KCE REPORT 287S

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

LOW BACK PAIN AND RADICULAR PAIN: ASSESSMENT AND MANAGEMENT

SUPPLEMENT

SPINE SOCIETY Belgium

SSBe

BVOT

SORBCOT

KCE REPORT 287S
GOOD CLINICAL PRACTICE

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

LOW BACK PAIN AND RADICULAR PAIN: ASSESSMENT AND MANAGEMENT

SUPPLEMENT

PETER VAN WAMBEKE, ANJA DESOMER, LUC AILLIET, ANNE BERQUIN, CHRISTOPHE DEMOULIN, BART DEPREITERE, JOHAN DEWACHTER, MIEKE DOLPHENS, PATRICE FORGET, VIRGINIE FRASELLE, GUY HANS, DAVY HOSTE, GENEVIÈVE MAHIEU, JEF MICHIELSEN, HENRI NIELENS, THOMAS ORBAN, THIERRY PARLEVLIET, EMMANUEL SIMONS, YANNICK TOBBACKX, JAN VAN ZUNDERT, JACQUES VANDERSTRAETEN, PATRICK VANSCHAEYBROECK, JOHAN VLAEYEN, PASCALE JONCKHEER

COLOPHON

Title:	Low Back Pain and radicular pain: assessment and management – Supplement
Authors:	Peter Van Wambeke (UZ Leuven, GDG president), Anja Desomer (KCE), Luc Ailliet (Belgische Vereniging van Chiropractors), Anne Berquin (Cliniques universitaires Saint-Luc), Christophe Demoulin (Université de Liège, CHU de Liège), Bart Depreitere (UZ Leuven), Johan Dewachter (Universiteit Antwerpen), Mieke Dolphens (Universiteit Gent), Patrice Forget (UZ Brussel, VUB), Virginie Fraselle (Cliniques universitaires Saint-Luc), Guy Hans (Universitair ziekenhuis Antwerpen), Davy Hoste (AZ Sint Lucas, Brugge), Geneviève Mahieu (Unité du Dos CHU UCL Namur), Jef Michielsen (UZ Antwerpen), Henri Nielens (Cliniques universitaires Saint-Luc), Thomas Orban (SSMG), Thierry Parlevliet (UZ Gent), Emmanuel Simons (CHU/UVC Brugmann), Yannick Tobbackx (VUB), Jan Van Zundert (ZOL, Genk), Jacques Vanderstraeten (SSMG), Patrick Vanschaeybroeck (Imelda Ziekenhuis, RZ Tienen), Johan Vlaeyen (UZ Leuven), Pascale Jonckheer (KCE).
Project coordinator	Marijke Eyssen (KCE)
Reviewers:	Raf Mertens (KCE), Dominique Roberfroid (KCE)
Experts externes :	Michael Bruneau (Hopital Erasme ULB), Pierre Duquenne (CHC Liège; GRID), Philippe Mairiaux (Université de Liège), Everard Munting (Clinique St Pierre Ottignies; UCL), Etienne Pendeville (UCL), Benoît Pirotte (Chirec; ULB), Irène Salamun (Université de Liège), Johan Van Lerbeirghe (AZ Sint-Lucas, Gent), Dominique Verhulst (ZNA, Antwerpen)
Stakeholders:	Geoffrey Brands (CHC Liège), John Collin (APBMT), Jean-Raphael De Caluwé (AXXON, WVVK), Saskia Decuman (RIZIV – INAMI), Lies De Ruddere (Universiteit Gent), Patrick Dufrane (INAMI – RIZIV), Lode Godderis (KU Leuven), Greta Haelterman (FOD Volksgezondheid – SPF Santé Publique), Martine Jeunehomme (AXXON), Caroline Larock (AXXON), Vincianne Magotteaux (VIVALIA), Michel Muller (SSST), Aline Ollevier (VIVES University College), Yves Paulus (INAMI – RIZIV), Nathalie Pauwen (AXXON), Alain Piette (SPF Emploi – FOD Werkgelegenheid), Olivier Poot (Fedris), Nathalie Roussel (Universiteit Antwerpen), Nicolas Sabbe (AXXON), Pierre-René Somville (CHU de Liège; Université de Liège), Veerle Stevens (Militair Hospitaal Koningin Astrid - Hôpital Militaire Reine Astrid), Koen Van Boxem (Sint-Jozef Kliniek, VAVP), Erik Van de Kelft (AZ Nikolaas), Dominique Van de Velde (Universiteit Gent), Michel Van den Abeele (UKO), Omer Van Haute (FOD Volksgezondheid – SPF Santé Publique)
External assessors:	An De Sutter (Universiteit Gent), Maurits Van Tulder (Vrije Universiteit Amsterdam)
External validators:	Fons De Schutter (CEBAM), Trudy Bekkering (CEBAM), Patrick Vankrunkelsven (CEBAM)
Acknowledgements:	Nicolas Fairon (KCE)

Particular aknowledgments:

The authors of this guideline wish to thank the National Institute for Health and Care Excellence (NICE) for the impressive work they have devoted to the preparation of a low back pain guideline, and their permission for the KCE and the Belgian health care workers to make use of this work.

The original NICE (National Institute for Health and Care Excellence) guideline to which this document refers, was produced by the British National Collaborating Centre for Cancer in 2016. It is available from http://www.nice.org.uk/guidance/ng2. NICE guidance is prepared for the National Health Service in England and Wales and does not necessarily apply to Belgium. NICE has not been involved in the development or adaptation of any guidance for use in Belgium.

Other reported interests:

Membership of a stakeholder group on which the results of this report could have an impact: Peter Van Wambeke (RBSPRM, BPS, SSBe), Luc Ailliet (BVC), Anne Berquin (BPS; RBSPRM), Geoffrey Brands (CHC de Liège; Absym; GBS), Michaël Bruneau (doctor at Hôpital Chirec), Jean-Raphaël De Caluwé (AXXON ; WVVK), Mieke Dolphens (BBS), Virginie Fraselle (physician in rehabilitation UCL ; SSBe), Patrice Forget (anesthesiologist, BPS et Cochrane collaboration), Lode Godderis (BBvAg & VWVA), Davy Hoste (SSBe), Martine Jeunehomme (AXXON), Geneviève Mahieu (BBS, SSBe, Eurospine), Philippe Mairiaux (APBMT), Michel Muller (occupational physician, SSST), Aline Ollevier (VE; OKE), Thomas Orban (SSMG), Erik Van de Kelft (BSN), Michel Van den Abeele (UKO), Johan Van Lerbeirghe (SSBe), Patrick Van Schaeybroeck (SSBe), Jan Van Zundert (BPS, VAVP, WIP)

Fees or other compensation for writing a publication or participating in its development: Luc Ailliet (grant for doctoral degree VU Amsterdam 2011 - 2015)

Participation in scientific or experimental research as an initiator, principal investigator or researcher: Luc Ailliet (doctoral degree VU Amsterdam 2011 – 2015 «*Rol van biopsychosociale factoren in het herstel van mensen met nekpijn en /of low back pain* »), Anne Berquin (validation French version of questionnaire Örebro (OMPSQ)), Mieke Dolphens (investigator IWT-TBM financed project «*A modern neuroscience approach to chronic spinal pain »* (1 nov. 2013 – 31 oct 2017), Lode Godderis (development of instruments for the evaluation of needs of disabled people (financed by FPS Social Security) ; development of questionnaire to evaluate the prognosis for resumption of work), Aline Ollevier (coordinator and principal investigator of « eUlift »), Veerle Stevens (manager of the programme « *Optimizing physical and psychosocial assessment in patients with non-specific chronic low back pain* »), Maurits Van Tulder (multiple scientific studies in the field of low back pain, financed by ZonMW ; principal investigator of studies about radiofrequency denervation for facet join pain and sacro-iliacale joints, endoscopic transforaminal discectomy and epidural injections McKenzieplus ; investigator at NHMRC in Australia), Johan Vlaeyen (Methusalem programme « *From acute aversive sensations to chronic bodily symptons* » (FNO)).

A grant, fees or funds for a member of staff or another form of compensation for the execution of research: Aline Ollevier (Erasmus + EPOS fund)

	Consultancy or employment for a company, an association or an organisation that may gain or lose financially due to the results of this report: Lode Godderis (Knowlegde, Information and Development Manager at IDEWE), Virginie Fraselle (BPS), Martine Jeunehomme (Keep Moving; Commission Risk prevention) Presidency or accountable function within an institution, association, department or other entity on which the results of this report could have an impact: Peter Van Wambeke (board member of RBSPRM, SSBe), Michaël Bruneau (board member of Hôpital chirec), Mieke Dolphens (BBS), Pierre Duquennes (president of GRID), Christophe Dumoulin (BBS), Patrice Forget (vice-president of BPS), Lode Godderis (board member of BBvAg & VWVA), Guy Hans (president of BPS), Martine Jeunehomme (member of AXXON), Philippe Mairiaux (board member of SSST), Aline Ollevier (board member of VE; président OKE), Thomas Orban (president of SSMG), Thierry Parlevliet (Board member of SSBe, treasurer RBSPRM), Michel Van den Abeele (president of UKO), Omer Van Haute (health economic evaluations of programmes for chronic diseases, vice-president ICF-Platform), Johan Van Lerbeirghe (former president of SSBe, treasurer SSBe), Jan Van Zundert (medical head of department multidisciplinary pain centre, ZOL, Genk), Dominique Verhulst (president of BSS) Other possible interests that could lead to a potential or actual conflict of interest: Martine Jeunehomme (thesis), Maurits van Tulder (co-editor of the Cochrane Back and Neck Group)
Layout:	Ine Verhulst
Disclaimer:	• **The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.** • **Subsequently, a (final) version was submitted to the validators. The validation of the report results from a consensus or a voting process between the validators. The validators did not co-author the scientific report and did not necessarily all three agree with its content.** • **Finally, this report has been approved by common assent by the Executive Board (see http://kce.fgov.be/content/the-board).** • **Only the KCE is responsible for errors or omissions that could persist. The policy recommendations are also under the full responsibility of the KCE.**
Publication date:	19 May 2017
Domain:	Good Clinical Practice (GCP)
MeSH:	Low back pain, sciatica, practice guideline
NLM Classification:	WE 755
Language:	English
Format:	Adobe® PDF™ (A4)

Legal depot: D/2017/10.273/37

ISSN: 2466-6459

Copyright: KCE reports are published under a “by/nc/nd” Creative Commons Licence http://kce.fgov.be/content/about-copyrights-for-kce-reports.

How to refer to this document? Van Wambeke P, Desomer A, Ailliet L, Berquin A, Demoulin C, Depreitere B, Dewachter J, Dolphens M, Forget P, Fraselle V, Hans G, Hoste D, Mahieu G, Michielsen J, Nielens H, Orban T, Parlevliet T, Simons E, Tobbackx Y, Van Zundert J, Vanderstraeten J, Vanschaeybroeck P, Vlaeyen J, Jonckheer P. Low Back Pain and radicular pain: assessment and management – Supplement. Good Clinical Practice (GCP) Brussels: Belgian Health Care Knowledge Centre (KCE). 2017. KCE Reports 287S. D/2017/10.273/37.

How to refer to this document? This document is available on the website of the Belgian Health Care Knowledge Centre.

TABLE OF CONTENTS

1. COMPOSITION OF EXPERTS AND STAKEHOLDERS GROUPS 6
1.1. COMPOSITION OF THE GUIDELINE DEVELOPMENT GROUP 6
1.2. COMPOSITION OF THE STAKEHOLDERS GROUP 8
1.3. COMPOSITION OF THE KCE EXPERT TEAM 9
2. INITIAL INTERVENTIONS PROPOSED FOR THE SCOPE OF THE GUIDELINE 10
3. SEARCH STRATEGIES FOR GUIDELINES 12
4. QUALITY APPRAISAL OF 17 SELECTED GUIDELINES 13
5. QUALITY APPRAISAL OF THE NICE GUIDELINE 15
6. EXAMPLE OF LIME SURVEY 18
7. SUMMARY SHEETS 22
7.1. CLINICAL EXAMINATION 22
7.2. RISK ASSESSMENT AND STRATIFICATION 26
7.3. IMAGING 40
7.4. SELF-MANAGEMENT 51
7.5. EXERCISE THERAPIES 64
7.6. POSTURAL THERAPIES 109
7.7. ORTHOTICS AND APPLIANCES 116
7.8. MANUAL THERAPIES 122
7.9. ACUPUNCTURE 164
7.10. ELECTROTHERAPIES 172
7.11. PSYCHOLOGICAL INTERVENTIONS 195
7.12. MULTIDISCIPLINARY BIOPSYCHOSOCIAL REHABILITATION (MBR) PROGRAMS 210
7.13. RETURN TO WORK PROGRAMMES 231
7.14. PHARMACOLOGICAL INTERVENTIONS 244
7.14.1. General issues 244
7.14.2. Specific points of discussion for NSAIDs 256
7.14.3. Specific points of discussion for paracetamol 268

7.14.4. Specific points of discussion for opioids 274
7.14.5. Specific points of discussion for antidepressants 289
7.14.6. Specific points of discussion for anticonvulsants 292
7.14.7. Specific points of discussion for muscle relaxants 294
7.14.8. Specific points of discussion for antibiotics 295
7.14.9. Specific point of discussion for oral methylprednisolone 296
7.15. SPINAL INJECTIONS 297
7.16. RADIOFREQUENCY DENERVATION FOR FACET JOINT PAIN 313
7.17. EPIDURAL INJECTIONS FOR RADICULAR PAIN 333
7.18. SURGERY AND PROGNOSTIC FACTORS 360
7.19. DISC REPLACEMENT 366
7.20. SPINAL FUSION 376
7.21. SPINAL DECOMPRESSION FOR RADICULAR PAIN 387
8. EXTERNAL REVIEW 400

LIST OF TABLES

Table 1 – List of non-invasive interventions for low back pain according to four sources (KCE 2006, NICE 2009, APTA 2012, SIGN 2013) 10
Table 2 – Number of guidelines related to back pain by search engines consulted 12
Table 3 – Appraisal of 17 selected guidelines 13
Table 4 – AGREE scores of the NICE guidelines on low back pain and sciatica (based on the draft edited on March 2016) 15
Table 5 – Predicting results of 11 risk assessments tools (NICE 2016) 27
Table 6 – Clinical effectiveness of imaging by outcome according to the population and the comparator 41
Table 7 – Clinical effectiveness of biomechanical exercise compared to usual care in patients with low back pain without sciatica 65
Table 8 – Clinical effectiveness of biomechanical exercise compared to placebo, usual care and spinal manipulation in patients with low back pain with sciatica 68
Table 9 – Clinical effectiveness of biomechanical exercise compared to placebo, usual care and active comparators in patients with low back pain with or without sciatica 71
Table 10 – Clinical effectiveness of aerobic exercise compared to usual care and active comparator in patients with low back pain without sciatica 75

Table 11 – Clinical effectiveness of aerobic exercise compared to usual care and active comparators in mixed population (LBP with or without sciatica) 77
Table 12 – Clinical effectiveness of mind-body exercise compared to usual care and active comparators in patients with low back pain without sciatica 79
Table 13 – Clinical effectiveness of mind-body exercise compared to usual care and active comparators in mixed population (LBP with or without sciatica) 81
Table 14 – Clinical effectiveness of mixed exercise compared to placebo, usual care and active comparator in patients with low back pain without sciatica 85
Table 15 – Clinical effectiveness of mixed exercise compared to usual care and active comparators in mixed population (low back pain with or without sciatica) 88
Table 16 – Clinical effectiveness of exercise as therapy adjunct compared to active comparators in patients with low back pain without sciatica 93
Table 17 – Clinical effectiveness of exercise as therapy adjunct in mixed population (low back pain with or without sciatica) 96
Table 18 – Clinical effectiveness of soft tissue techniques compared to sham, usual care and active comparators in patients with low back pain without sciatica 124
Table 19 – Clinical effectiveness of traction compared to sham, usual care and active comparators in mixed population (low back pain with or without sciatica) 127
Table 20 – Clinical effectiveness of manipulation/mobilisation compared to sham, usual care and active comparators in patients with low back pain without sciatica 129
Table 21 – Clinical effectiveness of manipulation/mobilisation compared to usual care and active comparators in mixed population (low back pain with or without sciatica) 133
Table 22 – Clinical effectiveness of mixed modality manual therapy compared to usual care, sham and active comparators in patients with low back pain without sciatica 137
Table 23 – Clinical effectiveness of manual therapy (manipulation) as component in a multimodal intervention compared to exercises in patients with low back pain without sciatica 140
Table 24 – Clinical effectiveness of manual therapy (manipulation) as component in a multimodal intervention in mixed population (low back pain with or without sciatica) 142
Table 25 – Clinical effectiveness of manual therapy (mixed modality) as component of a multimodal intervention in mixed population (low back pain with or without sciatica) 145
Table 26 – Clinical effectiveness of acupuncture as component in combined interventions 167
Table 27 – Clinical effectiveness of TENS in patients with low back pain without sciatica 174
Table 28 – Clinical effectiveness of TENS in mixed population (low back pain with or without sciatica) 176

Table 29 – Clinical effectiveness of Laser in patients with low back pain with sciatica 180
Table 30 – Clinical effectiveness of electrotherapy as adjunct in low back pain population without sciatica 183
Table 31 – Clinical effectiveness of electrotherapy as adjunct in mixed population (low back pain with or without sciatica) 186
Table 32 – Clinical effectiveness of cognitive behavioural approaches compared to other sham, usual care/waiting list or behavioural therapy in mixed population (LBP with or without sciatica) 197
Table 33 – Clinical effectiveness of behavioural therapy compared to other sham or usual care/waiting list in mixed population (LBP with or without sciatica) 199
Table 34 – Clinical effectiveness of 3-element MBR in mixed population (low back pain with or without sciatica) 213
Table 35 – Clinical effectiveness of 2-element MBR (physical + psychological) in mixed population (low back pain with or without sciatica) 217
Table 36 – Clinical effectiveness of 2-element MBR (physical + education) in mixed population (low back pain with or without sciatica) 221
Table 37 – Clinical effectiveness of individual RTW programmes in patients with low back pain without sciatica 234
Table 38 – Clinical effectiveness of NSAIDS in low back pain: three systematic reviews. 259
Table 39 – Clinical effectiveness of paracetamol in low back pain: three systematic reviews. 269
Table 40 – Clinical effectiveness of steroids for low back pain: three systematic reviews 278
Table 41 – Clinical effectiveness of facet joint injections in patients with low back pain 299
Table 42 – Clinical effectiveness of spinal injections (intradiscal) in patients with non-specific low back pain 301
Table 43 – Clinical effectiveness of prolotherapy in patients with low back pain and sciatica 303
Table 44 – Clinical effectiveness of radiofrequency denervation in patients with low back pain 315
Table 45 – Clinical effectiveness of image-guided epidural injections with steroid + anesthetic in patients with low back pain and sciatica 336
Table 46 – Clinical effectiveness of image-guided epidural injections with steroids + anesthetic according to the cause of sciatica 340
Table 47 – Clinical effectiveness of non-image guided epidural injections with steroid + anesthetic in patients with low back pain and sciatica 344

Table 48 – Clinical effectiveness of non-image guided epidural injections with steroids in mixed population/unclear spinal pathologies 347
Table 49 – Clinical effectiveness of discectomy in patients with sciatica 389

1. COMPOSITION OF EXPERTS AND STAKEHOLDERS GROUPS

1.1. Composition of the Guideline Development Group

Clinicians	Fields of expertise, affiliations
Ailliet Luc	Physiotherapist – Chiropractor (Belgiian Chripractors' Union)
Berquin Anne	Pain therapist (Cliniques universitaires Saint-Luc)
Bruneau Michael	Neurosurgeon (Hôpital Erasme ULB)
Demoulin Christophe	Physiotherapist (Université de Liège, CHU de Liège)
Depreitere Bart	Neurosurgeon (UZ Leuven)
Dewachter Johan	General practitioner (Universiteit Antwerpen)
Dolphens Mieke	Physiotherapist (Universiteit Gent)
Duquenne Pierre	Anaesthesiologist-algologist (CHC Liège)
Forget Patrice	Anaesthesiologist-algologist (UZ Brussel, VUB)
Fraselle Virginie	Specialist in physical medicine and rehabilitation (UCL, Cliniques universitaires Saint-Luc)
Hans Guy	Anaesthesiologist-algologist (Universitair ziekenhuis Antwerpen)
Hoste Davy	Orthopaedic surgeon (AZ Sint Lucas Brugge)
Mahieu Geneviève	Specialist in physical medicine and rehabilitation (CHU UCL Namur)
Mairiaux Philippe	Occupational medicine (Université de Liège)
Michielsen Jef	Orthopaedic surgeon (UZ Antwerpen)
Munting Everard	Orthopaedic surgeon (Clinique St Pierre Ottignies; UCL)
Nielens Henri	Specialist in physical medicine and rehabilitation (Cliniques universitaires Saint-Luc)
Orban Thomas	General practitioner (SSMG)
Parlevliet Thierry	Specialist in physical medicine and rehabilitation (UGent) (UZ Gent)
Pendeville Etienne	Physiotherapist (UCL)
Pirotte Benoit	Neurosurgeons (Chirec; ULB)
Salamun Irène	Psychologist - Service d'Algologie du CHU de Liège (Université de Liège)
Simons Emmanuel	Physiotherapist (CHU/UVC Brugmann)
Tobbackx Yannick	Physiotherapist – Acupunctor (VUB)

Van Lerbeirghe Johan	Orthopaedic surgeon (AZ Sint-Lucas, Gent)
Van Wambeke Peter	Specialist in physical medicine and rehabilitation - Président GDG (UZ Leuven, GDG president)
Van Zundert Jan	Anaesthesiologist-algologist (ZOL, Genk)
Vanderstraeten Jacques	General practitioner (SSMG)
Van Schaeybroeck Patrick	Neurosurgeon (Imelda Ziekenhuis, RZ Tienen)
Verhulst Dominique	Orthopaedic surgeon (ZNA, Antwerpen)
Vlaeyen Johan	Psychologist (UZ Leuven)

1.2. Composition of the Stakeholders Group

Clinicians	Affiliations
Geoffrey Brands	CHC Liège
John Collin	APBMT
Jean-Raphael De Caluwé	AXXON, WVVK
Saskia Decuman	RIZIV – INAMI
Lies De Ruddere	Universiteit Gent
Patrick Dufrane	INAMI – RIZIV
Lode Godderis	KU Leuven
Greta Haelterman	FOD Volksgezondheid – SPF Santé Publique
Martine Jeunehomme	AXXON
Caroline Larock	AXXON
Vincianne Magotteaux	VIVALIA
Michel Muller	SSST
Aline Ollevier	VIVES University College
Yves Paulus	INAMI – RIZIV
Nathalie Pauwen	AXXON
Alain Piette	SPF Emploi – FOD Werkgelegenheid
Olivier Poot	Fedris
Nathalie Roussel	Universiteit Antwerpen
Nicolas Sabbe	AXXON
Pierre-René Somville	CHU de Liège; Université de Liège
Veerle Stevens	Militair Hospitaal Koningin Astrid - Hôpital Militaire Reine Astrid
Koen Van Boxem	Sint-Jozef Kliniek, VAVP
Erik Van de Kelft	AZ Nikolaas
Dominique Van de Velde	Universiteit Gent
Michel Van den Abeele	UKO
Omer Van Haute	FOD Volksgezondheid – SPF Santé Publique

1.3. Composition of the KCE expert team

KCE member	Specific role
Dominique Paulus	Program Director
Marijke Eyssen	Project Coordinator
Pascale Jonckheer	Principal Investigator
Anja Desomer	Scientific researcher

2. INITIAL INTERVENTIONS PROPOSED FOR THE SCOPE OF THE GUIDELINE

Non-pharmacological and non-invasive interventions were the initial scope of the guideline. In order to prepare the discussion with the expert and stakeholders, we compared these interventions in 4 guidelines, two relatively old (KCE 2006 and NICE 2009) and two recent (the APTA 2012 and the SIGN 2013). As showed in Table 1, there is a variability among the selected interventions.

Table 1 – List of non-invasive interventions for low back pain according to four sources (KCE 2006, NICE 2009, APTA 2012, SIGN 2013)

	KCE 2006	NICE 2009	APTA 2012	SIGN 2013
PHYSICAL ACTIVITY & EXERCISES				
• **Bed rest**	Not effective (HQE)[a]			
• **Self-directed physical activity**		No evidence		Not alone, but in addition to exercise therapy
• **Alexander Technique and exercise prescription**		Effective (1+)		
• **Trunk coordination, strengthening & endurance exercises**			Effective (HQE)[e]	
• **Repeated exercises in a specific direction (determined by treatment response)**			Effective (HQE)[f]	
• **Flexion exercises (combined with other exercises)**			Effective (LQE)[g]	
• **Lower-quarter nerve mobilization procedures**			Effective (LQE)[g]	
• **Structured exercise programmes**	Effective (HQE)	Slightly effective (1++)		Effective (1++)
• **Hydrotherapy**	Effective (LQE)	Effective on function (1-)		
• **Yoga**		Effective (1+)		
PHYSICAL AGENTS				
• **Heat therapy**	No evidence			
• **Cold therapy**	No evidence			
• **Thermotherapy**	No evidence			
• **Electrotherapy**	No evidence	No evidence		
• **Ultrasound**	Not effective (LQE)	No evidence		
• **Laser**	Not effective (LQE)	Slight effective on pain (1++) but not strong enough		Effective (1++)
• **Transcutaneal Electrical Nerve Stimulation (TENS)**	Conflicting (LQE)	No sufficient evidence		Conflicting (1+)
• **Balneotherapy**	Effective[b] (MQE)			
MANUAL THERAPY				

• **Massage**	Effective (LQE)	Effective (LQE)		Effective (1++)
• **Spinal manipulation (high velocity)**	Conflicting [c] (MQE)	Effective (LQE)	Effective (thrust) (HQE)	No difference with other care (1++)
• **Spinal mobilization (low velocity)**	Conflicting (MQE)		Effective (nonthrust) (HQE)	
• **Osteopathic care (including manipulation)**		No difference with standard care (1-)		
• **Chiropractic manipulation**		Conflicting (1-)		
LUMBAR SUPPORTS	Conflicting (VLQE)	Not effective (1++)		
TRACTIONS	Not effective (HQE)	Not effective (1++)	Conflicting evidence	Not effective (1++)
BEHAVIORAL/EDUCATION				
• **Back schools**	Effective (LQE)	Effective (1++)		
• **Brief educational interventions to promote self-care**	Effective[d] (MQE)			Effective (1++)
• **Patient education and counselling strategies**				
• **Intensive educational programme**		Effective (1**+**)		
• **Relaxation**				Effective (1++)
• **EMG Biofeedback**	Not effective (HQE)			Effective (1++)
PSYCHOTHERAPY				
• **Psychotherapeutic cognitive-behavioral interventions**	Effective (MQE)	No evidence as mono-therapy		Effective (1++)
ERGONOMIC INTERVENTIONS (KCE)				
MULTIDISCIPLINARY PROGRAMS (KCE)				
• **High intensive multidisciplinary biopsychosocial rehabilitation**	Effective (HQE)	Conflictong (1-)		Conficting (1++)

In red, interventions not recommended; in green, interventions clearly recommended.
[a]for acute and subacute LBP; [b]in older patients (>60 years); [c]more effective than no treatment and only at short-term but not more effective than NSAIDs, physical therapy, exercise and back school; [d]to reduce disability and increase return to work but not to reduce pain level; [e]in patients with movement coordination impairments; [f]in patients with mobility deficits; [g]in patients with radiating pain.

3. SEARCH STRATEGIES FOR GUIDELINES

The search strategy for guidelines was performed in Augustus 2015 and focused on guidelines published after 1st January 2010. Several search engines were used.

Table 2 – Number of guidelines related to back pain by search engines consulted

Date	Augustus 2015	
Search engine	**Search term**	**Number of hits**
GIN – Guidelines international network: http://www.g-i-n.net	back pain	39
NGC - National Guideline Clearinghouse from US: http://www.guideline.gov/	low back pain	80
	sciatica	11
	backache	12
NICE - National Institute for Health and Care Excellence from UK: http://www.nice.org.uk/	back pain + guidance	126
SIGN - Scottish Intercollegiate Guidelines Network: http://www.sign.ac.uk/	orthopaedics	3
	other	19
NHMRC - National Health and Medical Research Council from Australia: http://www.nhmrc.gov.au/	back pain	4
Ministry of Health Library from New Zealand: http://www.moh.govt.nz/notebook/nbbooks.nsf/mohwebsearch?readform	back pain	6
ICSI - Institute for Clinical Systems Improvement from US: http://www.icsi.org/index.asp	musculo-skeletal	3
ACP - American college of physicians: https://www.acponline.org/clinical_information/guidelines/	full list of guidelines	0
CMA - Canadian Medical association: https://www.cma.ca/En/Pages/clinical-practice-guidelines.aspx	low back pain	3
KNGF - Koninklijk Nederlands Genootschap voor Fysiotherapie from The Netherlands: https://www.fysionet-evidencebased.nl/	full list of guidelines	16
HAS - Haute Autorité de Santé from France: http://www.has-sante.fr/portail/jcms/c_1101438/fr/tableau-des-recommandations-de-bonne-pratique	full list of guidelines	1
Cochrane	low back pain	110

After removal of duplicate guidelines, 17 guidelines were selected based on title and abstract. Of these, 14 guidelines were excluded because they focused only on a specific question or because of unclear or insufficient methodology, assessed with the 8 items of the third domain 3 ‘Rigour of development’ from the AGREE II checklist (see Table 3 in this document).

4. QUALITY APPRAISAL OF 17 SELECTED GUIDELINES

Table 3 – Appraisal of 17 selected guidelines

Guidelines	Assessment
Management of chronic pain. A national clinical guideline. SIGN 2013.[1]	Very high quality, date search 2007-2012; focus on chronic pain but with clear identification of LBP (manual therapy LBP chapter 7.1.1 and other treatments in other parts)
Low back pain: clinical practice guidelines linked to the International Classification of Functioning, Disability, and Health. Orthopaedic Section of the APTA 2012.[2]	High quality, date search a little bit old (1966-2010); focus mainly on several kind of exercises in LBP
Kreuzschmerz - Nationale VersorgungsLeitlinie (NVL) [Low back pain - National disease management guideline]. AQuMed 2013.[3]	High quality, assessed by one reviewer alone because methodology in German. but mainly ADAPT of old guidelines (2001-2006) except for some search questions (but not cleary identified)
Low back disorders. 1997 (revised 2011). ACOEM 2011.[4]	Medium quality (overall methods mentioned, but not specified for this guideline); comprehensive search but a little bit old (search date 1966-2010); specific population of workers, no free access to the full guideline
Lage rugpijn - KNGF-richtlijn [KNGF Guideline for Physical Therapy in patients with low back pain]. KNGF 2013.[5]	Medium quality; focus on physiotherapy and LBP, but the lack on information on methods and evidence behind recommendations hampers ADAPTE/update
Adult acute and subacute low back pain. 1994 Jun (revised 2012 Nov). ICSI 2012.[6]	Medium quality; focus on acute and subacute LBP which hampers an ADAPT/Update
Assessment and management of chronic pain. Health care guideline 2005 Nov (revised 2013 Nov). ICSI 2013.[7]	Medium quality; focus on chronic pain and refers to another specific guideline from ICSI on LBP (ICSI 2012)
Assessment: efficacy of transcutaneous electric nerve stimulation in the treatment of pain in neurologic disorders (an evidence-based review). Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. 2010 Jan.[8]	Medium quality but old search date (until 2009); focus on one intervention (TENS) and on neurologic disorders (with clear identification if associated with LBP or not)
Evidence-Based Clinical Practice Guideline for Management of Persistent non-specific low back pain. King Saud University 2013.[9]	Medium quality; not retained because it is an ADAPTE based on 3 existing GLs, mainly NICE (NICE, NCCPC, RCGP) without updating
Practice guidelines for chronic pain management. An updated report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine. 1997 Apr (revised 2010 Apr).[10]	Medium quality with old search date (1944-2009); concerns all chronic pain without clear identification of LBP
Best practices & practice guidelines. 2008 (revised 2013 Nov 22). International Chiropractors Association.[11]	Medium quality (search date 2008 – 2013) but focus on chiropractor's interventions (without other comparators)

Low back - lumbar & thoracic (acute & chronic). 2003 (revised 2013 Dec 4). Work Loss Data Institute.[12]	Low quality (but no access to the full guideline); focus on workers
Pain (chronic). 2003 (revised 2013 Nov 14). Work Loss Data Institute.[13]	Low quality (but no access to the full guideline); focus on workers and all chronic pain
Guideline for the evidence-informed primary care management of low back pain. 2009 Mar (revised 2011 Nov). Towards Optimized Practice 2011.[14]	Low quality; based on 8 old guidelines (date search 2010) rather than primary studies, difficult to be updated
Chronic pain disorder medical treatment guidelines. Colorado Division of Workers' Compensation 2011.[15]	Low quality; focus on chronic pain without clear identification of LBP
Manual medicine guidelines for musculoskeletal injuries. 2004 Dec 1 (revised 2013 Dec 1). Academy for Chiropractic Education.[16]	Low quality; no access on full methodology; not specific on LBP but on musculoskeletal injuries
Guidelines for the practice and performance of manipulation under anesthesia. American Association of Manipulation Under Anesthesia 2014.[17]	Low quality; based on three review articles on a specific topic: manipulation under anesthesia (MUA)

5. QUALITY APPRAISAL OF THE NICE GUIDELINE

The appraisal of the NICE guideline was based on the comprehensive AGREE checklist (Table 4).

Table 4 – AGREE scores of the NICE guidelines on low back pain and sciatica (based on the draft edited on March 2016)

Critical appraisal of clinical practice guidelines - AGREE II	Score	Comments
Domain 1. Scope and Purpose		
1. The overall objective(s) of the guideline is (are) specifically described.	7,0	Expected benefit is clearly described, seperate section on scope of the guideline
2. The health question(s) covered by the guideline is (are) specifically described.	7,0	Clinical review protocols contains a clear description of research questions, PICO, searched databases, study designs, exclusion criteria
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	7,0	There is a specific section on population with in- and excluded criteria
Domain 2. Stakeholder Involvement		
4. The guideline development group includes individuals from all the relevant professional groups.	6,5	The GDG is composed by: Neurosurgeon, Musculoskeletal physician and general practitioner, Nurse chronic pain, Psychologist, Patient representative, Orthopaedic Surgeon, Rheumatologist, Consultant in pain medicine. No occupational physician?
5. The views and preferences of the target population (patients, public, etc.) have been sought.	5,5	Three patients representative were included in the GDG (one until January 2015 and one from February 2015). However, the impact of the patients' values is difficult to be estimated in the guideline.
6. The target users of the guideline are clearly defined.	4,5	It is not detailed and appears very large: p 20: "With this broadened scope and using updated NICE methodology to examine the latest research evidence we hope to address the inconsistent provision and implementation of the recommendations of CG88 and to provide patients, carers and healthcare professionals with a sensible, practical and evidence based framework for the management of this important and common problem".
Domain 3. Rigour of Development		
7. Systematic methods were used to search for evidence.	6,5	Full search strategies are available, per research questions also mentioned in review protocols

Critical appraisal of clinical practice guidelines - AGREE II	Score	Comments
8. The criteria for selecting the evidence are clearly described.	7,0	In-and exclusion criteria are mentioned per research question
9. The strengths and limitations of the body of evidence are clearly described.	6,5	The software (GRADEpro163) developed by the GRADE working group was used to assess the quality of each outcome, taking into account individual study quality and the meta-analysis results. Clinical evidence statements are summary statements that are included in each review chapter, and which summarise the key features of the clinical effectiveness evidence presented. The wording of the evidence statements reflects the certainty or uncertainty in the estimate of effect.
10. The methods for formulating the recommendations are clearly described.	7,0	The main points of the GDG discussion are presented for each recommendation. The strength of the recommendation (for example the word 'offer' was used for strong recommendations and 'consider' for weaker recommendations).
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	5,5	Per research question the benefits/side effects/risks are reported and taken into account in the formulation of the recommendation.
12. There is an explicit link between the recommendations and the supporting evidence.	6,0	The main considerations specific to each recommendation are outlined in the 'Recommendations and link to evidence' sections within each chapter. We can find before that, for each research question, the number and kind of studies selected (clinical evidence), the GRADE analysis for each outcome (summary tables), the economic evidence and a text with interpretation of the results but witout the references (evidence statements).
13. The guideline has been externally reviewed by experts prior to its publication.	4,5	This guidance is subject to a 6-week public consultation and feedback as part of the quality assurance and peer review of the document. All comments received from registered stakeholders are responded to in turn and posted on the NICE website.
14. A procedure for updating the guideline is provided.	6,0	In general, NICE proposes an update after 5 years or whether the evidence base has progressed significantly to alter the guideline recommendations. Not specifically mentioned for this guideline.

Critical appraisal of clinical practice guidelines - AGREE II	Score	Comments
Domain 4. Clarity of Presentation		
15. The recommendations are specific and unambiguous.	5,0	The recommendations are sometimes vague on the specific modalities behind a specific intervention (e.g. exercise therapy)
16. The different options for management of the condition or health issue are clearly presented.	4,5	All types of interventions are taken into consideration. However some categories of options are broad (e.g. medications)
17. Key recommendations are easily identifiable.	5,5	No differentiation was made between the summary of recommendations and the key recommendations but maybe not necessary for this topic
Domain 5. Applicability		
18. The guideline describes facilitators and barriers to its application.	-	Not available within the draft verion of March 2016
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	-	Not available within the draft verion of March 2016, except an algorithm
20. The potential resource implications of applying the recommendations have been considered.	6,5	Cost estimations are taken into account by the GDG for in each of the research questions
21. The guideline presents monitoring and/ or auditing criteria.	-	Not available within the draft verion of March 2016
Domain 6. Editorial Independence		
22. The views of the funding body have not influenced the content of the guideline.	7,0	The National Institute for Health and Care Excellence (NICE) is a public institution sponsored by the Department of Health, but operationally NICE is independent of government.
23. Competing interests of guideline development group members have been recorded and addressed.	7,0	Mentioned per GDG member
Final appraisal		
Overal quality	6,5	High quality, transparent methodology, clear presentation of results and formulation of recommendations
Number of items scoring ³ 5	17	

6. EXAMPLE OF LIME SURVEY

Guideline LowBackPain - first round

We thank you very much for participating in our guideline development group and in the survey.

The survey focuses on 6 research questions dealing with clinical examination, risk assessement/stratification, imaging, self-management, orthotics and acupuncture. You can move through different sections according your skill and professional experience.

Section 1: Clinical examination

Section 2: Risk assessement tools and stratification

Section 3: Imaging

Section 4: Self-management

Section 5: Orthotics and appliances

Section 6: Acupuncture

We ask you to indicate if you agree, do not agree, have no opinion or consider the recommendation out of your competence (e.g. as a surgeon you may not have an opinion on the use of acupuncture; but of course, it is possible that you may have). We also ask you to judge if you think the recommendation should be strong or weak, based on 4 criteria: Balance between clinical benefits and harms, Quality of evidence, Costs (resource allocation), Patients values and preferences. Interpretation of strong and conditional (weak)* recommendations is given in the table below. We are very interested in comments and arguments in favour or against a strong or weak recommendation. You may however not always have an opinion

Implications	Strong recommendation	Weak recommendation
For patients	Most individuals in this situation would want the recommended course of action, and only a small proportion would not. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful helping individuals making decisions consistent with their values and preferences.
For policy makers	The recommendation can be adopted as policy in most situations.	Policy-making will require substantial debate and involvement of various stakeholders.

All these methodological issues can be found back using the help button at each step of the survey.

You can interrupt the survey at the end of each step. Please click on 'resume later' and leave the survey. When you come back, all your answers were saved. In case of technical problem, please feel free to contact us.

The survey will be definitively closed at **15th June (Midnight).**

There are 61 questions in this survey

Section 1: Clinical examination

Clinical examination

Introduction

Clinical examination of people with back pain or sciatica is routinely performed by primary health care professionals, therapists, specialist physicians and surgeons. NICE emphasised the role of clinical examination in people with suspected sciatica because there is uncertainty as to whether any of the clinical tests that are commonly used in this context are more beneficial than others, or compared to a taking a comprehensive history.

Search question (NICE 2016)

"In people with suspected (or under investigation for) sciatica, what is the clinical and cost effectiveness of clinical examination* compared to history alone or history with imaging, when each is followed by treatment for sciatica, in improving patient outcomes?"

*Clinical examination included: straight leg raise (may be referred to as sciatic nerve stretch test), femoral nerve stretch test, crossed straight leg raise, motor muscle strength, dermatome sensory loss, reflex impairment and, slump test

Literature review (NICE 2016)

- No relevant clinical studies were identified. This search was not extended to diagnostic accuracy studies as the GDG agreed that there is no agreed reference standard for diagnosis of sciatica and such a review would therefore not be informative for setting guideline recommendations.
- No relevant economic evaluations were identified.

Considerations from the NICE GDG (NICE 2016)

- The GDG discussed the Cochrane review on clinical examination from Van Der Windt DAWM 2008. However, it was noted that this was a diagnostic accuracy review, which used a combination of different reference standards including imaging and findings at surgery rather than patient outcomes. The GDG agreed that it was not possible to make a recommendation due to the lack of evidence.
- The only other studies the GDG were aware of on this topic were based on clinical opinion using Delphi consensus. The GDG believed that there was insufficient evidence to recommend a substantial change to normal clinical practice and therefore agreed not to make a recommendation.
- The GDG discussed the possibility of making a recommendation for future research, due to the lack of evidence in this area. They agreed that feasibility of such a trial would be an issue, and therefore unlikely to be funded, unlikely to change practice or add value to the treatment pathway. The group were also aware of a clinical cohort study that would be published in the near future and concluded that it was sensible to wait for the results of this rather than making a recommendation for future research.

Recommendation:

No recommendation

Do you agree with NICE who has decided not to formulate a recommendation on the clinical examination in patients with suspected sciatica?

Only answer this question if the following conditions are met:
Answer was 'Enter this section' at question '3 [Achi1]' (The following section is dedicated to clinical examination.)

Please choose **only one** of the following:

- ○ I agree
- ○ I do not agree
- ○ I do not have an opinion
- ○ This topic is out of my competence

If you do not agree with the lack of recommendation on clinical examination in patients with suspected sciatica, please explain why ? *

Only answer this question if the following conditions are met:
Answer was 'Enter this section' at question '3 [Achi1]' (The following section is dedicated to clinical examination.) *and* Answer was 'I do not agree' at question '4 [S1]' (Clinical examination Introduction Clinical examination of people with back pain or sciatica is routinely performed by primary health care professionals, therapists, specialist physicians and surgeons. NICE emphasised the role of clinical examination in people with suspected sciatica because there is uncertainty as to whether any of the clinical tests that are commonly used in this context are more beneficial than others, or compared to a taking a comprehensive history. Search question (NICE 2016) "In people with suspected (or under investigation for) sciatica, what is the clinical and cost effectiveness of clinical examination" compared to history alone or history with imaging, when each is followed by treatment for sciatica, in improving patient outcomes?" *Clinical examination included: straight leg raise (may be referred to as sciatic nerve stretch test), femoral nerve stretch test, crossed straight leg raise, motor muscle strength, dermatome sensory loss, reflex impairment and, slump test Literature review (NICE 2016) No relevant clinical studies were identified. This search was not extended to diagnostic accuracy studies as the GDG agreed that there is no agreed reference standard for diagnosis of sciatica and such a review would therefore not be informative for setting guideline recommendations. No relevant economic evaluations were identified. Considerations from the NICE GDG (NICE 2016) The GDG discussed the Cochrane review on clinical examination from Van Der Windt DAWM 2008. However, it was noted that this was a diagnostic accuracy review, which used a combination of different reference standards including imaging and findings at surgery rather than patient outcomes. The GDG agreed that it was not possible to make a recommendation due to the lack of evidence. The only other studies the GDG were aware of on this topic were based on clinical opinion using Delphi consensus. The GDG believed that there was insufficient evidence to recommend a substantial change to normal clinical practice and therefore agreed not to make a recommendation. The GDG discussed the possibility of making a recommendation for future research, due to the lack of evidence in this area. They agreed that feasibility of such a trial would be an issue, and therefore unlikely to be funded, unlikely to change practice or add value to the treatment pathway. The group were also aware of a clinical cohort study that would be published in the near future and concluded that it was sensible to wait for the results of this rather than making a recommendation for future research. Recommendation: No recommendation Do you agree with NICE who has decided not to formulate a recommendation on the clinical examination in patients with suspected sciatica?)

Please write your answer here:

Any comment?

Only answer this question if the following conditions are met:
Answer was 'Enter this section' at question '3 [Achi1]' (The following section is dedicated to clinical examination.) *and* Answer was 'I agree' *or* 'I do not have an opinion' *or* 'This topic is out of my competence' at question '4 [S1]' (Clinical examination Introduction Clinical examination of people with back pain or sciatica is routinely performed by primary health care professionals, therapists, specialist physicians and surgeons. NICE emphasised the role of clinical examination in people with suspected sciatica because there is uncertainty as to whether any of the clinical tests that are commonly used in this context are more beneficial than others, or compared to a taking a comprehensive history. Search question (NICE 2016) "In people with suspected (or under investigation for) sciatica, what is the clinical and cost effectiveness of clinical examination" compared to history alone or history with imaging, when each is followed by treatment for sciatica, in improving patient outcomes?" *Clinical examination included: straight leg raise (may be referred to as sciatic nerve stretch test), femoral nerve stretch test, crossed

straight leg raise, motor muscle strength, dermatome sensory loss, reflex impairment and, slump test Literature review (NICE 2016) No relevant clinical studies were identified. This search was not extended to diagnostic accuracy studies as the GDG agreed that there is no agreed reference standard for diagnosis of sciatica and such a review would therefore not be informative for setting guideline recommendations. No relevant economic evaluations were identified. Considerations from the NICE GDG (NICE 2016) The GDG discussed the Cochrane review on clinical examination from Van Der Windt DAWM 2008. However, it was noted that this was a diagnostic accuracy review, which used a combination of different reference standards including imaging and findings at surgery rather than patient outcomes. The GDG agreed that it was not possible to make a recommendation due to the lack of evidence. The only other studies the GDG were aware of on this topic were based on clinical opinion using Delphi consensus. The GDG believed that there was insufficient evidence to recommend a substantial change to normal clinical practice and therefore agreed not to make a recommendation. The GDG discussed the possibility of making a recommendation for future research, due to the lack of evidence in this area. They agreed that feasibility of such a trial would be an issue, and therefore unlikely to be funded, unlikely to change practice or add value to the treatment pathway. The group were also aware of a clinical cohort study that would be published in the near future and concluded that it was sensible to wait for the results of this rather than making a recommendation for future research. Recommendation: No recommendation Do you agree with NICE who has decided not to formulate a recommendation on the clinical examination in patients with suspected sciatica?)

Please write your answer here:

7. SUMMARY SHEETS

7.1. Clinical examination

Clinical examination in patients with radicular pain

NICE search question

"In people with suspected (or under investigation for) sciatica, what is the clinical and cost effectiveness of clinical examination compared to history alone or history with imaging, when each is followed by treatment for sciatica, in improving patient outcomes?"

Introduction based on the draft version of NICE guideline (March 2016)

- Clinical examination of people with back pain or sciatica is routinely performed by primary health care professionals, therapists, specialist physicians and surgeons.
- **Clinical examination included:** straight leg raise (may be referred to as sciatic nerve stretch test), femoral nerve stretch test, crossed straight leg raise, motor muscle strength, dermatome sensory loss, reflex impairment and, slump test.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with suspected (or under investigation for) sciatica
Intervention(s)	• Clinical tests (+ treatment): 1. straight leg raise (may be referred to as sciatic nerve stretch test) 2. femoral nerve stretch test 3. crossed straight leg raise 4. motor muscle strength 5. dermatome sensory loss 6. reflex impairment 7. slump test 8. combination of above
Comparison(s)	• History alone (+ treatment) • History with imaging (+ treatment) • Clinical tests compared to each other (+ treatment).
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (> 30% improvement in pain or function)

	• Adverse events: morbidity • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

- No relevant clinical studies were identified.
- This search was not extended to diagnostic accuracy studies as the GDG agreed that there is no agreed reference standard for diagnosis of sciatica and such a review would therefore not be informative for setting guideline recommendations**.**
- No relevant economic evaluations were identified.

NICE GDG considerations (March 2016)

- The GDG discussed the Cochrane review on clinical examination Van Der Windt DAWM 2010. However, it was noted that this was a diagnostic accuracy review, which used a combination of different reference standards including imaging and findings at surgery rather than patient outcomes. The GDG agreed that it was **not possible to make a recommendation** due to the lack of evidence. The only other studies the GDG were aware of on this topic were based on clinical opinion using Delphi consensus. The GDG believed that there was insufficient evidence to recommend a substantial change to normal clinical practice and therefore agreed not to make a recommendation.
- The GDG discussed the possibility of making a recommendation for future research, due to the lack of evidence in this area. They agreed that feasibility of such a trial would be an issue, and therefore unlikely to be funded, unlikely to change practice or add value to the treatment pathway. The group were also aware of a clinical cohort study that would be published in the near future and concluded that it was sensible to wait for the results of this rather than making a recommendation for future research.

NICE 2016 proposition: not to formulate a recommendation on this topic

Belgian GDG considerations mentioned in the Lime survey at the beginning of June 2016

Agreement with the lack of recommendation on clinical examination: 10 Yes; 8 No; 1 no opinion; 0 out of competence, 0 no answer, 0 not completed

- **Comments from those who do not agree:**
  - In my practice, physical exam can reveal other disease such as posterior lamina irritation which orient diagnosis and treatment with no need of imaging
  - Clinical examination is mandatory in each cases and should allow to orientate the diagnosis.
  - I do strongly believe that the SLRT , slump test and FNS can identify patients with radicular pressure
  - Although there isn't actually a reference standard in the clinical examination for sciatica, I think it's important to perform always a clinical examination in spinal problems. Probably a combination of different clinical tests can guide you more specific to a diagnosis of sciatica and clinical examination remains very important together with history taking in ruling out other specific causes of back pain or sciatica (red flags).
  - Two reasons :
    - clinical examination is necessary to rule out some red flags (i.e. neurological deficits: sciatica with severe motor deficit may be an indication for surgery)
    - as stressed by NICE (p58): "People consulting healthcare professionals may expect an examination as part of the consultation, and this contributes to satisfaction with the consultation. It is thought that the repercussions of not performing an examination would lead to dissatisfaction and unwarranted demand for tests or further referrals."
    - This is something I often hear for patients: "il ne m'a même pas examiné!" (understand : this doctor did not take my situation seriously)
  - Wat bedoelen ze in de studie met "rather than patient outcomes"?
  - The "minimum minimum" is to check whether a motor deficit is present.
  - Although not much evidence may be found in the literature, straight leg raise and slump tests may also be useful in the diagnosis and follow-up of sciatica.
  - A diagnosis based upon history (and imaging) is incomplete in my opinion. The relationship between imaging and actual "disease" has been proven to be very uncertain

- **Other comments**
  - It doesn't mean that we don't have to do it.
  - It will be very interesting to compare cross examinations of the same patient by different clinicians.
  - There are no solid scientific recommendations but we should note that a comprehensive clinical examination is always mandatory.

KCE proposition in June 2016:
A reminder at the beginning of the KCE guideline with:
Before any treatment decision can be made, an assessment should be undertaken including:
- **an history taking on patient's overall health status, his individual life expectancy and comorbidities**
- **a comprehensive clinical examination**

Belgian GDG comments during the GDG meeting on the 29th June 2016

- The Belgian GDG confirmed that a history taking and a clinical examination (including testing motor) is needed to exclude the presence of symptoms or signs suggestive of possible serious underlying pathology (red flags). The patient's expectation is another argument to perform a clinical examination.
- However, the GDG highlighted the lack of a single physical test that would combine high sensitivity and sensibility to identify a radiculopathy (except perhaps the Crossed Straight Leg Raising test (XSLR) or crossed Lasègue's test). They reminded the results of the Cochrane review on clinical examination from Van Der Windt DAWM 2010 and the potential utility of a combination of clinical tests.
- The Belgian GDG considered that the NICE recommendation 6 "Think about alternative diagnoses when examining or reviewing people with low back pain, particularly if they develop new or changed symptoms. Exclude specific causes of low back pain, for example, cancer, infection, trauma or inflammatory disease such as spondyloarthritis. If serious underlying pathology is suspected, refer to relevant NICE guidance on: Metastatic spinal cord compression in adults, Spinal injury, Spondyloarthritis, Suspected cancer" concerned the clinical examination of the patient rather than imaging. This recommendation could be used as a basis for formulating a consensus-based recommendation on clinical examination for low back and radicular pain. However, the references to the other NICE guidances should be removed in the Belgian version.
- The red flags proposed by NICE in the appendix P appears not sufficient for the Belgian GDG. A list of red flags will be provided by an experts group who will emphasised the lack of sensitivity and specificity of each red flags alone and the need to consider them by clusters.

⇨ The proposition of a consensus based recommendation is accepted. This would be preceded by a brief **explanation** on the utility of a clinical examination with a combination of tests in order to exclude red flags. Utility of the crossed Lasègue's test is suggested.

KCE additional information on clinical examination after the GDG meeting

In the Cochrane review from van Der Windt, it was stressed that several aspects of physical examination in isolation (scoliosis, paresis or muscle weakness, muscle wasting, impaired reflexes, sensory deficits) do not accurately distinguish between low-back pain patients with or without lumbar radiculopathy due to disc herniation. For other tests (forward flexion, hyper extension test, and slump test), there was insufficient evidence to provide recommendations regarding their diagnostic accuracy or usefulness. The Straight Leg Raising (SLR) or Lasègue's test showed high sensitivity (and variable specificity), whereas the XSLR showed high specificity in surgical studies but coupled with low sensitivity. The crossed SLR (XSLR) or crossed Lasègue's test is usually only positive in patients with major nerve root impingement, and the authors of the Cochrane review emphasised that "these results were obtained in populations characterised by a very high prevalence of disc herniation (>75% in nearly all studies) and a severe spectrum of disease, and cannot be generalised to populations with a lower prevalence of the target condition". This why they concluded that there was still insufficient evidence for the clinical usefulness of the SLR and XSLR in the diagnosis of disc herniation in primary care populations and other populations of patients not (yet) referred for surgery.

⇨ Conclusion: The diagnosis of lumbar disc herniation should not be based on the results of one single physical examination test. Better performance may be obtained with combinations of tests (even if evidence is still needed)

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30th November 2016):

- Warwick Clinical Trials Unit: "The guideline identifies the importance of red flags for screening for serious causes of back pain. Whilst how to screen out serious causes is out of scope the GDG should be aware that **a systematic review of red flags for malignancy and fracture suggest that these are largely uninformative**. Downie A, Williams CM, Henschke N, Hancock MJ, Ostelo RW, de Vet HC, Macaskill P, Irwig L, van Tulder MW, Koes BW, Maher CG. Red flags to screen for malignancy and fracture in patients with low back pain: systematic review BMJ. 2013 Dec 11;347:f7095. doi: 10.1136/bmj.f7095. Here the reader is directed to Appendix P for a list of red flags. Appendix P actually reproduces a guide to appropriate referral to specialist services produced by NICE in 2001. We have been unable to locate this on the NICE website and confirm if it has been reviewed since then. It is not listed on page 21 as part of related NICE guidance. We have concerns that this guidance may no longer be valid; and at the very least it needs to be easily accessible on the NICE website so people can appraise quality of the guidance. The GDG might here wish to consider a link to more recent NICE guidance on the recognition of, and referral for, suspected cancer. https://www.nice.org.uk/guidance/ng12"

  NICE reply: Thank you for your comment. We have added the reference of the report referred to in appendix P. (p4/222)

NICE changes in the final version of the guideline (November 2016) (see p. 61-63 full guideline https://www.nice.org.uk/guidance/ng59/evidence/full-guideline-assessment-and-noninvasive-treatments-2726158003)

Not in the guideline but In the final presentation of the recommendations by Bernstein et al. in the BMJ (BMJ 2017;356:i6748 doi: 10.1136/bmj.i6748 (Published 2017 January 05)), the recommendation 6 which focuses on alternative diagnosis was removed from the imaging topic and place at the first place of all recommendations.

NICE final recommendations on imaging (November 2016)

6. Think about alternative diagnoses when examining or reviewing people with low back pain, particularly if they develop new or changed symptoms. Exclude specific causes of low back pain, for example, cancer, infection, trauma or inflammatory disease such as spondyloarthritis. If serious underlying pathology is suspected, refer to relevant NICE guidance on:

- Metastatic spinal cord compression in adults
- Spinal injury
- Spondyloarthritis
- Suspected cancer

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

- "Think about" appaers too weak; "Always recall" is proposed.
- Change "alternative diagnosis" in "differential diagnosis".
- Because the terms "specific causes" are unclear, they have to be replaced by "signs suggestive of possible serious underlying pathology (identified as red flags)". This change allows to be more coherent trougth the text. A list of this red flags will be developed for the Belgian guideline, based on expert opinion. Moreover, the need for considering clusters of red flags rather than single red flag should be emphasised in the text linked to the recommendation.
- The Belgian red flags list included neurological emergencies. Therefore, they have to be listed within the examples of the recommendation.
- Add "radicular pain" after "low back pain" to be clearer.
- Remove the references to the other NICE guidances.

KCE 2017 final recommendation on clinical examination for low back pain and radicular pain

1. Allways take into account differential diagnoses when examining or reviewing patients with low back or radicular pain, particularly if they develop new or changed symptoms. Exclude signs suggestive of possible serious underlying pathology (identified as red flags), for example, cancer, infection, trauma, inflammatory disease such as spondyloarthritis, or severe neurological problems such as cauda equina syndrome.

(consensus-based experts opinion).

7.2. Risk assessment and stratification

Risk assessment and stratification in patients with low back pain ± radicular pain

NICE search question 1

"Which validated risk assessment tools are the most accurate for identifying people with low back pain or sciatica at risk of poor outcome/delayed improvement?"

NICE search question 2

"What is the clinical and cost effectiveness of stratifying management of non-specific low back pain or sciatica according to outcome of a risk assessment tool/questionnaire?"

Introduction based on the draft version of NICE guideline (March 2016)

- The aim of risk assessment tools is to **identify risk factors or prognostic features** that may make a person more likely to suffer from chronic, disabling back pain. These tools are used to **predict delayed improvement or poor outcome.**
- The desire to get away from a 'one size fits all' approach has led to considerable interest in **stratified care strategies**. There are many different proposed methods of stratification but in general they divide patients into one of 3 groups: Stratification by risk of on-going disability (e.g. OMPSQ and STarT Back); Stratification by underlying mechanism for back pain based on anatomy, pathology, pain mechanisms or psychosocial factors (e.g. Classification Based Cognitive Functional Therapy approach**);** Stratification by likelihood of response to treatment (e.g. those patients who might respond to spinal manipulation or spinal stabilisation). The question is whether **management stratified according to the tool is effective.**

PICO used by NICE for the research question 1 on risk assessment (March 2016)

Population	• People aged 16 or above with non-specific low back pain • People aged 16 or above with sciatica
Intervention(s)	• Validated risk assessment/clinical prediction tools, including; STarT Back, DRAM, Örebro
Comparison(s)	• Risk of poor outcome/delayed improvement (as reported by study)
Outcomes	• Area under the curve (c-statistic) • Sensitivity, specificity, predictive values (define thresholds) • Predicted risk versus observed risk (calibration) • Other outcomes e.g., D statistic, R2 statistic and Brier score • Reclassification

PICO used by NICE for the research question 2 on risk stratification (March 2016)

Population	• People aged 16 or above with non-specific low back pain • People aged 16 or above with sciatica
Intervention(s)	• Validated risk assessment/clinical prediction tools, including; STarT Back, DRAM, Örebro, Gatchel, Hicks/Delitto, Childs/Flynn, Hancock, O'Sullivan
Comparison(s)	• Control (no risk tool, receive the same intervention as those who have undergone a risk tool) □ • Tools compared to each other (groups receive the same intervention)

Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris disability questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BPI, BDI, STAI) **Important** • Responder criteria (> 30% improvement in pain or function) • Adverse events: 1. Morbidity • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit

Literature quoted by NICE 2016 guideline (March 2016)

- **Risk assessment:** 16 studies reporting evidence for 11 risk assessment tools**.** All of the studies were conducted in a low back pain population (2 of which had a mixed population of people either with or without additional sciatica).

  NICE use several outcomes such as **discrimination (DIS)** by calculating the area under the receiver operating characteristic curve[a] and **calibration (CAL)** = predicted risk versus observed risk. Eleven tools were analysed (see Table 5):

Table 5 – Predicting results of 11 risk assessments tools (NICE 2016)

Tools	Predicting functional improvement	Predicting pain	Quality evidence	Nb studies Population	NICE GDG Comments
ÖREBRO tool	Moderate DIS Low CAL		High to low	single studies, n=61 to n=296	Insufficient evidence Insufficient accuracy 21 questions= time Not for routine use in primary care
Acute LBP screening questionnaire ÖREBRO	Poor DIS[b] Low CAL	Low CAL	High to low	single studies, n=56 to n=296	
STarT Back tool	High DIS Moderate CAL	Moderate DIS Low CAL	High to low	max 2 studies, n=53 to n=1594	Sufficient evidence Sufficient level of DIS & CAL Rapid to complete Feasible to use in routine

[a] According to NICE, the following cut-offs have been used for discrimination: 90%-100% = perfect discrimination; 70%-89% = moderate discrimination; 50-69% = poor discrimination; <50% = not discriminatory at all.

However, when we read the result, a category of high discrimination exists, appearing to be around 80%

[b] Presented as Moderate by NICE but equals to 64%

Functional rating index (FRI) questionnaire	High DIS		Very low	a single study, n=131	Insufficient evidence Fairly quick to use
ODI questionnaire	High DIS		Very low	a single study, n=131	Insufficient evidence (no evidence for pain, no data for CAL)
Chronic pain risk item set		High DIS	Low	a single study, n=571	Insufficient evidence 22 questions= time
Hancock CPR		Moderate DIS	Low	a single study, n=937	Insufficient evidence Easy to use
Fear Avoidance Beliefs questionnaire	Moderate CAL	Low CAL	Low	a single study, n=146	Insufficient evidence 11 questions= time
Pain catastrophising scale	Moderate CAL	Low CAL	Low	a single study, n=146	Insufficient evidence 13 questions= time
Tampa scale of kinesiphobia	Moderate CAL	Low CAL	Low	a single study, n=146	Insufficient evidence 11 questions= time
Patient health questionnaire	Moderate CAL	Low CAL	Low	a single study, n=146	Insufficient evidence Easy to use

DIS: discrimination; CAL: calibration

No relevant economic evaluations were identified for risk assessment tools.

- **Risk stratification:** 6 studies (published in 8 papers) for the effectiveness of stratifying management. All of the studies were conducted in a population of low back pain with or without sciatica. As there was only one randomised trial identified, cohort studies were also searched for. However, none of the cohort studies identified met the inclusion criteria specified in the protocol**.**

  3 tools were analysed but one in two different settings

  - **Hicks/Delitto classification versus no risk tool**
    - no clinical difference for quality of life (mental and physical component scores of the SF-36) (2 studies, very low quality, n=234) except a clinical benefit favouring stratified treatment at ≤ 4 month for the physical component score (Mean diff PCS 0-100: 6.20 [95%CI -8.74, 21.14], 1 study, n=78).
    - no clinical difference for the majority of outcomes reported (pain, function and healthcare utilisation) although clinical benefit for stratified treatment for responders to pain improvement at ≤ 4 months (a single low quality study, n=156) and improvement in function at > 4 months (1 study, very low quality, n=156).
  - **O'Sullivan classification system versus no risk tool**
    - clinical benefit of stratified treatment for pain in both the short (≤ 4 months) and long term (> 4 months) (Mean diff VAS 0-10: -2.10 [95%CI -2.83, -1.37] & -1.50 [95%CI -2.33, -0.67, 1 study, low-very low quality, n=94).
    - clinical benefit of stratified treatment for function in the short term only, not at the >4 months' time period (Mean diff ODI 0-100: -10.90 [95%CI -13.94, -7.86] & -9.80 [95%CI -14.21, -5.39], 1 study, low-very low quality, n=94).

- **STarT Back risk tool versus no risk tool in secondary care**
  - no clinical difference for most of the outcomes: quality of life (mental component score), pain, function, psychological distress (a single, low quality study, n=851).
  - clinical benefit with the stratified treatment for quality of life measured by the physical component score of the SF-12 at both the short (≤ 4 months) and long (>4 months) term time points (Mean diff: 2.30 [95%CI 0.42, 4.18] & 2.30 [95%CI 0.73, 3.87], a single study Hill 2011, low quality study, n=851)..

When the individual stratified groups from the STarT Back classification of low, medium and high risk category patients were compared with no risk tool

- clinical benefit favouring stratified treatment for **quality of life measured by EQ-5D 0-1 in the high risk category patients at ≤ 4 months** (Mean diff: 0.11 [CI95% 0.01, 0.21], 1 study of Hill 2011, very low quality, n=236) and in the **medium and high risk category patients at > 4 months** (Mean diff: 0.05 [CI95% -0.01, 0.12] & 0.08 [CI95% -0.02, 0.18], 1 study, very low quality, n=394 and n=236).
- clinical benefit favouring stratified treatment for **quality of life measured by the physical component score of the SF-12 0-100 in both the medium and high risk patients at the ≤ 4 months'** (Mean diff: 2.70 [95%CI 0.39, 5.01] & 2.50 [CI95% -1.71, 6.71], 1 study, very low quality, n=394 and n=236) as well as in the **medium risk patients at > 4 months (**Mean diff: 3.10 [95%CI 0.66, 5.54] 1 study, very low quality, n=392).
- clinical benefit in responder criteria for improvement in pain and function was seen in the overall group as well each stratified risk group at the ≤ 4 month follow up (1 study from Beneciuk 2015), low-very low quality, n=99 according to the Forest plot, Appendix K, p20/624 and not 951 as quoted by NICE in the text p111/816).
- no clinical difference between the STarT Back risk tool compared to no risk tool for all other outcomes reported at any time point. NICE quoted a clinical benefit in function favouring stratified treatment for the high risk category patients in the short term (≤4 months) (1 study, very low quality, n=236) but we did not find this.

- **STarT Back risk tool (IMPaCT cohort) versus no risk tool in primary care**
  - no clinical difference for any outcome reported (quality of life, pain, function and psychological distress) (a single study Foster 2014, very low quality evidence, n=922).

When the individual stratified groups from the STarT Back classification of low, medium and high risk 11 category patients were compared with no risk tool,

- clinical benefit favouring stratified treatment for **quality of life** measured by EQ-5D 0-1 in the high risk category patients at ≤ 4 months (Mean diff: 0.06 [95%CI 0.01, 0.12]) and > 4 months' (Mean diff: 0.01 [CI95% -0.03, 0.04]) time points (1 study very low quality, n=922).
- clinical benefit for stratified treatment in patients identified as being at high risk for **quality of life** measured by the physical component score of the SF-12 (PCS 0-100 Mean diff: 3.80 [95%CI -0.19, 7.79]), **pain severity** (VAS 0-10, Mean diff: -1.00 [95%CI -1.84, -0.16]) and **function** (RMDQ 0-24, Mean diff: -2.50 [CI95% -4.30, -0.70]) at the > 4 month follow-up (very low quality evidence, n=189).
- no clinical difference between the STarT Back risk tool compared to no risk tool for all other outcomes reported at any time point.

Conclusion regarding the literature review: For the risk assessment, analysis showed evidence in terms of discrimination and calibration for the Start Back screening tool. Evidence for the other tools is judged insufficient. The results regarding the effectiveness of the risk stratification found poor evidence for the use of the Hicks/Delitto classification (few clinical benefits), some evidence for the use of the O'Sullivan classification (clinical benefit in pain in both short and long term and in function at short term in a single study). With the Start back screening tool, when the individual stratified groups of low, medium and high risk category were compared with no risk tool, a clinical benefit was mentioned, in several outcomes for the medium and the high risk groups.

Economic evaluation

- One cost-utility analysis found that in adults with low back pain (with or without sciatica) Hicks/Delitto classification based intervention dominated (less costly and more effective) compared to usual physical therapy care. This analysis was assessed as partially applicable with potentially serious limitations.
- Two cost-utility analyses found that in adults with low back pain (with or without sciatica) STarT Back stratification based intervention based intervention dominated (less costly and more effective) compared to current best practice/usual care. These analyses were assessed as directly applicable with potentially serious limitations.

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:**
  - The GDG agreed that **calibration and reclassification** were the outcomes that were critical for decision-making in **risk assessment**. Discrimination was considered as important. No evidence was found for reclassification.
  - For the **risk stratification** review, the GDG agreed that **health-related quality of life, pain severity, function, and psychological distress** were the outcomes that were critical for decision-making. Responder criteria, adverse events (morbidity and mortality), and healthcare utilisation were also considered as important. Evidence was found for all of the outcomes except for adverse events (morbidity and mortality).
- **Trade-off between clinical benefits and harms:**
  - **Risk assessment:** The GDG is in favour of the StartBack tool. The **sensitivity** of the STarT Back tool was 80% comparing people of low risk versus those of medium + high risk. Therefore, the false negative rate was 20%. In terms of **predicting functional outcomes**, the AUC results were found to be best for STarT Back, functional rating index and ODI; in terms of predicting the outcome of **pain intensity**, the AUC results were best for STarT Back, and Hancock CPR. The GDG noted that in terms of **calibration**, for all the tools reviewed, the R2 values were generally low (particularly for pain outcomes). However, the GDG considered that because no test will be both highly sensitive and highly specific, an R2 value of 40% (as shown by STarT Back trial for function) would be sufficient for the purposes of this review. The GDG considered that for most of the tools there was either no evidence or poor evidence for the accuracy of either one of the outcomes of function or pain. However STarT Back had both calibration and discrimination evidence for both of these outcomes, and several studies reported this tool. The evidence for STarT Back was also amongst the more accurate of the tools. The GDG considered that people whose treatment was stratified based on the STarT Back tool fared better when considering the intervention population as a whole, but noted that some people would be misclassified by the tool. The GDG therefore reflected this in recommending that a stratification tool should be considered as an assessment tool at point of first contact, thereby allowing people re-presenting to be considered for further treatment. The GDG also reflected the predictive value of the tool by recommending that the tool should support but **not replace clinical decision-making.**
  - **Risk stratification:**
    - For the Hicks/Delitto tool, the GDG mentioned the results (clinically important difference for the outcomes of quality of life (SF-36 physical component) only in the short term but no difference for the SF-36 mental component, pain or function at any time point). They also reminded that the rules combine key information from clinical history and physical examination studies but are only validated for people suffering from low back pain and not a sciatica population.
    - For the O'Sullivan tool, the GDG mentioned only the result (clinically important difference for the outcomes of pain (short and longer term) and for function (ODI) in the short term, which was not carried through in the longer term).
    - For the STarTBack, the GDG mentioned several issues:
      - Clinically important effect is showed for the following: Quality of life; SF-12 physical component in both the short term for the overall population and the medium and high risk stratified groups and in the longer term for the overall population and the medium risk stratified group;EQ-5D in the short term for the high risk stratified group and in the longer term for the medium and high risk stratified groups; responder criteria for improvement in pain and function in the short term for both the overall population as well as all stratified risk groups.
      - The GDG emphasised the very low quality of the evidence due to being non-randomised and therefore prone to selection bias and lack of blinding to key confounders. The GDG felt it was appropriate that less weight be placed on evidence from this non-randomised study due to the high risk of bias attached to the effects.
      - There is a concern that the intervention in the low risk group might be misinterpreted as 'no treatment'. The GDG noted that the low risk group identified in the RCT assessing STarT Back received a package of care comprising advice and education (with booklet and video) delivered by a physiotherapist during the course of a 30 min appointment in addition to usual care.

- Patients stratified to the low risk group who continued to experience pain have to return to their general practitioner (or other healthcare provider). It was emphasised that STarT Back is a decision support tool and not a substitute for clinical acumen.
- One of the trials relating to STarT Back is only validated in a **primary care setting at first** point of contact. It was clarified that this did **not imply first consultation for low back pain, and may represent a range of durations of pain** for different people and at different stages in the patient pathway. As the questionnaire is only validated at first point of contact, it was agreed that it was **not appropriate to apply the tool again** if the person returned for the **same episode**. The second trial however was based on the implementation of STarT Back in a secondary care outpatient setting. The GDG felt that this range of settings balanced the evidence. The GDG agreed that one of the strengths of the tool was that it correctly identified more patients who were in the low risk category compared to non-use of the tool, thus giving the healthcare provider confidence in the management of the patient after the first initial treatment. It was acknowledged that **avoidance of overtreatment** in patients where it was not required was a real benefit of the tool with potential to save time and money if implemented correctly.
- The GDG also noted that STarT Back performs better than non-use of the tool in people at high risk compared to medium or low risk groups. The GDG discussed that the value of the tool may be in identifying those with a **poorer prognosis** and ensuring they get more intensive treatment without delay.
- The GDG agreed that an essential part of stratification was not just identifying subgroups at risk of poor outcome but also informing appropriate management and therefore agreed it was important to make clear in the recommendation that management should be tailored as a result of stratification.
- Overall it was agreed that benefit was demonstrated for stratification using STarT Back but that if stratification is used it should be considered as a package of both a risk stratification tool and stratified management.
- NEW: The GDG was not able to recommend any specific risk assessment tool or sets of interventions for stratified management based on the evidence included in this review. However the GDG agreed that based on risk stratification, simpler and less intensive support should be considered for people with low back pain or sciatica likely to improve quickly and have a good outcome (for example, reassurance, advice to keep active and guidance on self-management), while more complex and intensive support should be offered to those at higher risk of a poor outcome (for example, exercise programmes with or without manual therapy or using a psychological approach).

- **Trade-off between net clinical effects and costs.** Based on the 3 economic evaluations, the GDG recommended that a risk stratification tool should be considered at first consultations in primary care for stratification and risk-adjusted interventions for people in whom a specific treatment is being considered. The GDG discussed the importance of assessment tools that are easy and quick to conduct in practice. It was noted that the STarT Back tool is short and can be completed in a few minutes and was therefore given as an example of the tool that could be used in the recommendation.
- **Quality of evidence:**
  - **For the risk assessment, t**he evidence was rated as low or very low quality for all of the outcomes and risk assessment tools (due **to** outcome reporting bias, and attrition bias**)**, except for ÖREBRO which was graded as high quality (for both discrimination and calibration).
  - **For the risk stratification**, the evidence was rated as low or very low quality for all of the outcomes, mainly due to risk of bias (and sometimes due to additional imprecision): mainly lack of appropriate blinding to the key confounders for randomized studies and selection bias coupled with lack of appropriate blinding for the single non-randomised study. The GDG also expressed concern regarding the evidence for the O'Sullivan classification tool versus no risk tool stratification as it was from a single study that only included people who had already been assessed by the O'Sullivan tool and stratified into treatment groups accordingly. Information on people that did not meet the specific inclusion criteria for the risk tool were not reported which led the GDG to question the applicability of this evidence.
- **Other considerations:** The GDG agreed on that the STarT Back tool over the other clinical prediction tools included in this review demonstrated superior specificity, sensitivity and usability in a clinical setting. STarT Back is quick and easy to conduct in practice unlike the ÖREBRO tool, for example, which is more complicated and less practical to use in a consultation. It was also the most relevant as it was based and validated in a primary care setting in the UK. There was also concern raised about the inability of some risk tools to subgroup the full spectrum of low back pain patients leaving a large portion of the population unclassified. The evidence for STarT Back

exhibited positive results favouring stratified care for some critical outcomes such as function and was also supported by an IMPaCT study testing the implementation of stratified care for low back pain within in a primary care physician setting, although it was noted that this evidence was of poorer quality due to being from a non-randomised study. The GDG therefore agreed that stratification should be considered, and that the STarTBack tool could be given as an example of a tool that may be used.

-

NICE 2016 draft recommendation on risk stratification (March 2016)

1. Consider using risk stratification (for example, the STarT Back risk assessment tool) at first point of contact with a healthcare professional for each new episode of non-specific low back pain with or without sciatica to inform shared decision-making about stratified management.

Belgian GDG considerations mentioned in the Lime survey at the beginning of June 2016

Agreement with the NICE draft recommendation 1: 15 Yes, 1 No, 2 no opinion, 1 out of competence, 0 no answer, 0 not completed

- **Comments from the one respondent who does not agree:**
  - Not clinical and especially cost effective
- **Comments from other respondents:**
  - They state "The STarT Back risk tool versus no risk tool in primary care (IMPaCT cohort) showed no clinical difference for any outcome reported (quality of life, pain, function and psychological distress) (a single study, very low quality evidence, n=922)." Yet, in the abstract of the article it is mentioned: "Mean time off work was 50% shorter (4 vs 8 days, p = 0.03) and the proportion of patients given sickness certifications was 30% lower (9% vs 15%, P = 0.03) in the post-intervention cohort. Health care cost savings were also observed." (Foster 2014 Annals of Family Medicine http://www.ncbi.nlm.nih.gov/pubmed/24615305)
    Besides, I consider the classification of Hicks/Delitto as a different classification from the one resulting from the use of the Orebro or Start Back Q.
    Finally I do not consider all the tools presented in Table 5 as "risk assessment tools".
  - Very important.
  - Lichte discrepantie tussen de studie STarT in "primary care" en aanbeveling om bij elk nieuw contact te starten. Nederlandse vertaling leest moeilijk en trapsgewijs is geen korrekte weergave want suggereert een chronologisch doorlopen van verschillende behandelingen.
  - 'New' episode needs to be clearly defined in this recommendation.
  - I certainly agree to consider using risk stratification. However, it is unclear to me whether the NICE recommendation relates to 'eerstelijns-' and/or 'tweedelijnsgezondheidszorg' (health care professionals in first and/or second care). Furthermore, when putting in the Belgian context, more information (evidence) will be needed on the Dutch/French/German translations of the tools that are available, e.g. STarT Back).

Strength of the recommendation 1 on risk stratification: According to NICE formulation, it is a weak recommendation

GRADE Factors	
Balance between desirable and undesirable effects	Benefit if package of both risk stratification and stratified management
Quality of evidence	Mainly low or very low
Costs (resource allocation)	Positive analysis for Start Back tool
Values and preferences	Importance of easy and quick tool

Agreement with the strength of the NICE draft recommendation 1: 7 strong, 7 weak, 0 no opinion, 2 no answer, 3 not completed

- **Comments for a weak recommendation**
  - Based on patient's values and preferences the ultimate point of efficacy is motivation.

- Although the clinical benefits outweigh the harms and using risk stratification leads to a more cost-effective approach, my recommendation would be weak because of the actual rather low quality of evidence. Further research seems necessary.
- My "feeling" is that it should be a strong recommendation. But, although the evidence for stratification tools is quite good, there is still insufficient evidence as to what we should propose to high risk patients.

- **Comments for a strong recommendation**
  - All the patients with LBP should not be considered as a single group and be proposed the same treatment. I think the scientific literature agrees with that and with the necessity to identify the risks of chronicity in order to propose an adequate treatment to the patient
  - Low cost, easy to use as a tool, good balance between desirable and undesirable effects, leads to stratification in treatment approach.

Belgian GDG comments during the GDG meeting on the 29th June 2016

Although the **StarT Back tool** is quoted by NICE as an **example**, it appeared that the wording of the recommendation concerned mainly the StarT Back tool.

- The terms “first point of contact” and “new episode” are relative to the StarT Back tool that has to be used during the first encounter with the patient.
- There are few other tools used for risk stratification in practice, except the Örebro tool.

However several issues are mentioned concerning the Start Back tool:

- For some GDG members, chronic LBP patients (with a non-stop duration of pain) could not need the StarT Back tool (because there are already “high risk” patients). However, some GDG members argued that some patients have chronic LBP with low disability and low psychosocial factors; therefore they do not belong to the “high” risk group.
- In recurrent LBP, an episode is “new” if it occurred after at least one month without pain and have a duration of at least 24h. (see addendum below)
- One GDG member mentioned that the efficacy of the risk stratification tool appeared mainly measured on pain even if it is not the critically outcome for these kind of tools. However, function was often measured. For the StarT Back tool, a benefit was demonstrated on quality of life.
- Some physicians at emergency department mentioned that the length of the StarT Back tool is a barrier for its use. But the Örebro is longer than Start Back tool.
- It is not sure that there is a validated Dutch-version either of the StarT Back tool nor the Örebro tool. Idem for the German-version. (see addendum below)
- The StarT Back Tool is certainly useful in general practice and at emergency department. It is designed to assess several psychosocial dimensions that can be related to pain.
- The StarT Back Tool is poorly known by Belgian practitioner.

Concerning the **strength of the recommendation**, it was decided to keep a weak recommendation such as NICE.

- In front of a perfect dissensus in the survey (7 strong and 7 weak), it is proposed to select the weakest strength.
- Moreover, the level of evidence is not high.

⇨ **The NICE recommendation 1 is accepted** without any change.

1. “Consider using risk stratification (for example, the StarT Back risk assessment tool) at first point of contact with a healthcare professional for each new episode of non-specific low back pain with or without sciatica to inform shared decision-making about stratified management”.

KCE additional information after the meeting

On screening test

This type of research questions needs a specific approach, as there is no direct relationship between the test and the clinically important outcome since the clinical effectiveness of a test depends on the availability and efficacy of treatment. The value of a test depends on its characteristics compared to the test that is considered standard and the purpose for which it is considered. The diagnostic accuracy of two tests can be compared but a new test can also replace another test with the same diagnostic accuracy

because it is more safe or cheaper. Furthermore, a test can be evaluated as an extra test (add-on) in the clinical pathway in addition to the tests already used. Results of the evidence thus always have to be interpreted in view of the clinical context.

Performing a screening test can have positive but also negative impact:

- Independent of the test results, patients may suffer from the morbidity caused by a given test and many patients will experience some anxiety when awaiting test results.
- Patients with a true positive result may benefit from an effective treatment to improve important clinical outcomes but treatment interventions may also have important side effects. The supporting evidence for the treatment efficacy may be of low quality with uncertainty around its true effect.
- False positive results lead to needless anxiety and patients who have a false positive result will be exposed to unnecessary therapeutic interventions and associated risks.
- False negative results may lead to delayed help seeking when (minor) symptoms occur, resulting in poorer clinical outcomes.
- Finally, when results are inconclusive or 'borderline', further follow-up and additional tests may be necessary and may be associated with additional side effects and anxiety.

All these factors need to be taken into account when considering the use of a diagnostic test or implementing a screening strategy. Evaluating the diagnostic accuracy of a test (sensitivity, specificity, predictive values in a population etc.) will provide insufficient information to judge its clinical value.

On recurrent pain

- In the Clinical Orthopaedics and Related Research (February 2006, page 152) recurrent back pain is defined as "the repetition of two or more episodes of disability from normal activity over a period of 12 months that are separated by at least 3 months of normal functioning."

On the StarT Back screening Tool

- On the website of the StarT Back tool, several translations are proposed http://www.keele.ac.uk/sbst/startbacktool/translations/: one formal translation in French, another formal translation in Dutch and an informal translation in German.
- The term non-specific is unclear for the GDG and should be remove from all recommendations.
- The time window for the use of the StarT Back tool is questioned: It is proposed by NICE at the first contact but 4 questions/9 in the StarT Back questionnaire concern the last 2 weeks. It would be strange to ask these questions in the first hours of pain. According to Jonathan Hill contacted by e-mail during November 2016, "*the STarT Back Tool was originally developed with each item having a reference time frame for patients to consider - "last 2 weeks" and validated within questionnaires as part of a large cohort study ... so those who have concerns are right in some ways... However, the tool has since be tested among patients in many first contact care situations and there are no reported problems among very acute patients. For example NHS Scotland uses the tool as part of a central telephone triage service which has around 10,000 calls per month who all complete the SBT. We do find the prediction cut-offs in those with less duration than 48 hours is not as accurate as in those who have had pain for longer - mainly because we find that symptoms in very acute high risk patients can settle fairly quickly if their risk factors are appropriately managed (i.e. with good reassurance and pain medication). The STarT Back Trial is the highest quality evidence we have for SBT and included patients with less than 2 weeks duration... Also our implementation study - IMPaCT Back included very acute patients. When we did a moderation analysis (published by Benecuik et al 2016) it showed that the only moderator of outcome was socioeconomic status - not duration. The message from that study was that among people from deprived areas who have low health literacy - caution is required to only provide one low risk session of advice - as these people need more support. This makes some sense…*"

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30th November 2016)

Risk assessment with Start Back tool

- **Question on symptom duration**: British Institute of Musculoskeletal Medicine "If you had an acute back for one week and were asked whether you agreed or disagreed with the following statement (which contains the questionable conflation of two questions): "My back pain is terrible and it's never going to get any better." What would you think of your interviewer? – I find myself apologising to the patient and promising never to use the tool again. **NICE reply**: The GDG considered that the evidence for STarT Back was amongst the more accurate of the tools. The GDG acknowledged that people could be misclassified by the tool, and recommended that a stratification tool should be considered as an assessment tool at point of first contact, thus allowing for people to be re-assessed for eventual further treatment. Furthermore, the GDG recommended

that the tool should inform, but not be a substitute of, clinical decision-making, The GDG acknowledged the predictive value of the STarTBack risk assessment tool. These issues are discussed in section 6.6 (Recommendations and link to evidence) in the Risk assessment and stratification chapter. (p12/222)

- **Limited accuracy:** British Institute of Musculoskeletal Medicine: It is used to identify patients with high levels of distress and unhelpful perceptions to allow a more psychologically directed management – but distress may derive from high levels of symptoms and impairment that the tool would not identify. (p12/222). **NICE reply**: the STarT Back was amongst the more accurate of the tools according to the GDG. The GDG acknowledged that people could be misclassified by the tool, and recommended that a stratification tool should be considered as an assessment tool at point of first contact, thus allowing for people to be re-assessed for eventual further treatment. Furthermore, the GDG recommended that the tool should inform, but not be a substitute of, clinical decision-making, The GDG acknowledged the predictive value of the STarTBack risk assessment tool. These issues are discussed in section 6.6 (Recommendations and link to evidence) in the Risk assessment and stratification chapter.
- **Risk of misuse and equity:** British Institute of Musculoskeletal Medicine: There is reputed to be a 20% error in group allotment. The presence of the tool on the internet with its scoring system and intent could result in some of those it is applied to "gaming" the system, supplying the answers that would get them more attention and validation. If some patients are going to have more resources devoted to their management than others they will need to have confidence that this is decided by individual clinical judgement and not a hasty short questionnaire with what many may find uncomfortable forced-choice questions that do not have a very reliable outcome. **NICE reply**: The GDG acknowledged that people could be misclassified by the tool, and recommended that a stratification tool should be considered as an assessment tool at point of first contact, thus allowing for people to be re-assessed for eventual further treatment. Furthermore, the GDG recommended that the tool should inform, but not be a substitute of, clinical decision-making, The GDG acknowledged the predictive value of the STarTBack risk assessment tool. These issues are discussed in section 6.6 (Recommendations and link to evidence) in the Risk assessment and stratification chapter. (p12/222)
- **General reluctance from GPs to use the tool in clinical practice due to time pressures, lack of training and diversity of the patient population.**

  Guy's and St. Thomas NHS Foundation Trust: We acknowledge the potential benefit of stratification in targeting treatment provision. We anticipate barriers to the use of StartBack in primary care at the point of first contact. We conducted an audit which showed that GPs in our local area found it difficult to use. There was a general reluctance from GPs to use the tool in clinical practice due to time pressures and the diversity of the patient population in our area… **NICE reply:** Your comments will be considered by NICE where relevant support activity is being planned. (p197/222)

  Primary Care Rheumatology Society: The choice of risk stratification tool (such as the Keele STarT Back) should be considered for its ease and speed of use in relevant, commonly used electronic patient record systems (such as SystmOne and EMIS) as well as the tool's validity…. The tool in patients electronic record as SystmOne is clunky and too slow. **NICE reply**: STarT Back is suggested in the recommendation as an example of risk assessment tool to inform shared decision-making about stratified management. Your comments will be considered by NICE where relevant support activity is being planned. (p61/111)

  Extended Scope Practitioners Professional Network: The STartBack Tool has been available for GPs for a number of years but is frequently omitted. Could this tool be put onto systmone for ease of use? Could a national back pain website be created incorporating the STartBack tool and subsequent self-management advice for patients and self-referral forms for patients dependant on their scoring? **NICE reply:** Your comments will be considered by NICE where relevant support activity is being planned. (p39/111)

  Homerton University Hospital NHS Foundation Trust: The STarT Back risk assessment tool, is currently embedded within our electronic choose and book GP referral form and questionnaires given to new patients. Homerton's Locomotor referral pathway advises that only moderate and high risk patients are referred to physiotherapy/pain service, internal audit has found this to be the case. However in practice, GPs report feeling able to guess the risk factors so that this as well as time constraints mean the STarT form is rarely completed by GPs. It is however used by Homertons physiotherapists in the service. The STarT back tool contributes to Physiotherapists consideration as to whether to refer to the interdisciplinary pain service that is embedded within our Physiotherapy department. **No NICE reply on this topic.** (p191/222)

  British Institute of Musculoskeletal Medicine: Clinicians of first contact should have the training to elicit the various aspects of a bio-psychosocial assessment with more accuracy and sensitivity [in all aspects of the word] than this tool. **No NICE reply on this topic.** (p12/222**)**
- **Not for sciatica:**

  Extended Scope Practitioners Professional Network: Our understanding is this tool was designed for back pain alone and not sciatica. Due to the high levels of distress experienced by patients with acute sciatica this could mean patients are stratified incorrectly into the high risk group and subsequently miss out on more active and hands on treatment. Currently, there is no research evidence about superior outcomes using a risk stratification approach specifically for patients with spinal radiculopathy and

so the recommendation for stratification would be more closely matched to best evidence if it were to be recommended for patients with NSLBP. We assume this is what the GDG is intending, i.e. that stratification (for example with the STarT Back tool) be considered in patients with 'non-specific LBP with or without sciatica' in the context of the clinician applying clinical judgement and that radiculopathy may require other specific interventions. We would like to draw attention to the GDG that a current randomised trial is ongoing that is testing a stratified care intervention specifically for patients with sciatica (NIHR HTA funded SCOPiC trial, Chief Investigator Prof Nadine Foster at Keele University; 2014-2018). Due to the high levels of distress experienced by patients with acute sciatica this could mean patients are stratified incorrectly into the high risk group and subsequently miss out on more active and hands on treatment. (p39/111). **NICE reply:** The GDD acknowledged that all of the tools reviewed are validated in either solely low back pain populations or mixed populations of people with low back pain and/or sciatica, but none are validated for sciatica specifically. This is reflected in the 'Other considerations' box, section 6.6 on page 114. . STartBack is provided as an example of a stratification tool that may be used, but other risk stratification tools could be considered. As there was evidence for the use of stratification tools in populations with low back pain and sciatica, the GDG agreed it was appropriate to state 'low back pain with or without sciatica' in the recommendation.(p18/111; p39/111)

Stratified care

- **Need of combination between risk stratification tool (e.g., STarT Back) and matched treatments.** British Institute of Musculoskeletal Medicine: There is no evidence that stratification alone improves outcome. However stratification improves consistency of care; a biopsychosocial approach is indicated at all stages; the low risk group had treatment: advice, education and information, reassurance, pain relief. There needs to be guidance for recommendations appropriate for initial primary care. **NICE reply**: The GDG considered that the evidence for STarT Back was amongst the more accurate of the tools. The GDG acknowledged that people could be misclassified by the tool, and recommended that a stratification tool should be considered as an assessment tool at point of first contact, thus allowing for people to be re-assessed for eventual further treatment. Furthermore, the GDG recommended that the tool should inform, but not be a substitute of, clinical decision-making, The GDG acknowledged the predictive value of the STarTBack risk assessment tool. These issues are discussed in section 6.6 (Recommendations and link to evidence) in the Risk assessment and stratification chapter. (p12/222)
- **Importance of the tool both in stratifying subgroups and informing appropriate management.** Chartered Society of Physiotherapy: The capability of the tool to inform management should be made more explicit throughout the guideline by linking/referring to the stratification tool in later recommendations e.g. psychological interventions, multidisciplinary biopsychosocial rehabilitation (MBR). **NICE reply**: The GDG recommended to consider the use of a stratification tool that may be used to inform shared decision- making about stratified management. The GDG felt there was not enough evidence to recommend a specific tool, nor specific sets of interventions for stratified management. However, the recommendation has now been edited for clarity as follows: Based on risk stratification, consider simpler and less intensive support for those likely to improve quickly and have a good outcome (for example, reassurance, advice to keep active and guidance on self-management) and more complex and intensive support for those at higher risk of a poor outcome (for example, exercise programmes with or without manual therapy or using a psychological approach). For more details please see section 6.6 (Recommendations and link to evidence). (p12/222)
- **Sense of the terminology "stratified' management".** Faculty of Sport and Exercise Medicine: 'Stratified' management: will this terminology make sense to the lay reader? Or consider providing a definition in 'Terms used in this document' section page 8, line 17. **NICE reply**: The 'Information for the public' document published alongside this guideline explains this in lay terms. (p200/222)
- **Need of link with interventions:** Warwick Clinical Trials Unit: The main STarTBack paper tested the combination of risk stratification and bespoke treatment packages compared to 'standard' physiotherapy. Positive results were obtained on the primary outcome at four and 12 months. It is not, however, clear to what extent these benefits were derived from the use of a stratification tool and how much were from the improved physiotherapy approach. Thus any recommendation of the STarTBack approach should support the use of the whole package and not just parts of the package. We note here that the mean difference between groups in RMDQ at one year is 1.06 (95% CI 0.25 to 1.86). This effectively excludes the GDG's pre-set minimally important difference of 2.0 points on the RMDQ. If such a smaller difference is accepted there should be an explicit discussion from GDG as to why this is not consistent with planned methods. Since the comparator is another physiotherapy package, such a small difference may well represent worthwhile added value; but only if it is the whole package that was used. The GDG appear, in fact to be advising that the STarTBack tool should be used to inform stratified management without providing the STarTBack interventions. Neither 'standardised individual physiotherapy addressing symptoms and function' for the medium risk group or the 'individual psychologically informed physiotherapy' for those in the high risk group are recommended in the guideline. Indeed, evidence to support these approaches has not been specifically sought. **NICE reply: T**he GDG recommended STarTBack tool as an example of a stratification tool that may be used

to inform shared-decision making about stratified management. The GDG felt there was not enough evidence to recommend a specific tool, nor specific sets of interventions for stratified management. However, the recommendation has been edited for clarity and the following has been added: "Based on risk stratification, consider:
  - simpler and less intensive support for people likely to improve quickly and have a good outcome (for example, reassurance, advice to keep active and guidance on self-management)
  - more complex and intensive support for people at higher risk of a poor outcome (for example, exercise programmes with or without manual therapy or using a psychological approach)." (p98/111))
- **Importance of psychosocial factors.** Faculty of Pain Medicine**:** The "Startback tool" demonstrates that psychosocial factors are very important for some but not all patients in the outcome of treatment for back pain. This, and similar questionnaire systems (e.g DRAM) are useful tools to help guide early therapeutic interventions, but are simple statistical models. Large numbers of patients will not be reliably treated using these direction indicators alone. Oxford's large suite of pain rehabilitation programmes are now split by level of psychosocial distress and psychological interventions matched. Whilst the GDG recommends its use, the resultant PICO's are not adjusted to take splitting of the population into account and thus the reasoning is fundamentally flawed. **NICE reply**: **T**he GDG recommended STarTBack tool as an example of a stratification tool.... (p40-41/111)
- **Timing of treatments and stratification.** Faculty of Pain Medicine**:** There is little consideration of the risk and costs of overtreatment (eg CPP) or of invasive treatment (eg RF) applied to those who will get better anyway. The timing of treatments and stratification to risk is crucial yet relatively underemphasised which threatens best patient care for chronic back pain.to risk is crucial yet relatively underemphasised which threatens best patient care for chronic back pain**. NICE reply:** Regarding people at low risk of poor outcome, the GDG recommended that risk stratification at first point of contact with a healthcare professional for each new episode of non-specific low back pain with or without sciatica be considered to inform shared decision-making about stratified management. This recommendation has now been edited to add the following sentence: Based on risk stratification, consider simpler and less intensive support for those likely to improve quickly and have a good outcome (for example, reassurance, advice to keep active and guidance on self-management) and more complex and intensive support for those at higher risk of a poor outcome (for example, exercise programmes with or without manual therapy or using a psychological approach). (p43/111)
- **Challenges:** Guy's and St. Thomas NHS Foundation Trust: We acknowledge the potential benefit of stratification in targeting treatment provision. We anticipate barriers to the use of StartBack in primary care at the point of first contact. We conducted an audit which showed that GPs in our local area found it difficult to use. There was a general reluctance from GPs to use the tool in clinical practice due to time pressures and the diversity of the patient population in our area**… There are challenges in the low risk group (e.g. a**ddressing the pati**ent expectation of 'Treatment', e**nsuring information is accessible to all in a multi-ethnic population**) and in the high risk group (e.g. o**btaining psychological support for this group, using physiotherapists who have trained in psychologically informed treatments**). S**upport needed to overcome these barriers:

  1) Adequate resourcing/ national education initiatives targeting LBP (As for Stroke and OA), to manage patient expectation and change locus of control to self management first.

  2) Building on any current language provision at a local and national level

  3) Nationally scoping the use of digital support: EG 'patient support appt ,' to provide motivational support in self management

  4) Review resourcing to ensure pyschological support is adequate nationally

  5) Review a national drive for self referral to physiotherapy

  6) Drive the direct referral to physiotherapists as first contact for LBP to avoid the GP as an 'extra step ' if StartBack can not be administered at the GP level.

  NICE reply: Your comments will be considered by NICE where relevant support activity is being planned. (p197-198/222)

NICE changes in the final version of the guideline (November 2016)

In the Trade-off between clinical benefits and harms, a **summary** was added:

"The GDG agreed that an essential part of stratification was not just identifying subgroups at risk of poor outcome but also informing appropriate management and therefore agreed it was important to make clear in the recommendation that management should be tailored as a result of stratification. The GDG was not able to recommend any specific risk assessment tool or sets of interventions for stratified management based on the evidence included in this review. However the GDG agreed that based on risk

stratification, simpler and less intensive support should be considered for people with low back pain or sciatica likely to improve quickly and have a good outcome (for example, reassurance, advice to keep active and guidance on self-management), while more complex and intensive support should be offered to those at higher risk of a poor outcome (for example, exercise programmes with or without manual therapy or using a psychological approach)."

In the Trade-off between net clinical effects and costs, in the $ dedicated to one cost-utility analysis and another paper based on cohort study, a sentence was added: "The GDG agreed that these studies show that stratifying people into risk groups and offering intervention based on them is cost effective, however the details of the interventions to be offered to each risk group could not be established as studies did not compare alternative options for each group."

NICE final recommendations on risk stratification (November 2016)

1. Consider using risk stratification (for example, the STarT Back risk assessment tool) at first point of contact with a healthcare professional for each new episode of low back pain with or without sciatica to inform shared decision-making about stratified management.
2. Based on risk stratification, consider:
   - simpler and less intensive support for people with low back pain with or without sciatica likely to improve quickly and have a good outcome (for example, reassurance, advice to keep active and guidance on self-management)
   - more complex and intensive support for people with low back pain with or without sciatica at higher risk of a poor outcome (for example, exercise programmes with or without manual therapy or using a psychological approach).

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

- A recent meta-analysis (Karan et al. Can screening instruments accurately determine poor outcome risk in adults with recent onset low back pain? A systematic review and meta-analysis. BMC Medicine 2017. DOI 10.1186/s12916-016-0774-4.2017) was quoted by several GDG member that questioned the sentence "The STarT Back tool over the other clinical prediction tools demonstrated superior specificity, sensitivity and usability in a clinical setting". In this review, 5 studies investigated the STarT Back Tool and 7 the Orebro Musculoskeletal Pain Screening Questionnaire. The results were:

  For the Start Back tool

  - 'non-informative' performance for discriminating pain outcomes at follow-up (pooled AUC = 0.59 [95%CI 0.55, 0.63], n = 1153)
  - 'acceptable' performance for discriminating disability outcomes (pooled AUC = 0.74 [95%CI 0.66–0.82], n = 821).

  For the Orebro Musculoskeletal Pain Screening Questionnaire (short or long version)

  - 'poor' performance for discriminating pain (pooled AUC = 0.69 [95%CI 0.62–0.76], n = 360),
  - 'acceptable' performance for disability outcomes (pooled AUC = 0.75 [95%CI 0.69–0.82], n = 512),
  - 'excellent' performance for absenteeism outcomes (pooled AUC = 0.83 [95%CI 0.75–0.90], n = 243)

  For the Belgian GDG, this review suggested that we should recommend at least the Orebro Musculoskeletal Pain Screening Questionnaire for absenteeism outcomes.
- The acceptability for the clinicians of the long version of the Örebro is very low but there is a short version of the Örebro Musculoskeletal Pain Screening Questionnaire (10 items only) (see Fuhro F. et al. Orebro Musculoskeletal Pain Screening Questionnaire Short-Form and STarT Back Screening Tool: Correlation and Agreement Analysis. Spine 2016, 41(15), E931-936; Linton S. at al. Development of a short form of the Orebro Musculoskeletal Pain Screening Questionnaire. Spine 2011, 36(22), 1891-1895). However, this last tool uses a single cutoff score to distinguish two groups of patients only (low and high risk of chronicity), while our literature review show that distinguishing three patients groups might be more meaningful.
- This short version is currently tested for validation in French by a Belgian team. Preliminary results show psychometric properties quite similar to the long version. It should be verified that a Dutch short version also exist by asking to Steven Linton.

Additional GDG members information after the meeting (by e-mail)

- Steven Linton, the developer of the ÖMPSQ replied: "*I am not sure if anyone is/has looked at the psychometrics of the short form in those languages. However, the short form is based on a selection of 10 items from the long form. Consequently, constructing the short form is straightforward. There are a few studies now looking at the short form and although I have not properly reviewed them, it seems to work pretty well. My sense is that you lose a little predictive ability as compared to the long form. Btw: it is being used in the large study Mike and we are doing in Sydney. And the best cut-off there turned out to be 49 (while we determined it to be 50). The bottom line is that there is probably actually no real good screening instrument for risk stratification. Perhaps the Orebro is one of the best at least for work related risks, but it is longer than the Start Back.*"
- In sum: there is a Dutch version of the Short Form that can be derived from the full version (which exist in Dutch). It would be recommended, however, to pursue an additional study testing the predictive value of this short form in the near future. As is the case in other languages, the results will be quite similar, probably with some loss of predictive ability as compared to the long form.
- A critical criteria in choosing a screening tool is the purpose for which this tool has initially been designed. The OMPSQ is probably a better prognostic tool than the SBT (confirmed by the results of Karran 2017), while the SBT is probably more accurate than the OMPSQ for treatment allocation in a stratified perspective. In SBT, only potentially treatment-modifiable prognostic indicators were chosen and three potential patients subgroups with three corresponding treatment approaches were identified: low risk subgroup (suitable for primary care management according to guidelines), high physical risk subgroup (high levels of physical prognostic indicators, appropriate for physiotherapy), and high psychosocial risk subgroup (high levels of psychosocial prognostic indicators, appropriate for a combination of physical and cognitive-behavioural treatments). Analysis of the results showed that in fact these three subgroup corresponded respectively to low, medium, and high risks of chronicity. By contrast, the OMPSQ does not make any distinction between physical and psychosocial risk factors and patients groups are probably more heterogeneous, making treatment allocation more difficult.
- The Keele team working on the SBT and the stratified approach has posted useful resources online (**https://www.keele.ac.uk/sbst/**) and provided their therapists with a detailed manual.

KCE 2017 final recommendations on risk stratification (February 2017)

1. Consider using risk stratification (for example, the STarT Back risk assessment tool as presented in Box 2 and the Orebro Musculoskeletal Pain Screening Questionnaire in Box 3) for each new episode of low back pain with or without radicular pain. This risk stratification should not be performed during the first 48h after the pain onset*. The aim of the risk stratification is to inform shared decision-making about stratified management.

*It is advised to perform the risk stratification during the second consultation, approximately 2 weeks after onset.

(weak recommendation based on low to very low quality evidence from RCTs)

2. Based on risk stratification, consider:

- simpler and less intensive support for patients with low back pain with or without radicular pain likely to improve quickly and have a good outcome (for example, reassurance, advice to keep active and guidance on self-management)
- more complex and intensive support for patients with low back pain with or without radicular pain at higher risk of a poor outcome (for example, exercise programmes with or without manual techniques and a psychological intervention such as cognitive-behavioral approach).

(weak recommendation based on low to very low quality evidence from RCTs)."

7.3. Imaging

Imaging in patients with non-specific low back pain ± radicular pain

NICE search question

"What is the clinical and cost effectiveness of performing imaging (X-ray or MRI*) compared with no investigation to improve functional disability, pain or psychological distress in people with low back pain and/or sciatica?" *MRI (or CT where MRI is contraindicated)

Introduction based on the draft version of NICE guideline (March 2016)

- There are several methods that can be used to image the spine.
- Whether or not imaging is of benefit in terms of improving patient related outcomes for people with non-specific back pain or sciatica, either at initial presentation or later in the pathway, remains an area of uncertainty. This review intends to address this uncertainty.
- **Included imaging: s**imple X-ray, CT-scans, MRI scans**.**

PICO used by NICE (March 2016)

Population	• People aged 16 or above with non-specific low back pain • People aged 16 or above with sciatica
Intervention(s)	• Imaging with MRI (or CT where MRI is contraindicated), X-ray for low back pain • Imaging with MRI for sciatica
Comparison(s)	• No initial imaging • Deferred imaging
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (> 30% improvement in pain or function) • Adverse events: morbidity • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

- Five randomised trials were included in the review (reported in 9 studies). All included mixed populations of people with low back pain with and without sciatica. One of the trials included an indirect population (including people from 14 years of age). Four trials compared X-ray to no imaging, while one compared MRI or CT to no imaging.
- The search was extended to cohorts for all comparisons due to insufficient evidence and 5 additional studies were identified. Most of the cohort studies included a mixed population of people with low back pain with and without sciatica. One study had a population with low back pain only and another with a sciatica only population. Two

studies compared imaging (X-ray) to no imaging, one compared MRI only to no imaging or deferred imaging and another compared X-ray and MRI or CT separately, to no imaging or deferred imaging. One study compared MRI to no imaging and to deferred MRI separately.

- One economic evaluation relating to imaging versus no imaging has been included in this review.

Table 6 – Clinical effectiveness of imaging by outcome according to the population and the comparator

Imaging versus no imaging for mixed population (LBP with or without sciatica)		
Outcome	Short term <4mo	Long term 4mo-1y
QoL	**CIB favouring X-ray** for SF-36 (general health perception, vitality, social functioning, mental health, emotional functioning) and in the EQ-5D (1 RCT, low to very low quality, n=153) No diff. after X-ray for QoL (1 cohort study, very low quality; n=506)	**CIB favouring X-ray or MRI or CT** for SF-36 (bodily pain, physical functioning, vitality, role-physical functioning, emotional functioning) (2 RCTs, low to very low quality, n=935) and in the EQ-5D (1 RCT, very low quality, n=782) No diff. after X-ray for QoL (1 cohort study, very low quality, n=506)
Pain		No diff. after MRI or CT for pain severity (1 RCT, very low quality, n=782).
Function	No diff. after X-ray (1 RCT and 1 cohort study, low to very low quality; n=153 and 506 respectively)	No diff. after X-ray (1 RCT and 1 cohort study, low to very low quality; n=153 and 506 respectively)
Psychological distress	No diff. after X-ray (1 RCT and 1 cohort study, low to very low quality; n=153 and 506 respectively)	No diff. after X-ray (1 RCT and 1 cohort study, low to very low quality; n=153 and 506 respectively)
Healthcare utilisation outcomes	No diff. after X-ray (1 or 2 RCTs, low to very low quality; n=153 and 421) **CIB favouring no imaging** compared to either X-ray or MRI or CT (2 cohort studies; very low quality; n=506 and 3022).	No diff or **CIB favouring no imaging** (3 RCTs; 2 comparing X-ray to no imaging, 1 comparing MRI to no imaging, low to very low quality, range of n=153-782) and 2 observational studies, 1 comparing X-ray to no imaging, 1 comparing MRI to no imaging, very low quality, n=506 and 3022).
Imaging versus no imaging or deferred imaging for mixed population (LBP with or without sciatica)		
Outcome	Short term <4mo	Long term 4mo-1y
QoL	No diff. after X-ray, MRI or CT for EQ-5D (1 cohort, very low quality, n=5239).	No diff. after X-ray, MRI or CT for EQ-5D (1 cohort, very low quality, n=5239).
Pain	No diff. after X-ray, MRI or CT (1 cohort, very low quality, n=5239).	No diff. after X-ray, MRI or CT (1 cohort study, very low quality, n=5239).
Function	No diff. after X-ray, MRI or CT (1 cohort, very low quality, n=5239).	No diff. after X-ray, MRI or CT (1 cohort study, very low quality, n=5239).
Healthcare utilisation outcomes		Less in the groups that did not receive imaging (1 cohort study, very low quality; n=1770).

Imaging versus deferred imaging for mixed population (LBP with or without sciatica)		
Outcome	Short term <4mo	Long term 4mo-1y
Healthcare utilisation outcomes	**CIB of deferred MRI** (41-180 days post-onset) compared to early MRI (within the first 30 days post- onset) (a single cohort study, very low quality, n=3022). No clinical difference between imaging and deferred imaging in healthcare utilisation of injections ((a single cohort study, very low quality, n=3022).	**CIB of deferred MRI** (41-180 days post-onset) compared to early MRI (within the first 30 days post- onset) (a single cohort study, very low quality, n=3022). No clinical difference between imaging and deferred imaging in healthcare utilisation of nerve testing (a single cohort study, very low quality, n=3022).
Imaging versus no imaging or deferred imaging for LBP patients without sciatica		
Outcome	Short term <4mo	Long term 4mo-1y
QoL		**CIB favouring no imaging or deferred** MRI (after 6 weeks of injury) compared to MRI (within 6 weeks of injury) for SF-36 physical functioning and role-physical (1 cohort study, very low quality, n=1226)
Pain		No diff between MRI and no imaging or deferred MRI in pain severity (1 cohort study, very low quality, n=1226)
Function		**CIB favouring no imaging or deferred** MRI (after 6 weeks of injury) compared to MRI (within 6 weeks of injury) (1 cohort study, very low quality, n=1226)
Imaging versus no imaging or deferred imaging for sciatica		
Outcome	Short term <4mo	Long term 4mo-1y
QoL		**CIB favouring no MRI or deferred MRI** (after 6 weeks of injury) compared to MRI (within 6 weeks of injury) for SF-36 physical functioning and role-physical (1 cohort study, very low quality, n=1226).
Pain		No diff between no MRI or deferred MRI (after 6 weeks of injury) compared to MRI (within 6 weeks of injury) in pain severity. (1 cohort study, very low quality, n=1226).
Function		**CIB favouring no MRI or deferred MRI** (after 6 weeks of injury) compared to MRI (within 6 weeks of injury) (1 cohort study, very low quality, n=1226).

CIB: clinically important benefit

Conclusion regarding the literature review: No clear evidence favouring imaging (compared to no imaging or deferred imaging) was found in people with low back pain or radicular pain. In terms of healthcare utilization, no clinical difference or a clinical benefit favouring no imaging or deferred imaging was shown compared to imaging within the first 30 days (very low quality evidence)

Economic evaluation

- One cost-utility analysis found that **early imaging is cost effective compared to delayed, selective imaging** (ICER: £1,527 per QALY gained). This analysis was assessed as partially applicable with potentially serious limitations.

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:** The GDG agreed that health-related quality of life, pain severity, function and psychological distress were the outcomes that were critical for decision making. Responder criteria (for pain and function), adverse events and healthcare utilisation were also considered as important but there was no evidence for adverse events or responder criteria for any of the comparisons.
- **Trade-off between clinical benefits and harms: several issues were mentioned by the GDG**
  - For most of the comparisons, there was limited evidence from a small number of studies.
  - A considerable amount of evidence came from cohort studies (difficulty in determining cause and effect in interpreting outcomes.)
  - Further limitations are: the available evidence could be outdated, as x-rays were the imaging modality studied in most papers, rather than MRI. One RCT used bed rest as concomitant treatment to imaging.
  - The evidence from 3 studies would not necessarily be applicable to the UK healthcare setting where data relating to quality of life and healthcare utilisation were collected from US settings of care (eg workers' complaints registers).
  - Most of the evidence in favour of imaging was obtained from a single RCT performed in a secondary care setting (maybe to not be generalised to all patients with low back pain and/or sciatica). This was contrary to the evidence from cohort studies which reported imaging to have no clinical benefit over no imaging.
  - It was considered that primary care clinicians might be less likely to be experts in musculoskeletal evaluation compared to clinicians within specialist settings of care and as such, have a greater degree of diagnostic uncertainty.
  - The GDG agreed that imaging should be performed based on clinical appropriateness. It was discussed that imaging is often unable to confirm or refute a provisional diagnosis and that many of the imaging findings some would associate with low back pain causation (for example; disc and joint degeneration) are frequently found in asymptomatic individuals. In view of the limited and conflicting evidence, the GDG agreed that imaging should only be carried out where it was likely to change future management of the condition (for example if epidural or spinal surgery was being considered), and not in response to diagnostic uncertainty.
  - In instances where imaging was not likely to change management, it was considered that people might accept the decision not to image more readily from expert specialist clinicians. The GDG noted that people often seek imaging for reassurance, as they lack confidence in a clinical diagnosis. However, on the basis of the clinical and cost-effectiveness evidence reviewed, the GDG discussed that imaging in this circumstance would not be appropriate.
  - The GDG were concerned that the recommendation that imaging should only be performed in specialist settings of care could lead to referrals with the expectation that imaging would be performed. The GDG therefore advised that health professionals should make it clear that if they are to refer to a specialist service, they do so primarily for a clinical opinion and not necessarily for imaging.
- **Trade-off between net clinical effects and costs:** The GDG discussed the opportunity cost of providing imaging with MRI to people with low back pain, which could result in a longer wait for imaging or treatments for other conditions. They also discussed the cause for the higher QALY gain in the imaging arm of the included economic study and concluded that this could be the alteration in management following from the imaging test. The population of this study was also discussed; the fact that this was people in a secondary care setting was considered important as the results may be different for people presenting in a primary care setting. For these reasons the GDG considered imaging unlikely to be cost effective in a primary care setting, while it could be cost effective in those cases where imaging in specialist settings of care could lead to a change in management.
- **Quality of evidence:** ranged from a GRADE rating of low to very low for the majority of the evidence due to the high number of drop outs or crossover of participants from each group resulting in a high risk of bias rating, as well as the imprecise nature of the results extracted and analysed.
- **Other considerations:**

- The GDG discussed which people with low back pain should be imaged. The presence of symptoms or signs suggestive of possible serious underlying pathology (red flags), including a past history of cancer or trauma may warrant early imaging, however it is beyond the scope of this guideline to review the use of imaging for these conditions.
- The GDG noted that when imaging is requested from primary care, it is often for x-ray. However, the GDG discussed that MRI is more likely to change management than x-rays. Thus they debated in which setting (i.e. primary care or secondary care) and for what reason (e.g. diagnosis or treatment pathway) should imaging be delivered to people with non-specific back pain and agreed it should be in a specialist setting only.
- The GDG agreed on the importance of considering alternative diagnoses when examining and reviewing people with low back pain or sciatica. Similarly, the GDG recognised that new or changed signs and symptoms could suggest alternative diagnoses and may be an indication of possible serious underlying pathology. They discussed that health professionals should make people aware that they should seek further advice if people developed new or changed symptoms, and agreed to make a consensus recommendation in this regard.

NICE draft recommendations on imaging (March 2016): Four clinical recommendations

2. Do not routinely offer imaging in a non-specialist setting for low back pain with or without sciatica.
3. Explain to people with low back pain with or without sciatica that if they are being referred for a specialist opinion, they may not need imaging.
4. Consider imaging in a specialist care setting for people with low back pain with or without sciatica only if the result is likely to change management.
5. Consider alternative diagnoses when examining or reviewing people with non-specific low back pain, particularly if they develop new or changed symptoms.

Belgian GDG considerations mentioned in the Lime survey at the beginning of June 2016

NICE draft recommendation 2. Do not routinely offer imaging in a non-specialist setting for low back pain with or without sciatica

Agreement with the content of the NICE draft recommendation 2: 18 Yes, 0 No, 0 no opinion, 0 out of competence, 0 no answer, 1 not completed

- **Comments:**
  - Add: "offer imaging if "red flags" suggesting specific LBP?
    Potential harmfulness of early imaging has been reported: http://www.ncbi.nlm.nih.gov/pubmed/22415000; http://www.ncbi.nlm.nih.gov/pubmed/23883826; http://www.ncbi.nlm.nih.gov/pubmed/23484834
    I would like also to emphasize the fact that the interpretation of the results are very important! One need to consider the frequent degenerative changes also observed in asymptomatic people: http://www.ncbi.nlm.nih.gov/pubmed/22357893
  - This recommendation should also be taken into account in a specialist setting.

Strength of the recommendation 2: According to NICE formulation, it is a weak recommendation (but presented as a strong in the Lime survey by error)

GRADE Factors	
Balance between desirable and undesirable effects	Positive results in favour of imaging in second care setting (in US), not confirmed by cohort study in primary care in UK
Quality of evidence	Low to very low, small number of studies (RCTs and cohort study)
Values and preferences	Need of reassurance leading to expectation of imaging by patients (and physicians)
Costs (resource allocation)	Imaging unlikely to be cost-effective in primary care according to NICE 2016

Agreement with the strength of the NICE draft recommendation 2: 16 strong, 2 weak, 0 no opinion, 0 no answer, 1 not completed

- **Comments for a strong recommendation**
  - All the guidelines agree that imaging should not be done systematically. It is even more evident in primary care.
  - It can be used as a quality indicator.
  - Reduce costs and balance between clinical benefits and harms
  - When there are no red flags, imaging is not to be done before 6 weeks
  - Since most cases of low back pain with or without sciatica will be either non-specific or a non-complicated radiculopathy, imaging shouldn't be offered routinely neither in primary nor in specialist care.
  - 1/ cost effectiveness
  - There is ample evidence for the inability of imaging to identify the cause of the pain. Studies show that imaging has no consequence on treatment decisions.
- **No comments for a weak recommendation**

NICE draft recommendation 3. Explain to people with low back pain with or without sciatica that if they are being referred for a specialist opinion, they may not need imaging.

Agreement with the content of the NICE draft recommendation 3: 17 Yes, 1 No, 0 no opinion, 0 out of competence, 0 no answer, 1 not completed

- **Comments from the one respondent who does not agree:**
  - If the patient is referred to a specialist, it means that the problem is severe or has started several weeks ago. In these situations, I would be in favour of performing an imaging study.
- **Other comments:**
  - It's indeed relevant to change some expectations of the patients and change potential misbeliefs by explaining them (if necessary) why imaging is not useful in their case
  - The specialist is best placed to decide which investigation has or does not has to be done
  - As I mentioned in my previous comment, also in a specialist setting imaging should not be routinely offered.

Strength of the recommendation 3: According to NICE formulation, it is a strong recommendation (same table as above)

Agreement with the strength of the NICE draft recommendation 3: 11 strong, 4 weak, 2 no opinion, 0 no answer, 2 not completed

- **Comments for a strong recommendation**
  - Reduce costs and quality of evidence
  - See above (Since most cases of low back pain with or without sciatica will be either non-specific or a non-complicated radiculopathy, imaging shouldn't be offered routinely neither in primary nor in specialist care.
  - Values and preferences
  - I completely agree with the discussion of the NICE GDG
- **Comments for a weak recommendation**
  - Very logical, but not needed in most patients as they don't ask for this.

NICE draft recommendation 4. Consider imaging in a specialist care setting for people with low back pain with or without sciatica only if the result is likely to change management.

Agreement with the content of the NICE draft recommendation 4: 17 Yes, 0 No, 0 no opinion, 0 out of competence, 1 no answer, 1 not completed

- **Comments:**
  - Imaging can help in making a differential diagnose between, disc pathology, facetartrosis, radicular compression, etc.

- I am not convinced that deciding on imaging should only be reserved for a specialist setting.
- There is no use to make imaging if it has no impact on management. Moreover, unnecessary imaging may generate anxiety if benign findings are interpreted by the patient (or the clinician) as indicating a serious pathology.

Strength of the recommendation 4: According to NICE formulation, it is a weak recommendation (same table as above)

Agreement with the strength of the NICE draft recommendation 4: 11 strong, 4 weak, 1 no opinion, 1 no answer, 2 not completed

- **Comments for a weak recommendation**
  - Lack of evidence
- **Comments for a strong recommendation**
  - Very logical.
  - Balance between clinical benefits and harms
  - From a clinical and cost effective perspective it's obvious that imaging should only be performed if it's likely to change management and/or outcome.

NICE draft recommendation 5. Consider alternative diagnoses when examining or reviewing people with non-specific low back pain, particularly if they develop new or changed symptoms.

Agreement with the content of the NICE draft recommendation 5: 15 Yes, 0 No, 2 no opinion, 0 out of competence, 1 no answer, 1 not completed

- **Comments:**
  - The Dutch translation in not totally correct! I have no comments on the English version.

Strength of the recommendation 5: According to NICE formulation, it is a weak recommendation

Agreement with the strength of the NICE draft recommendation 5: 8 strong, 4 weak, 1 no opinion, 3 no answer, 3 not completed

- **Comments for a weak recommendation**
  - This is medicine.
- **Comments for a strong recommendation**
  - It is always important to consider an alternative diagnosis when reviewing and re-examining patients with low back pain, especially when they have new or changed symptoms. But this should be done by a thorough history taking and clinical examination looking for signs and or symptoms of specific or serious underlying pathology and not by imaging. Technical investigations (imaging...) will only be necessary if there is a suspicion on specific or serious pathology.

Belgian GDG comments during the GDG meeting on the 29th June 2016

The GDG stressed the contextual difference between the UK and the Belgian healthcare system. In Belgium, the general practitioners are not gate-keepers and patients can have a direct access to specialist setting. This led the GDG to propose minor changes in the wording of the first three NICE recommendations on imaging.

NICE draft recommendation 2: "Do not routinely offer imaging in a non-specialist setting for low back pain with or without sciatica"

- The GDG proposed to delete the words "in a non-specialist setting" because in Belgium, specialized physician can be the first clinician consulted by a patient with a first episode of low back pain.
- The word « routinely » should be highlighted.
- Because the duration of the complaint could define the management, it was proposed to add the notion of immediately (or « d'emblée » in French). It is mainly important if there is a long waiting time before having access to the specialist.
- There was no discussion on the strength of the recommendation.

NICE draft recommendation 3: "Explain to people with low back pain with or without sciatica that if they are being referred for a specialist opinion, they may not need imaging.

- The GDG emphasised the utility of this recommendation. It is a support for the specialist who loses time to convince patients that they do not need an imaging. According to many patients, a physician who does not prescribe an imaging is not a "good" physician.
- Because this recommendation could also support the general practitioner in the same situation, the recommendation should not focus on specialist setting only.
- However, if the word « specialist » is deleted, there is a risk that one believes that specialists are not concerned by the recommendation. The GDG proposed to add "even" in front of "if they are being referred for a specialist opinion".
- There was no discussion on the strength of the recommendation**.**

NICE draft recommendation 4: "Consider imaging in a specialist care setting for people with low back pain with or without sciatica only if the result is likely to change management."

- For the same reason as above, the GDG proposed to delete the terms "in a specialist care setting".
- The Belgian GDG proposed to be stronger and to emphasise the condition allowing an imaging because:
  - The cost of imaging
  - The risk of cumulative medical radiation
  - The known overuse of imaging in Belgium: medical radiation exposure is particularly high in Belgium compared with other European countries (KCE report 2015 on performance of the Belgian healthcare system: https://kce.fgov.be/sites/default/files/page_documents/KCE_259C_performancereport2015.pdf)
  - The fact that imaging can be iatrogenic, favouring patients' misbeliefs.
- One expert commented the sentence "imaging can help in making a differential diagnose between, disc pathology, facetartrosis, radicular compression, etc." and reminded this kind of degenerative changes are also found in asymptomatic people.

NICE draft recommendation 5. "Consider alternative diagnoses when examining or reviewing people with non-specific low back pain, particularly if they develop new or changed symptoms."

- The GDG was not in favour to link this recommendation with imaging and proposed to place it in the chapter clinical examination.
- The recommendation should be strong because it is a part of clinical vigilance, it is common sense.

⇨ **The NICE recommendations 2, 3 & 4 are accepted with minor changes**

2. "Do not immediately and routinely offer imaging for low back pain with or without sciatica."

3. "Explain to people with low back pain with or without sciatica that, even if they are being referred for a specialist opinion, they may not need imaging."

4. "Only prescribe imaging for people with low back pain (with or without sciatica) if its (expected) result may lead to change management."

⇨ The NICE recommendation 5 is accepted but will be placed in the clinical examination chapter:

5. Seek alternative diagnoses when examining or reviewing people with non-specific low back pain, particularly if they develop new or changed symptoms**."**

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30th November 2016)

Importance of the 'red flag' signs and need for urgent imaging (usually MRI)

- Spine intervention society: There are recommendations based on risk stratification regarding the likelihood of underlying systemic disease as the cause of the patient's back or limb pain. This stratification is based on signs, symptoms, and historical features (red flag features) which identify risk of neoplasm, infection, traumatic injury or inflammatory spondyloarthropathy. (See the American College of Radiology, American Pain Society, and American College of Physicians recommendations for the use of imaging in spine pain patients). The draft guideline acknowledges this (page 150) but chooses to purposely avoid the discussion. This is a disservice to the reading

physicians not to provide this established guidance from the literature. **NICE reply**: The red flag features are outside of the scope of the guideline. This is now detailed within the algorithm for clarity. The recommendation for imaging relates specifically for its use in people with suspected non-specific low back pain and sciatica, once these aforementioned conditions have been excluded. (p80/111) This has been highlighted in section 7.1, lines 24-26 on page 116 (Full guideline- Assessment and non-invasive). Furthermore, section 7.6, 'Other consideration' box states that 'the presence of symptoms or signs suggestive of possible serious underlying pathology (red flags), including a past history of cancer or trauma may warrant early imaging. (p13/222) Reference to common red flags was included in the introduction of the guideline and a list of these taken from NICE Referral Advice: A guide to appropriate referral from general to specialist services in appendix P. (p37/111)

Need for a diagnosis

- Faculty of Pain Medicine: There is confusion over a general theme to avoid imaging, and a clear need to establish a diagnosis (and obtain any diagnosis or perform any intervention safely). **NICE reply:** The recommendation on imaging states that imaging should not be routinely offered in a non-specialist setting for low back pain with or without sciatica, but should be considered in a specialist setting of care if the result is likely to change management. Please see section 7.6 (Recommendations and link to evidence) for more details. (p43/111)
- Medtronic: Appropriate imaging is required to attribute a diagnosis of specific versus non-specific low back pain (before disc replacement). **NICE reply**: The importance of assessing an individual's signs and symptoms when considering the appropriate form of imaging has been highlighted in section 7.1, lines 24-26 on page 116 (Full guideline- Assessment and non-invasive). Furthermore, section 7.6, 'Other consideration' box states that 'the presence of symptoms or signs suggestive of possible serious underlying pathology (red flags), including a past history of cancer or trauma may warrant early imaging'. However guidance on assessment of such underlying pathology is beyond the scope of this guideline. (p111/222) Medtronic: Same remarks for the algorithm. **NICE reply**: The suspected underlying pathology that require further investigation and management have been added to the algorithm for clarity(p57/111)
- Medtronic: Imaging is for example required to diagnose conditions such as spondylolisthesis and spondylosis and thereby identify patients who are excluded from the scope of this guideline. **NICE reply**: Imaging may be used to identify some of these conditions, however their diagnosis and management is not directly covered by this guideline, and they remain out of scope. The review on imaging within the guideline focussed only on whether imaging improved functional disability, pain or psychological distress in people with non-specific low back pain or sciatica, not its use as a diagnostic tool. (p7/222)
- Guy's and St. Thomas NHS Foundation Trust: A barrier to reducing imaging for patients with non specific LBP is their need to seek a tissue based diagnosis. A cultural shift is needed (p201/222)**. NICE reply:** Your comments will be considered by NICE where relevant support activity is being planned.
- Society of British Neurological Surgeons**:** Some recommendation on when to use imaging would be useful (like pain severity, duration, effect on life etc).Usefulness of recommendations on when to use imaging (like pain severity, duration, effect on life etc). **NICE reply:** The aim of the review was to establish clinical and cost effectiveness of imaging in people with low back pain or sciatica. It is recommended that imaging is not routinely offered in a non-specialist setting, and it is considered in a specialist setting of care if the result is likely to change management. The identification of which subgroup of patients would benefit more from the use of imaging was beyond the scope of the review.(p183/222)

Setting in which imaging should be considered

- Society for Back Pain Research: The setting in which imaging should be considered needs more clarity. In the UK diagnostics are often arranged/commissioned from primary care/interface musculoskeletal services**.** There are risks of substantial cost implications if all diagnostics required secondary care referral as this would attract a tariff for a secondary care consultation and a tariff for the diagnostic. The evidence indicates that it is not cost effective for general clinicians to arrange diagnostics. However, it would be helpful if the GDG could offer a definition of a "specialist setting". Even if specialist clinicians may have less diagnostic uncertainty, in the UK specialist clinicians increasing use diagnostics for defensive medicine (rising litigation). Hence none can assume that the use of diagnostics will be lower. It would be helpful if the focus of the recommendation was WHEN to do imaging. **NICE reply:** This has been discussed further with the GDG and the imaging recommendation has been edited to read; for example, a musculoskeletal interface clinic or hospital to clarify the recommendation. The objective of the review was to determine the clinical and cost effectiveness of imaging techniques in the management of non-specific low back pain and sciatica. Analysing the timing of imaging was beyond the scope of the review. (p67/111)

- Medtronic: **Restricted appropriate access for Primary Care** (MSK/ESP) triage services that require access to imaging to ascertain the specific mechanical spinal pathology and facilitate appropriate referral to respective specialist MDT. **NICE reply**: The definition of 'specialist setting of care' has been detailed in the recommendation for clarity as 'for example, a musculoskeletal interface clinic or hospital'.(p15/222)
- Society of British Neurological Surgeons**: Risk of waiting time for referral:** The recommendation that imaging should be decided by a specialist will result in a huge increase in the number of referrals to spinal surgery units. This will potentially delay the 18 week pathway to the extent that NHS targets will be adversely affected. It is suggested to include a protocols of referral to a specialist from Primary care and Physiotherapy/Allied therapists and a minimum time period before referral is considered unless clinical features dictate urgency. **NICE reply**: The objective of the review was to determine the clinical and cost effectiveness of imaging techniques in the management of non-specific low back pain and sciatica. Therefore, reviewing the timing of imaging was beyond the scope of the review. (p13/222)
- United Chiropractic Association: As chiropractors are specialists in primary contact with NMSK patients, the clinical skill and rationale for imaging referral/ procurement is well within the scope of practice. Imaging is an integral part of the precision of due diligence in the assessment and patients presenting with NSLBP and Sciatica. We are concerned that this recommendation may cause unnecessary delays to the timely, thorough and accurate assessment. **NICE reply:** Most of the evidence supporting the use of imaging in the review came from a single RCT performed in a secondary setting of care. The GDG considered that the level of diagnostic uncertainty in specialist settings is likely to be lower, therefore they agreed that imaging should not be carried out in primary care but in specialist settings of care only, for example, a musculoskeletal interface clinic or hospital.(p187/222)
- Medtronic: Further criteria are needed to guide selection of people in whom the result of imaging is likely to change management**. NICE reply: T**hese criteria are lacking in the guideline but beyond the scope of this review according to NICE. (p57/111)
- Warwick Clinical Trials Unit: One could perhaps be a bit more specific, such that there is a distinction made between imaging for back pain and sciatica in non-specialist setting**.** e.g. 1. Do not offer imaging in non-specialist setting for low back pain**,** 2. Consider imaging in a non-specialist setting for low back pain with sciatica after failed conservative treatment only when special referral is being considered. The point is that in some cases onward referral can be avoided if radiological changes are not congruent with symptoms. **NICE reply**: The GDG reviewed the evidence and found that it was the same for both populations. Recommendations 2 and 4 apply to people with low back pain with or without sciatica.(p98/111)
- Spine Intervention Society: The guideline states, "explain to people with low back pain with or without sciatica that if they are being referred for a specialist opinion, they may not need imaging" but at the same time suggests to "consider imaging in a specialist care setting for people with low back pain with or without sciatica only if the result is likely to change management". This approach may produce negative patient bias towards specialists**. NICE reply:** The GDG were concerned that people being referred to a specialist would expect imaging to be performed. The GDG therefore advised that the primary aim of a referral to a specialist service would be a clinical opinion and not necessarily imaging and agreed it was important to state this within a recommendation. However, they further agreed that the situations under which imaging might be considered should be clarified. The GDG do not agree that this would negatively bias towards specialists. The rational for these recommendations is discussed in more details in Section 7.6 (recommendations and link to evidence, 'trade-off between clinical benefits and harms'). (p82/111)

CT-scan/MRI

- **British Society of neuroradiologists:** CT can be used when MRI contra-indicated and when further assessment of a spondylolisthesis (bony defect) is required. **NICE reply:** The use of CT scans is detailed in the introductory paragraph above that for MRI: "CT scans are the preferred method when investigating bony pathology. With the advancement of faster and more powerful scanners, 3D reconstructions and multi-directional cuts are easier to obtain and use. This is useful for assessing trauma, deformity and planning surgery, as well as the follow-up of the treatment plans. CT scans carry high dose radiation and a simple un-contrasted CT scan of the lumbar spine equates to approximately 70 chest x-rays." (p37/111)

Patients expectation

- Chartered Society of Physiotherapy**:** This could be a challenge to implement due to patient expectations. However, we also recognise that it is the clinician responsibility to educate patients about the purpose of imaging, fully explaining why they do not feel a referral for imaging is necessary. Whilst this guideline will be helpful in supporting clinicians when explaining imaging choices to patients, we anticipate that **further resources** may be required to gain patient buy-in when imaging isn't indicated. **NICE reply**: Section 7.6 (recommendations and link to evidence, 'trade-off between clinical benefits and harms') reports the rationale for recommendation n.3. The GDG were

concerned that if imaging should only be performed in specialist settings, people being referred to a specialist would expect imaging to be performed. The GDG therefore advised that the primary aim of a referral to a specialist service would be a clinical opinion and not necessarily imaging. (p14/222)

- Homerton University Hospital NHS Foundation Trust: When patients do receive copies of their imaging reports the medical language used can elicit distress, fear and confusion. Imaging reports detailing clinically unimportant changes using potentially frightening terms such as 'degenerative' or 'tear' can be detrimental to patients recovery if not accompanied by considerable education and explanation by clinicians. Imaging reports can in this way become a risk factor for chronic pain. It would be helpful for NICE to recommend that patient information should be embedded within imaging reports, such as the % of symptom free patients in their age bracket that would be expected to present with this age related change. Patient information leaflet providing elements covered in the 'vomit poster' would be useful in helping patients accept that imaging is unnecessary and potentially counterproductive. (VOMIT (victims of modern imaging technology)—an acronym for our times BMJ 2003;326:1273). **NICE reply**: The issue of imaging reporting was not prioritised as an area to review within the scope of the guideline and NICE was therefore unable to comment on patient information in reports or the harms of interpretation of results. (p192/222)

NICE changes in the final version of the guideline (November 2016)

The change concerned only the specialist setting.

In the "Trade-off between clinical benefits and harms" chapter, a piece of sentence was added in the summary:

As the level of diagnostic uncertainty in specialist settings is likely to be lower, the GDG agreed that imaging should not be carried out in primary care but in specialist settings of care only, for example, a musculoskeletal interface clinic or hospital.

In the "Other considerations" chapter, the same piece of sentence was added:

The GDG noted that when imaging is requested from primary care, it is often for x-ray. However, the GDG discussed that MRI is more likely to change management than x-rays. Thus they debated in which setting (i.e. primary care or secondary care) and for what reason (e.g. diagnosis or treatment pathway) should imaging be delivered to people with back pain and agreed it should be in a specialist setting of care only, for example, a musculoskeletal interface clinic or hospital.

NICE final recommendations on imaging (November 2016)

3. Do not routinely offer imaging in a non-specialist setting for people with low back pain with or without sciatica.
4. Explain to people with low back pain with or without sciatica that if they are being referred for specialist opinion, they may not need imaging.
5. Consider imaging in specialist settings of care (for example, a musculoskeletal interface clinic or hospital) for people with low back pain with or without sciatica only if the result is likely to change management.
6. Think about alternative diagnoses when examining or reviewing people with low back pain, particularly if they develop new or changed symptoms. Exclude specific causes of low back pain, for example, cancer, infection, trauma or inflammatory disease such as spondyloarthritis. If serious underlying pathology is suspected, refer to relevant NICE guidance on:

- Metastatic spinal cord compression in adults
- Spinal injury
- Spondyloarthritis
- Suspected cancer

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

The GDG emphasised that exclusion of red flags with imaging is out of scope of this guideline and asked to insert this warning within the recommendation with the word "in absence of red flags"

KCE 2017 final recommendations on imaging (February 2017)

2. In the absence of red flags, do not routinely offer imaging for people with low back pain with or without radicular pain. Only prescribe imaging if its expected result may lead to change management, e.g. when an invasive intervention is being considered.

(weak recommendation based on low to very low quality evidence from RCTS and cohort studies)

5. Explain to people with low back pain with or without radicular pain that they may not need imaging, even if they are being referred for a specialist opinion.

(consensus-based experts opinion)

7.4. Self-management

Self-management in patients with low back pain ± radicular pain

NICE search question

"What is the clinical and cost-effectiveness of self-management in the management of non-specific low back pain and sciatica?"

Introduction based on the draft version of NICE guideline (March 2016)

- The lack of a clear definition of non-specific low back pain can produce increasing confusion, distress and, for many people, may result in an inability to adopt positive coping strategies. This can quickly result in vicious cycles of physical deconditioning, low mood, withdrawal from normal activity and, increased anxiety.
- Given these factors, the management of chronic non-specific low back pain can be placed largely outside the scope of a biomedical approach, into the unknown territory of self-management and counter-intuitive ideas such as 'living well' with a long-term health condition. The quality of life for people in this situation depends less on interventions from health professionals and more on the ability of the person to undertake self-management.
- The concept of self-management encompassed different approaches: self-management programmes including patient education, reassurance, such as the Back Book; self-management consisting on advice to stay active; self-management consisting on bed rest; and self-management consisting on unsupervised exercises. Two sections are presented: Self-management as single intervention and combination of interventions (self-management adjunct).

PICO used by NICE (March 2016)

Population	• People aged 16 or above with non-specific low back pain • People aged 16 or above with sciatica
Intervention(s)	• Self-management programmes (including patient education and reassurance for example, the Back Book) • Advice to stay active • Advice to bed rest • Unsupervised exercise (including exercise prescription, advice to exercise at home)
Comparison(s)	• Placebo/Sham/Attention control • Usual care/waiting list • To each other • Any other non-invasive interventions in the guideline

	• Combination of interventions: any combination of the non-invasive interventions in the guideline
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (> 30% improvement in pain or function) • Adverse events: morbidity • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

28 RCTs on single interventions, 7 RCTs on combined interventions.

NEW: Five Cochrane reviews on self-management were identified but could not be included due to methodological flaws. The included studies were individually assessed and included if they matched the review protocol.

Self-management as single intervention: self- management programmes (including patient education, advice, reassurance, exercise prescription)

- **Self-management programmes (education, advice, reassurance) versus usual care**
  - **Patients with LBP without sciatica:** no studies found
  - **Patients with LBP with sciatica:** no studies found
  - **Mixed population (LBP with or without sciatica)**
    - QoL (SF-36): a clinically important benefit for physical (1 RCT; low quality; n=49) and mental composites (1 RCT; very low quality; n=49) at the short term. At long term (> 4 months) a benefit of self-management compared to usual care for the well-being domain (1 RCT; moderate quality; n=80) and general health domain (1 RCT; low quality; n=80), but not for the energy domain of the SF-36 (1 RCT; low quality; n=80).
    - Pain (VAS, modified von Korff pain scale): no clinical differences at short term (VAS; very low quality; 2 RCTs; n=106) nor at long term (modified von Korff pain scale; moderate quality; 1 RCT; n=101).
    - Function (modified von Korff, number not working, RMDQ): no clinical benefit in function measured by different scores at short term (RMDQ; very low quality; 2 RCTs; n=106) and at long term (RMDQ; low quality; 1 RCT; n=421; modified von Korff; low quality; 1 RCT; n=101; number not working; very low quality; 1 RCT; n=419)
    - Responder criteria (>30% improvement in pain): no clinical differences at short term (low quality; 1 RCT; n=122) and at long term (low quality; 1 RCT; n=113).
    - Healthcare utilisation: a clinically important benefit at long term for number of consultations for back pain (very low quality; 4 RCTs; n= 1304), number of hospitalisations (very low quality; 1 RCT; n=936), number of physicians' visits for back pain (low quality; 1 RCT; n=421), number of physical therapist' visits for back pain (low quality; 1 RCT; n=421) and number of hospital days (low quality; 1 RCT; n=421). However, no difference could be found in number of chiropractor's visits for back pain (low quality; 1 RCT; n=421). No short term data were reported.
    - Not reported outcomes: psychological distress, adverse events
- **Self-management (education, advice and reassurance) versus sham (sham advice sessions)**
  - **Patients with LBP without sciatica:** no studies found
  - **Patients with LBP and sciatica**: no studies found

- **Mixed population (LBP with or without sciatica)**:
  - Pain (VAS): no differences at short term (low quality; 1 RCT; n=131) and long term (low quality; 1 RCT; n=131).
  - Function (RMDQ): no differences at short term (moderate quality; 1 RCT; n=131) and long term (moderate quality; 1 RCT; n=131).
  - Not reported outcomes: Psychological distress: not reported
  - Not reported outcomes: QoL, adverse events, responder criteria, healthcare utilisation

- **Self-management programme (education, advice, reassurance and exercise prescription) versus bed rest**
  - **Patients with LBP without sciatica**: no studies found
  - **Patients with LBP and sciatica**: no studies found
  - **Mixed population (LBP with or without sciatica)**: no differences in responder criteria (>30% improvement in pain) at short term (moderate quality; 1 RCT; n=119) and long term (very low quality; 1 RCT; n=112). The other outcomes (QoL, pain, function, psychological distress, adverse events and healthcare utilisation) were not reported.
- **Self-management programme versus other non-invasive interventions (exercise, acupuncture, massage, yoga)**
  - **Patients with LBP without sciatica**:
    - Self-management programme (education, advice and reassurance) versus (biomechanical and aerobic) exercise : no clinical difference for function (RMDQ; 1 RCT; low quality; n=180) at short term. No long term data for function was reported. Both responder criteria (>50% improvement in RMDQ at short term) (1 RCT; low quality; n=60) and healthcare utilisation (medication use at long term) (1 RCT; very low quality; n=61) showed **clinical important benefits in favour of exercise**. The other outcomes (QoL, pain, psychological distress, adverse events) were not reported.
    - Self-management programme (education, advice and reassurance) versus massage: **a clinical benefit for function in favour of massage** was seen at short term (RMDQ; 1 RCT; very low quality; n= 160), but not at long term (RMDQ; 1 RCT; low quality; n= 159). Also a **clinical benefit was seen in favour of massage for healthcare utilisation**: number of providers' visits at long term (1 RCT; low quality; n= 159) and number of low back pain medication fills at long term (1 RCT; low quality; n= 159). The other outcomes (pain, QoL, psychological distress, adverse events) were not reported.
    - Self-management programme (education, advice and reassurance) versus yoga: both responder criteria (>50% improvement in RMDQ at short term) (1 RCT; moderate quality; n=66) and healthcare utilisation (medication use at long term) (1 RCT; moderate quality; n=63) showed **clinical important benefits in favour of yoga**. The other outcomes (QoL, pain, function, psychological distress, adverse events) were not reported.
    - Self-management programme (education, advice and reassurance) versus acupuncture: no clinical difference for function at both short term (RMDQ; 1 RCT; very low quality; n= 172) and long term (RMDQ; 1 RCT; very low quality; n= 173). Also no clinical difference was seen for healthcare utilisation: number of providers' visits at long term (1 RCT; low quality; n= 173) and number of low back pain medication fills at long term (1 RCT; low quality; n= 173). The other outcomes (pain, QoL, psychological distress, responder criteria, and adverse events) were not reported.
    - Self-management programme (education, exercise prescription) versus mobilisation + electrotherapy: no clinical difference in function (improvement in ODI) both at short term (1 RCT; low quality; n=68) and long term (1 RCT; low quality; n=64). Also no clinical difference was found in healthcare utilisation (number of visits to healthcare centres at long term) (1 RCT; low quality; n=64). The other outcomes (QoL, pain, psychological distress, responder criteria, adverse events) were not reported.
    - Self-management programme (education, exercise prescription) versus manual therapy (mobilisation): no clinical difference in function (improvement in ODI) both at short term (1 RCT; low quality; n=78) and long term (1 RCT; low quality; n=76). Also no clinical difference was found in healthcare utilisation (number of visits to healthcare centres at long term) (1 RCT; low quality; n=76). The other outcomes (QoL, pain, psychological distress, adverse events) were not reported.
  - **Patients with LBP and sciatica**:
    - Self-management programme (education, advice and reassurance) versus biomechanical and home exercise: no clinical difference for QoL (15-D; 1 RCT; low quality; n=83), function (ODI; 1 RCT; low quality; n=83) in both short and long term and for pain (VAS; 1 RCT; low quality; n=83) in short term. **Only at long term a clinical benefit for pain in favour of self-management** was found (1 RCT; low quality; n=83). The other outcomes (psychological distress, adverse events, responder criteria, and healthcare utilisation) were not reported.
  - **Mixed population (LBP with or without sciatica)**:

- Self-management programme (bed rest + education, exercise prescription) versus usual care: no clinical difference for responder criteria (no pain) at short term (1 RCT; low quality; n=123) and long term (1 RCT; very low quality; n=114). The other outcomes (QoL, pain, function, psychological distress, adverse events, and healthcare utilisation) were not reported.
- Self-management programme (bed rest + education, exercise prescription) versus bed rest: no clinical difference for responder criteria (no pain) at short term (1 RCT; moderate quality; n=120) and long term (1 RCT; low quality; n=113). The other outcomes (QoL, pain, function, psychological distress, adverse events, and healthcare utilisation) were not reported.
- Self-management programme (bed rest + education, exercise prescription) versus self-management (education, exercise prescription): no clinical difference for responder criteria (no pain) at short term (1 RCT; moderate quality; n=125) and long term (1 RCT; low quality; n=119). The other outcomes (QoL, pain, function, psychological distress, adverse events, and healthcare utilisation) were not reported.

Self-management as single intervention: advice to stay active

- **Advice to stay active versus bed rest**
  - **Patients with LBP without sciatica:** a clinical benefit of bed rest over advice to stay active was seen in responder criteria (number of days to full activity at short term) (very low quality; 1 RCT; n=80). The other outcomes (QoL, pain, function, psychological distress, adverse events and healthcare utilisation) were not reported.
  - **Patients with LBP and sciatica**: no studies found
  - **Mixed population (LBP with or without sciatica)**: A clinical benefit for function (RMDQ) was seen in favour of advice to stay active at short term (1 RCT; very low quality; n=34). The other outcomes (QoL, pain, psychological distress, adverse events, responder criteria and healthcare utilisation) were not reported.

Self-management as single intervention: bed rest

- **Bed rest versus usual care**
  - **Patients with LBP without sciatica:** no studies found
  - **Patients with LBP and sciatica**:
    - Pain (VAS): no clinical difference in back pain at short term (1 RCT; low quality; n= 169). However a clinical benefit was seen for leg pain in favour of usual care (1 RCT; low quality; n= 169). No long term data were reported.
    - Function (ODI): no clinical difference at short term (1 RCT; low quality; n=169). No long term data was reported.
    - Not reported outcomes: QoL, psychological distress, adverse events, responder criteria, healthcare utilisation
  - **Mixed population (LBP with or without sciatica)**:
    - Function (ODI): no clinical difference at short term (1 RCT; low quality; n=134). No long term data was reported.
    - Responder criteria (no pain): no clinical difference at short term (1 RCT; low quality; n=117) and at long term (1 RCT; very low quality; n=107).
    - Not reported outcomes: QoL, pain, psychological distress, adverse events, healthcare utilisation

Self-management as single intervention: unsupervised exercise

- **Unsupervised (home) exercise versus usual care**
  - **Patients with LBP without sciatica:**
    - QoL (SF-36): no clinical difference at long term for the physical domain (1 RCT; very low quality, n= 111) and for the mental domain (1 RCT; very low quality; n= 111). Data at short term not reported.
    - Function (RMDQ): no clinical difference at long term (1 RCT; very low quality; n=111). No short term data was reported.
    - Not reported outcomes: pain, psychological distress, adverse events, responder criteria, healthcare utilisation
  - **Patients with LBP and sciatica**: no studies found
  - **Mixed population (LBP with or without sciatica)**: no clinical difference for function (ODI) at short term (1 RCT; low quality; n= 119). No long term data reported. The other outcomes (QoL, pain, psychological distress, adverse events, responder criteria, healthcare utilisation) were not reported.
- **Unsupervised (home) exercise versus postural therapy (Alexander technique)**

- **Patients with LBP without sciatica:**
  - QoL (SF-36): clinical benefit of either 6 sessions (1 RCT) or 24 sessions (1 RCT) in favour of the Alexander technique at long term for the physical (1 RCT; low quality; n= 221) and mental domain (1 RCT; low quality; n=221). No short term data reported.
  - Pain (von Korff): no clinical difference at long term (1 RCT; low quality; n= 221). No short term data reported.
  - Function (RMDQ): no clinical difference at long term (1 RCT; low quality; n=221). No short term data reported.
  - Not reported outcomes: psychological distress, adverse events, responder criteria, healthcare utilisation
- **Patients with LBP and sciatica**: no studies found
- **Mixed population (LBP with or without sciatica)**: no studies found

- **Unsupervised (home) exercise versus (group-based biomechanical) exercise**
  - **Patients with LBP without sciatica:** no studies found
  - **Patients with LBP and sciatica**: no studies found
  - **Mixed population (LBP with or without sciatica)**:
    - Pain (VAS): a clinical benefit in favour of biomechanical exercise for back pain at short term (1 RCT; moderate quality; n=116) and long term (2 RCTs; very low quality; n=156) and for leg pain at short term (1 RCT; moderate quality; n= 116) and long term (1 RCT; moderate quality; n= 116).
    - Function (ODI): no clinical difference at short term (1 RCT; moderate quality; n=116) and long term (1 RCT; moderate quality; n= 116)
    - Responder criteria (number of pain relapses, return to work): a clinical difference in number of pain relapses at long term in favour of exercise (1 RCT; low quality; n= 40), however no difference was seen in return to work at long term (1 RCT; very low quality; n=139). No short term data was reported.
    - Not reported outcomes: QoL, psychological distress, adverse events, healthcare utilisation
- **Unsupervised (home) exercise versus massage**
  - **Patients with LBP without sciatica:**
    - QoL (SF-36): no clinical difference for the physical domain (1 RCT; low quality; n= 115) and the mental domain (1 RCT; very low quality; n= 115) at long term. No short term data was reported.
    - Pain (McGill, Von Korff): no clinical difference measured by McGill questionnaire at short term (1 RCT; very low quality; n=24) neither measured by Von Korff scale at long term (1 RCT; low quality; n= 115). Other time points were not reported.
    - Function (RMDQ): no clinical difference at long term (1 RCT; very low quality; n= 115). No short term data was reported.
    - Not reported outcomes: psychological distress, adverse events, responder criteria, healthcare utilisation
  - **Patients with LBP and sciatica**: no studies found
  - **Mixed population (LBP with or without sciatica)**: no studies found

Combination of interventions-self-management adjunct

- **Self-management in combination with active comparisons versus usual care or active comparisons**
  - **Patients with LBP without sciatica**:
    - Self-management (exercise prescription) + postural therapy (Alexander technique-**6** lessons) versus postural therapy (Alexander technique-**6** lessons): a clinical benefit for physical domain of the SF-36 (QoL) at long term (1 RCT; low quality; n=115) in favour of the combined self-management and postural therapy, however not difference could be found for the mental component (1 RCT; moderate quality; n= 115). No clinical difference was found in pain severity (Von Korff scale; 1 RCT; low quality; n= 115), function (RMDQ; 1 RCT; low quality; n=115) and healthcare utilisation (number of primary care contacts; 1 RCT; moderate quality; n= 115 and number of prescriptions; 1 RCT; moderate quality; n= 115). No short term data of the above-mentioned outcomes were reported. Other outcomes (psychological distress, adverse events, and responder criteria) were not reported.
    - Self-management (exercise prescription) + postural therapy (Alexander technique-**24** lessons) versus postural therapy (Alexander technique-**6** lessons): a clinical benefit at long term was found for QoL physical domain (SF-36; 1 RCT; low quality; n= 114), for pain severity (Von Korff scale; 1 RCT; low quality; n= 114) and for function (RMDQ; 1 RCT; low quality; n=114) in favour of the combination of self-management with 24 lessons of Alexander technique. However, no difference was found for the mental component of SF-36 (QoL; 1 RCT; moderate quality; n=114) and in healthcare utilisation

(number of primary care contacts; 1 RCT; moderate quality; n=114 and number of prescriptions; 1 RCT; moderate quality; n=114). No short term data were reported. Other outcomes (psychological distress, adverse events, and responder criteria) were not reported.

- Self-management (exercise prescription) + postural therapy (Alexander technique-**6** lessons) versus postural therapy (Alexander technique-**24** lessons): a clinical benefit at long term was found for QoL physical domain (SF-36; 1 RCT; moderate quality; n= 116) and for QoL mental domain (SF-36; 1 RCT; moderate quality; n= 118) in favour of the 24 lessons of Alexander technique. No difference was found for pain severity (Von Korff scale; 1 RCT; moderate quality; n= 118), function (RMDQ; 1 RCT; low quality; n= 118) and healthcare utilisation (number of primary care contacts; 1 RCT; moderate quality; n=118 and number of prescriptions; 1 RCT; low quality; n=118). No short term data reported. Other outcomes (psychological distress, adverse events, and responder criteria) were not reported.
- Self-management (exercise prescription) + postural therapy (Alexander technique-**24** lessons) versus postural therapy (Alexander technique-**24** lessons): Only a clinical benefit at long term was found for the physical component of the SF-36 (QoL; 1 RCT; moderate quality; n= 117) in favour of the single intervention of postural therapy (24 lessons of Alexander technique). No difference was found for the mental component of the SF-36 (QoL; 1 RCT; moderate quality; n=117), pain severity (Von Korff scale; 1 RCT; moderate quality; n= 117), function (RMDQ; 1 RCT; moderate quality; n= 117) and healthcare utilisation (number of primary care contacts; 1 RCT; low quality; n=117 and number of prescriptions; 1 RCT; low quality; n=118). No short term data reported. Other outcomes (psychological distress, adverse events, and responder criteria) were not reported.
- Self-management (exercise prescription) + postural therapy (Alexander technique-**24** lessons) versus self-management (exercise prescription) + postural therapy (Alexander technique-**6** lessons): Only a clinical benefit at long term was found for the mental component of the SF-36 (QoL; 1 RCT; low quality; n= 113) in favour of the combined intervention of self-management and postural therapy (24 lessons of Alexander technique). No difference was found for the physical component of the SF-36 (QoL; 1 RCT; moderate quality; n=113), pain severity (Von Korff scale; 1 RCT; low quality; n= 113), function (RMDQ; 1 RCT; low quality; n= 113) and healthcare utilisation (number of primary care contacts; 1 RCT; low quality; n=113 and number of prescriptions; 1 RCT; moderate quality; n=113). No short term data reported. Other outcomes (psychological distress, adverse events, and responder criteria) were not reported.
- Overall: one study (Little 2008, RCT, range n=113-118, moderate to very low quality of evidence, UK) examined the effectiveness of the combination of self-management (exercise prescription) and postural therapy (Alexander technique) in different modalities (6 or 24 lessons of postural therapy) in people with low back pain without sciatica:
  - For most of the outcomes (QoL, pain, function, healthcare utilisation) and comparisons no clinical benefit was seen, except for some small benefits in one of the domains of QoL in the combined interventions and in the interventions with 24 lessons of postural therapy.
  - Only long term data reported, other outcomes (psychological distress, adverse events, and responder criteria) were not reported.

- **Patients with LBP and sciatica**: no studies found
- **Patients with LBP with or without sciatica**:
  - Self-management (home exercise) + electrotherapy (laser) versus electrotherapy (laser): No clinical difference in pain (VAS; 2 RCTs; very low quality; n=85) and function (ODI; 2 RCTs; very low quality; n=85) at short term. No long term data reported. Other outcomes (psychological distress, adverse events, healthcare utilisation and responder criteria) were not reported.
  - Self-management (home exercise) + electrotherapy (HILT laser) versus electrotherapy (HILT laser): at short term, a clinical benefit was found for pain (VAS; 1 RCT; low quality; n=48), however no difference was found for function measured by RMDQ (1 RCT; low quality; n=48) or by MODI (1 RCT; low quality; n=48). No long term data were reported. Other outcomes (psychological distress, adverse events, healthcare utilisation and responder criteria) were not reported.
  - Self-management (education) + biomechanical exercise versus biomechanical exercise (motor control): No clinical difference in pain (VAS; 1 RCT; low quality; n=21) and function (RMDQ; 1 RCT; low quality; n=21) at short term. No long term data reported. Other outcomes (psychological distress, adverse events, healthcare utilisation and responder criteria) were not reported.
  - Overall: Conflicting evidence was found on the effect of the addition of home exercises to laser therapy: 2 studies (RCTs, very low quality, n=85) found no clinical benefit on short term pain and function, whereas another study (RCT, low quality, n=48) found a clinical benefit on short term pain (not on

function). No clinical important benefits (on pain and function) were seen in the combination of self-management and biomechanical exercises compared to biomechanical exercises alone. No long term data and other outcomes (psychological distress, adverse events, and responder criteria) were reported.

Economic evidence

One cost-utility analysis (partially applicable; potentially serious limitations) in people with low back pain without sciatica found that:

- The combination of unsupervised exercise with usual care was cost effective compared to usual care alone, independently if they received massage or Alexander technique lessons.
- Among a selection of active treatment, the combination of Alexander technique (24 lessons) with unsupervised exercise was the most effective and cost effective option

No economic evaluation were found in people with sciatica or the mixed population of people with or without sciatica.

NICE GDG considerations (March 2016)

- **Relative values of different outcomes**
  - Most critical outcome was health-related QoL with pain severity, function and psychological distress as individually critical outcomes as well as components of QoL measure.
  - Responder criteria (for pain and function), adverse events and healthcare utilisation were considered important for decision-making.
  - No evidence was available for any adverse events.
- **Trade-off between clinical benefits and harms**
  - NEW: Comparison to placebo or sham-controlled evidence should inform decision-making, but due to lack of this kind of evidence, evidence against usual care is given priority when decision making.
  - No conclusive evidence was found in favour of self-management:
    - Compared to usual care: some benefit in QoL, but not for pain and function. Healthcare utilisation was reduced by the use of self-management but this could be biased by taking part in a trial.
    - Compared to supervised activity: additional benefit of supervised activity due to contact with healthcare professional and the associated contextual effects
    - Advice to stay active versus bed rest: the beneficial effects of bed rest in days to full activity are explained by the GDG by the study characteristics (single study, specific population of combat trainees). Review showed that there was no evidence that bed rest in the short term was harmful, but also no evidence to suggest that is was beneficial to do so.
  - Although the direct evidence was far from convincing, the GDG considered that, based on evidence from combination and multidisciplinary programmes reviews, self-management plays an important role in the management of a variety of chronic conditions.
  - The GDG agreed that although there was no conclusive evidence in favour of self-management (provided in isolation), it was still important to provide advice to people about their condition and encourage them to continue with normal activities.
  - It was noted that there is no evidence from this review that a more complex intervention was any more effective than simple advice.
  - The GDG therefore felt that a good practice statement to support self-management was justified. The GDG intended self-management to apply as a principal alongside all treatment for people with low back pain and sciatica as part of routine practice.
- **Trade-off between net clinical effects and costs**
  - The economic evaluation (a within-trial cost-utility analysis) showed that adding exercise prescription component to other interventions was always more cost effective than each intervention alone.
  - The GDG considered that although the provision of advice and information to promote self-management of low back pain may incur some minimal costs, this is an essential part of good patient care to ensure patients are adequately informed.

- **Quality of evidence:**

- Ranging from very low to moderate, with serious or very serious risk of bias, small trials, difficulty of adequate blinding, lack of information on background care increasing the risk of overestimating effects.
- The GDG noted that the included studies were not optimally designed to test self-management.
- The economic evidence was assessed as partially applicable with potentially serious limitations.

- **Other considerations**
  - Existing recommendation from the previous NICE recommendation 2008 should still stand: it was agreed important for clinicians to take into account people's concerns about their back pain and sciatica, and tailor the advice to the individual.
  - Overlap with multidisciplinary biopsychosocial rehabilitation programmes
  - GDG agreement there was no evidence to suggest sciatica should be treated differently to non-specific LBP in terms of providing advice to the person with pain
  - Existing NICE guidance: PH16 Managing long term sickness and incapacity to work and CG138 patient experience in adult NHS services

NICE draft recommendations on self-management (March 2016)

6. Provide people with advice and information, tailored to their needs and capabilities, to help them self-manage their non-specific low back pain with or without sciatica, including:
   - Information on the nature of non-specific low back pain and sciatica
   - Encouragement to continue with normal activities as far as possible.

Belgian GDG considerations mentioned in the Lime survey at the beginning of June 2016

Agreement with the content of the NICE recommendation 6: 16 Yes, 0 No, 2 no opinion, 0 out of competence, 1 no answer, 4 not completed

- **Comments:**
  - Exercise/physiotherapy should indeed not routinely be recommended unless for ongoing complaints without spontaneous recovery or in case of relapse.
  - Still too often rest is prescribed during days for non-specific back pain.
  - It might not be sufficient to provide people with information on the nature of non-specific low back pain/sciatica, and to encourage them to continue with normal activities as far as possible. For instance, when kinesiophobia is present, this should be tackled explicitly. In my opinion, in (chronic) patients with kinesiophobia, it won't be sufficient to inform them that 'movement and exercise is important' when a behavioural change is pursued.

Strength of the recommendation 6: According to the NICE formulation, this is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	NEW: Comparison to placebo or sham-controlled evidence should inform decision-making, but due to lack of this kind of evidence, evidence against usual care is given priority when decision making. No conclusive evidence was found in favour of self-management: • Compared to usual care: some benefit in QoL, but not for pain and function. Healthcare utilisation was reduced by the use of self-management but this could be biased by taking part in a trial. • Compared to supervised activity: additional benefit of supervised activity due to contact with healthcare professional and the associated contextual effects • Advice to stay active versus bed rest: the beneficial effects of bed rest in days to full activity are explained by the GDG by the study characteristics (single study, specific population of combat trainees). Review showed that there was no evidence that bed rest in the short term was harmful, but also no evidence to suggest that is was beneficial to do so.

	Although the direct evidence was far from convincing, the GDG considered that, based on evidence from combination and multidisciplinary programmes reviews, self-management plays an important role in the management of a variety of chronic conditions. The GDG agreed that although there was no conclusive evidence in favour of self-management (provided in isolation), it was still important to provide advice to people about their condition and encourage them to continue with normal activities. It was noted that there is no evidence from this review that a more complex intervention was any more effective than simple advice. The GDG therefore felt that a good practice statement to support self-management was justified. The GDG intended self-management to apply as a principal alongside all treatment for people with low back pain and sciatica as part of routine practice.
Quality of evidence	The quality of the 35 RCTs ranged from very low to moderate with serious or very serious risk of bias due to small trials, difficulty of adequate blinding, and lack of information on background care increasing the risk of overestimating effects. The GDG noted that the included studies were not optimally designed to test self-management. The economic evidence was assessed as partially applicable with potentially serious limitations.
Values and preferences	Existing recommendation from previous NICE guideline on low back pain (2008) should still stand: it was agreed important for clinicians to take into account people's concerns about their back pain and sciatica, and tailor the advice to the individual Overlap with multidisciplinary biopsychosocial rehabilitation programs GDG agreement there was no evidence to suggest radicular pain should be treated differently to LBP in terms of providing advice to the person with pain Regarding the potential barriers to self-management, NICE referred to two existing NICE guidances related to this area: NICE public health guidance on managing long term sickness and incapacity to work and NICE guideline on patient experience in adult NHS services: improving the experience of care for people using adult NHS services.
Costs (resource allocation)	Addition of exercise prescription to other interventions was more cost effective than the other interventions alone. The provision of advice would not be a change of practice. Promotion of self-management may incur some minimal costs, but is an essential part of good patient care to ensure patients are adequately informed.

Agreement with the strength of the NICE draft recommendation 6: 13 strong, 2 weak, 0 no opinion, 2 no answer, 6 not completed

- **Comments for a strong recommendation**
  - The biopsychosocial approach should be formally recommended.
  - Although the rather low to moderate quality of evidence I would recommend this strongly because of the minimal cost of this intervention and the probability of reducing the risk for chronicity.
  - Costs
  - As fear-avoidance is a strong factor for chronicity, patient education and advice are compulsory
- **Comments for a weak recommendation**
  - Quality of evidence

Belgian GDG comments during the GDG meeting on the 29th June 2016

No comment

- **Conclusion: recommendation NICE 2016 unchanged**

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30 November 2016)

Definition of self-management

- Institute of Osteopathy: Self-management as defined in these recommendations is **wide reaching**. It includes self-management programmes such as education leaflets and advice with group psychological therapies. According to our researchers, this may have raised the effectiveness of 'self-management approaches' as part of the multi-modal package recommended. While manual therapy clinicians routinely provide advice and self-management strategies, the definition as used here may have raised its importance for inclusion, rather than as an adjunct to others such as manual therapy and exercise.

  Reply NICE: The guideline reviewed self-management programmes (including patient education and reassurance for example, the Back Book), advice to stay active, advice to bed rest and unsupervised exercise (including exercise prescription, advice to exercise at home). Details of each intervention are given in the summary of included studies and in the evidence tables for the GDG to consider. The complexity of defining self-management is acknowledged and detailed in section 8.6 'Recommendations and link to evidence'. On reviewing this evidence the GDG agreed that the evidence was not strong, however that self-management should be a principle applied alongside all treatment options throughout the pathway. This has been clarified in the wording of the recommendation.

- National Council for Osteopathic Research/ Centre for Rehabilitation Research, University of Oxford*:* One would be hard pressed NOT to recommend self-management, but there is an issue with this chapter because the definition of self-management is too inclusive. The main evidence reviewed in this section centres on advice and guidance. Self-management interventions are more than just education leaflets and advice they usually involve some sort of active behaviour change component often using a cognitive behavioural approach (Self-management of long term conditions: PRISM NIHR HTA report 2014). Analysing the group self-management programmes with the group psychological therapies may have altered the effectiveness outcomes and raised the importance of these approaches as part of a multi-modal package of care, rather than as an adjunct to exercise. Suggestion: Review structured self-management programmes separately to and advice and guidance.

  Reply NICE: The GDG agreed to separately review self-management programmes (including patient education and reassurance for example, the Back Book), advice to stay active, advice to bed rest and unsupervised exercise (including exercise prescription, advice to exercise at home) from psychological therapies in alignment with the scope. Individual therapies within a 'class' of therapies (e.g. type of self-management programmes) were considered for subgroup analysis in case there was heterogeneity and were detailed in the summary of included studies and the evidence tables. The GDG acknowledged the complexity of defining self-management and this is detailed in section 8.6 'Recommendations and link to evidence'. This was taken into account when reviewing the evidence and as a contributing factor to the poor evidence for this intervention. However the GDG agreed that self-management should be a principle that is recommended across the treatment pathway for people with low back pain and sciatica. The wording of the recommendation has been amended to clarify this.

Methodological aspects

- Acupuncture Now Foundation: "Evidence from 1 study reporting at the longer-term time-point confirmed a benefit of self-management compared to usual care for quality of life in terms of well-being and general health domains of the SF-36." None of these outcomes were clinically significant. Furthermore, for the general health domain, the outcome was not statistically significant. Thus it would appear that results which do not meet NICEs definition of clinical significance are judged able to confirm a benefit in respect of self-management, whilst this is not the case in respect of acupuncture. Again, declared criteria have been applied inconsistently to different interventions, which suggests a biased approach.

  Reply NICE: The outcomes showing clinical benefit of self-management over usual care are detailed in the Clinical evidence statements section (8.5.1.1.2). There was evidence of benefit of self-management over usual care for quality of life and healthcare utilisation outcomes, in most cases at the longer term follow-up. The GDG have now edited the recommendation to clarify that self-management is intended to apply as a principle alongside all treatment for people with low back pain and sciatica as part of routine practice. They noted that the evidence from the review was weak, however it was also acknowledged that this review did not adequately capture true self-management approaches and that a good practice statement to support self-management was justified. This is further supported by evidence from the review of multidisciplinary programmes where self-management was often included as part of treatment packages demonstrating benefit. The LETR and recommendation have been updated to clarify this.

- Acupuncture Now Foundation: "There was evidence that healthcare utilisation (consultation for back pain, hospitalisation, physician visits, physiotherapist visits) was reduced by the use of self-management programmes." None of these results meet the GDG's criteria for clinical significance. For physiotherapy, the outcome crosses the line of no effect. Clinical significance would appear to be applied to some interventions and not others. Again, declared criteria have been applied inconsistently to different interventions, which suggests a biased approach.

  Reply NICE: The outcomes showing clinical benefit of self-management are detailed in the Clinical evidence statements section (8.5.1.1.2). The outcomes mentioned show clinical benefit of self-management over comparator.

- Society for Back Pain Research*:* We are not clear why self-management is such a strong recommendation "provide" and why it appears in box 1 of the algorithm. The effect size is negligible and the GDG concluded that: there was "uncertainty about this evidence", "no conclusive evidence in favour of self-management provided in isolation". Advice and education are not self-management. Advice and education may facilitate self-management. The terms can't be used interchangeably. It would be helpful if there was guidance about what information to provide. It is important to highlight that this is usually integrated with other intervention throughout the algorithm. It would be helpful if the GDG could support the importance of the consistency of information across the pathway. It would be helpful to highlight that there was no benefit of unsupervised exercise.

  Reply NICE: The GDG have clarified that the recommendation for self-management is intended to apply as a principle alongside all treatment for people with low back pain and sciatica as part of routine practice rather than a separate intervention that is offered. They noted that the evidence from the review was weak, however it was also acknowledged that this review did not adequately capture true self-management approaches and that a good practice statement to support self-management was justified. This is further supported by evidence from the review of multidisciplinary programmes where self-management was often included as part of treatment packages demonstrating benefit. The wording of recommendation 1.2.1 is now the following: All healthcare professionals should provide people with advice and information, tailored to their needs and capabilities, to help them self-manage their non-specific low back pain with or without sciatica, at all steps of the treatment pathway. This should include: information on the nature of non-specific low back pain and sciatica; encouragement to continue with normal activities as far as possible.

Evidence and formulation of the recommendation

- Arthritis research UK: We noted that self-management is recommended yet supervised exercise is only to be 'considered'. This does not match the evidence for these interventions quoted by the GDG, since the effect size from self-management is negligible/much smaller than the effect size for exercise (see next points below). It would be helpful to relook at these recommendations, to therefore consider recommending exercise, and having an explicit statement about how the evidence is being used and interpreted in relation to these recommendations:
  - There is inconsistent evidence for self-management and no benefit of it over sham.
  - Studies involving unsupervised exercise were considered by the GDG under self-management, yet these studies were heterogeneous and some included patient-clinician contact, which is not 'unsupervised exercise'.
  - There is no benefit of unsupervised exercise yet it is recommended for all patients with LBP in the draft guidance (and is in the top box of Figure 1 algorithm, page 15 along with some pharmacological interventions). This does not appear to be in line with the evidence underpinning self-management or exercise, presented in the guideline

  Reply NICE: The GDG have clarified that the recommendation for self-management is intended to apply as a principle alongside all treatment for people with low back pain and sciatica as part of routine practise. The GDG agreed that the evidence for supervised exercise, reviewed in the exercise chapter, supported a 'consider' recommendation, and believed this was consistent with the approach to the self-management recommendation. Unsupervised exercise has been categorised within self-management for the purpose of this review as stated in the protocol, and it included interventions such as exercise prescription and advice to exercise at home (Appendix C.4). The GDG acknowledged that for some of these there would be some clinician contact, but the distinguishing factor for determining where the intervention should be considered was the exercise component being carried out without supervision.

- Faculty of pain medicine*:* **Psychology** in the form of education around the concept of chronic pain and importance of self-management should be integral to pathway. Such a pain management programme should not be considered only at the end of the line or in the presence of significant psychological obstacles. Failure to understand and engage with fundamental chronic pain concepts is a barrier to progress in the majority of patients and fosters a persistent acute pain model and dependency on escalating and long-term medication as well as on intervention. Would a recommendation be to consider a significant public health campaign vis a vis the Buchbinder trial?

This used social marketing techniques and TV adverts as opposed to Health backs Scotland which used only radio so probably missed many people with sedentary behaviours. The place of the combined psychology/physiotherapy programme seems about right as Psychological techniques are about getting people to make changes when they are finding it difficult to do so. Education = advice on self-management which people need to know and some may find it easy to adapt and make changes and agree very much needs to be provided very early –as education is a very weak way to change behaviour (Price C1, Williams AC, Main CJ. Rehabilitation for chronic low back pain. Review was of little help in selecting treatment.BMJ. 2001 Nov 24;323(7323):1251-2.)

Reply NICE: The GDG felt that every healthcare professional is expected to provide advice and education to their patients and that every programme should contain some elements of self-management. The wording of the recommendation has been updated to clarify this. Furthermore, psychological therapies are considered if provided as a package of treatment including exercise with or without manual therapies. This has been recommended as a treatment early in the pathway. Please note that it is outside the remit of this guideline to consider public health campaigns.

- National Council for Osteopathic Research: There is inconsistent use of the UK BEAM trial data. UK BEAM trial had 4 arms: Best practice usual care (rebranded as self-management), exercise, manipulation package of care and manipulation package of care plus exercise. These data were extracted for mixed modality vs usual care but not extracted or included in the effectiveness analysis for exercise vs usual care. We would like more information and transparency about why studies were excluded (reasons not given for UK BEAM in Appendix L rejected studies).

  Reply NICE: We note that the UK BEAM trial had the following four arms: 1) self-management; 2) self-management plus exercise; 3) self-management plus manual therapy; 4) self-management plus exercise plus manual therapy. On considering this alongside the protocols for the reviews in this guideline, comparisons of self-management plus manual therapy versus self-management (3 versus 1) and self-management plus exercise plus manual therapy versus self-management (4 vs1) had been included in the manual therapy chapter. Comparison of self-management plus manual therapy versus self-management plus exercise (3 versus 2) has now been added to the manual therapy review (chapter 12). Comparison of self-management plus exercise versus self-management (2 versus 1) has now been added to the exercise review (chapter 9). We apologise for any omissions in the consultation version of the guideline.
- South Devon Healthcare NHS Foundation Trust*:* We are concerned that this does not recognise the complexities of helping patients to establish self-management and how far beyond "advice and information" this can go. If the support with self-management is "tailored" as it says to an individual's needs and capabilities, this is where the bulk of our physiotherapy and psychology input is focussed. Also the breadth of barriers (psychological, physical, social and economic) to self-management is not considered.

  Reply NICE: The complexity of identifying self-management is acknowledged and detailed in the guideline (section 8.6, Recommendations and link to evidence). The objective of the self-management review was to assess the clinical and cost effectiveness of self-management in the management of people with non-specific low back pain and sciatica. The analysis of barriers to self-management was beyond the scope of the review to analyse. However, the GDG acknowledged the existence of other NICE guidance related to this area. This is referred to in section 8.6, Recommendations and link to evidence.
- Chartered Society of Physiotherapy*:* We welcome this recommendation. Promoting self-management is well-established as part of physiotherapy management of low back pain. We agree with the GDG conclusion that although the evidence for self-management in isolation is far from conclusive, it is important to provide advice to people about their condition. This also helps aid shared-decision making and gives the individual more control over their condition. Could further information be provided on what self-management should look like? For example, it requires a skilled assessment and intervention, as opposed to just the provision of information.

  Reply NICE: Several types of self-management interventions were reviewed: self-management programmes (including patient education and reassurance for example, the Back Book), advice to stay active, advice to bed rest and unsupervised exercise (including exercise prescription, advice to exercise at home). The evidence reviewed did not enable a more specific definition of what self-management would look like beyond what was stated in the recommendation, although it was noted as important to state that it should be tailored to the individual.

NICE final recommendations on imaging (November 2016)

7. Provide people with advice and information, tailored to their needs and capabilities, to help them self-manage their low back pain with or without sciatica, at all steps of the treatment pathway. Include:
   - information on the nature of low back pain and sciatica

- encouragement to continue with normal activities.

Belgian GDG comments on the last formulation during the meeting on 24 January 2017

- A clear definition of self-management will be added in the communication for physicians.
- Tools are needed for patient information e.g. video, leaflets, book (see examples of Jo Nijs, mind-medico-coach?).
- A box with main messages what to say and what not will be developed with information sent by the GDG member.

KCE 2016 final recommendation on self-management

6. Provide each patient with advice and information, tailored to their needs and capabilities, to help them self-manage their low back pain with or without radicular pain, at all steps of the treatment pathway. Include:
    - information on the benign nature of low back pain and radicular pain
    - encouragement to continue with normal activities, exercise included.

(consensus-based experts opinion)

7.5. Exercise therapies

Exercise therapies in patients with low back pain ± radicular pain

NICE search question

"What is the clinical and cost-effectiveness of exercise therapies in the management of non-specific low back pain and sciatica?"

Introduction based on the draft version of NICE guideline (March 2016)

- The term "exercise therapy" encompasses a wide range of difference exercise types, environments and theoretical models and may be delivered by a range of healthcare professionals, on a one to one basis or in a group environment, in a specialist gym equipment or at home.
- Exercise may be directed at improving a variety of parameters of fitness and function, including muscle strength, timing or endurance, flexibility and range of motion, precision of movement, cardiovascular fitness, functional task performance and confidence.
- In this section only supervised exercise has been considered, unsupervised exercise was considered as self-management, and therefore included in the self-management review.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with non-specific low back pain • People aged 16 or above with sciatica
Intervention(s)	• Individual/group exercise: o Mind-body exercises (Yoga, Tai-Chi) o Biomechanical (Pilates, core stability, McKenzie, motor control, stretching, Feldenkrais) o Aerobics (swimming, walking programme, aerobic exercise) o Mixed modality exercise (aerobics and/or mind-body and/or biomechanical)
Comparison(s)	• Placebo/Sham/Attention control • Usual care/waiting list • To each other □ Any other non-invasive interventions in the guideline • Other treatment (interventions listed in our guideline review protocols) • Combination of interventions: any combination of the non-invasive interventions in the guideline
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (>30% improvement in pain or function) • Adverse events: morbidity; • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

- 76 RCTS on single interventions and 16 RCTS on combined interventions were included (75 in the final version of the NICE guideline). Single interventions are divided in biomechanical, aerobic, mind-body and mixed exercises.
- NEW: Two Cochrane reviews were identified but could not be included for the following reasons: review was not limited to RCTs, the population was stratified by chronicity of pain. The studies included in these Cochrane reviews were individually assessed and included if they matched the review protocol.

Biomechanical exercise

= include any exercise intervention that is primarily directed at altering or improving spinal mechanics, by muscle strengthening, stretching, range of motion exercise, motor control exercise (core stability programmes and Pilates) or programmes aimed at addressing specific problem movements (McKenzie exercise and Feldenkrais method)

- **Patients with low back pain without sciatica**
  - Only 1 comparison was found: **Biomechanical exercise (individual and group) versus usual care (UC)**
    - Individual biomechanical exercises versus UC: Both at short term and long term, a clinically important improvement in **QoL** composite scores (SF-36 0-100; 2 RCTs; low quality; n=99) and domain scores (except for 1 QoL domain functional capacity at short term) (SF-36 0-100; 1 RCT; very low to low quality; n=60) was seen with biomechanical exercises. Also for **pain**, a clinical important benefit favouring biomechanical exercises could be seen at short term (VAS 0-10; 4 RCTs; very low quality; n=246 and VAS change score full and limited range of motion VAS 0-10; 1 RCT; low quality; n=17-14) and at long term (VAS 0-10; 2 RCTs; very low quality; n=146). No clinical difference was seen in pain change score, both at short term (VAS 0-85; 1 RCT; low quality; n= 260) and at long term (VAS 0-85; 1 RCT; low quality; n= 271). Conflicting results were reported for **function**: no difference was found in 7 RCTs at short term and long term (RMDQ 0-24/0-23; low-very low quality: n=17-418) in contrary to a clinically important benefit favouring biomechanical exercises both at short term (RMDQ 0-24 mean difference; 1 RCT; moderate quality; n=86) and at long term (RMDQ 0-24; 1 RCT; very low quality; n= 60). More **adverse events** were reported in the group undertaking the biomechanical exercises (1 RCT; very low quality; n=40).
    - Group biomechanical exercises versus UC**:** At short term, a clinically important benefit of group biomechanical exercise was found for the composite score of **QoL** (SF-36 0-100; 1 RCT; moderate quality; n=18) but not for the subdomains (SF-12 0-100; 1 RCT; very low quality; n=34). No clinical difference for short term **pain** (VAS 0-10; 2 RCTs; very low quality; n= 52), however a clinically important benefit for **function** favouring group biomechanical exercises was demonstrated (ODI; 2 RCTs; very low quality; n= 52). No long term data for QoL, pain and function were reported.
    - Not reported outcomes: psychological distress, responder criteria, healthcare utilisation
  - Not reported comparisons in this patient group:
    - Biomechanical exercise (individual and group) versus placebo
    - Biomechanical exercise versus active comparator (including self-management, spinal manipulation (LAHV) and interferential therapy)

Table 7 – Clinical effectiveness of biomechanical exercise compared to usual care in patients with low back pain without sciatica

Biomechanical exercises (individual and group sessions)		
Outcomes	**Individual biomechanical exercise (IBME) versus usual care**	**Group biomechanical exercise (GBME) versus usual care**
QoL	At short term: • **Composite physical score (SF-36 0-100): CIB favouring IBME** (stretching, core stability) (2 RCTs; Low; n=99) • **Composite mental score (SF-36 0-100): CIB favouring IBME**	At short term: • **Composite physical score (SF-36 0-100): CIB favouring GBME** (resistance) (1 RCT; Moderate; n=18) • **Composite mental score (SF-36 0-100)**: **CIB favouring GBME**

	(stretching, core stability) (2 RCTs; Low; n=99) • **5 of 6 QoL domains (SF-36 0-100)**: **CIB favouring IBME** (stretching) (1 RCT; very low-low; n=60) At long term: • **Composite physical score (SF-36 0-100): CIB favouring IBME** (stretching) (1 RCT; low; n=60) • **Composite mental score (SF-36 0-100)**: **CIB favouring IBME** (stretching) (1 RCT; Low; n=60) • **All six QoL domains (SF-36 0-100)**: **CIB favouring IBME** (stretching) (1 RCT; Very low and Low; n=60)	(resistance) (1 RCT; Moderate; n=18) • **All six QoL domains (SF-12 0-100)**: **no diff** (Pilates) (1 RCT; Very low; n=34) At long term: Not reported
Pain	At short term: • **Fixed time point (VAS 0-10): CIB favouring IBME** (stretching, McKenzie, core stability) (4 RCTs; Very low; n=246) • **Evolution over time (change score, VAS 0-85): No diff** (core stability) (1 RCT; Low; n= 260) • **Evolution over time (change score, VAS 0-10): CIB favouring IBME** (core stability, full range of motion) (1 RCT; Low; n=17) • **Evolution over time (change score, VAS 0-10): CIB favouring IBME** (core stability, limited range of motion) (1 RCT; Low; n=14) At long term: • **Fixed time point (VAS 0-10): CIB favouring IBME** (stretching, individual Pilates) (2 RCTs; Very low; n=146) • **Evolution over time (change score, VAS 0-85): No diff** (core stability) (1 RCT; Low; n= 271)	At short term: • **Fixed time point (VAS 0-10): No diff** (resistance, Pilates) (2 RCTs; Very low; n= 52) At long term: Not reported

Function	At short term: • **Fixed time point (RMDQ 0-24): No difference** (McKenzie, core stability, stretching) (4 RCTs; Low; n= 418) • **Evolution over time (change score, ODI 0-100): No diff** (core stability, full range of motion) (1 RCT; Low; n=17) • **Evolution over time (change score, ODI 0-100): No diff** (core stability, limited range of motion) (1 RCT; Very low; n=14) • **Evolution over time (RMDQ 0-24 mean difference): CIB favouring IBME** (Pilates) (1 RCT; Moderate; n=86) • **Evolution over time (RMDQ 0-23): CIB favouring IBME** (stretching) (1 RCT; Very low; n=32) At long term: • **Fixed time point (RMDQ 0-24): CIB favouring IBME** (stretching) (1 RCT; Very low; n= 60) • **Evolution over time (RMDQ 0-24 mean difference): No diff** (Pilates) (1 RCT; Very low; n=86)	At short term: • **Fixed time point (ODI 0-100): CIB favouring GBME** (resistance, Pilates) (2 RCTs; Very low; n= 52) At long term: Not reported
Adverse events	At short term: **More morbidity reported in IBME** (stretching) (3 versus 0; 1 RCT; Very low; n=40) At long term: Not reported	

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y;

- **Patients with low back pain and sciatica**
  - **Biomechanical exercises (individual) versus placebo: study (Albert 2012) excluded due to incorrect interventions (sham= another form of exercise)**
    - ~~At short term, a clinical important benefit in **pain** was seen favouring individual biomechanical exercises (VAS 0-10; 1 RCT; low quality; n=170), however this benefit was not seen at long term (VAS 0-10; 1 RCT; moderate quality; n=170).~~
    - ~~Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation~~

- **Biomechanical exercises (individual) versus usual care (UC): Goren 2010 has been excluded from this analysis. In this study the exercise intervention can rather be classified as a mixed intervention.**
  - At short term, a clinical important benefit in **pain** (VAS 0-10; ~~2~~ 1 RCTs; low quality; n=~~82~~ 52) ~~and in leg pain (leg pain VAS 0-10; 1 RCT; low quality; n=30)~~ was seen in the individual biomechanical exercise group. No long term data were reported.
  - Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation
- **Biomechanical exercises (individual) versus active comparator (spinal manipulation (low-amplitude high-velocity))**
  - At short term no difference in **QoL** between individual biomechanical exercises and spinal manipulation (composite physical score SF-36; 1 RCT; very low quality; n=191 and composite mental score SF-36; 1 RCT; very low quality; n=191). At long term, only a clinical important benefit was seen in the composite physical score favouring individual biomechanical exercises (SF-36; 1 RCT; very low quality; n=164). No clinical differences in **pain** scores at short term (VAS 0-10; 1 RCT; low quality; n=191) and long term (VAS 0-10; 1 RCT; very low quality; n=164) and in **function** both at short term (RMDQ 0-24; 1 RCT; low; n=191) and at long term (RMDQ 0-24; 1 RCT; low; n=164).
  - Not reported outcomes: psychological distress, responder criteria, adverse events, healthcare utilisation
- Not reported comparisons in this patient group:
  - Biomechanical exercise versus active comparator (including self-management)
  - All comparisons with group biomechanical exercises

Table 8 – Clinical effectiveness of biomechanical exercise compared to placebo, usual care and spinal manipulation in patients with low back pain with sciatica

Biomechanical exercises (individual sessions)			
Outcomes	**~~Individual biomechanical exercise (IBME) versus placebo~~**	**Individual biomechanical exercise (IBME) versus usual care**	**Individual biomechanical exercise (IBME) versus spinal manipulation (low-amplitude high-velocity)**
QoL			At short term: • **Composite physical score (SF 36 0-100): No diff** (strength) (1 RCT; very low; n=191) • **Composite mental score (SF 36 0-100): No diff** (strength) (1 RCT; very low; n=191) At long term: • **Composite physical score (SF 36 0-100): CIB favouring IMBE** (strength) (1 RCT; very low; n=164) • **Composite mental score (SF 36 0-100): No diff** (strength) (1 RCT; low; n=164)
Pain	~~At short term:~~	At short term:	At short term:

	~~• VAS 0-10: CIB favouring IBME~~ ~~(McKenzie)~~ ~~(1 RCT; low; n=170)~~ ~~At long term:~~ ~~• VAS 0-10: No diff~~ ~~(McKenzie)~~ ~~(1 RCT; moderate; n=170)~~	• **Overall score (VAS 0-10): CIB favouring IBME** (stretching, core stability) (~~2~~ 1 RCTs; very low; n=~~82~~ 52) ~~• Leg pain (VAS 0-10): CIB favouring IBME~~ ~~(stretching)~~ ~~(1 RCT; low; n=30)~~ At long term: Not reported	• **VAS 0-10: No diff** (strength) (1 RCT; low; n=191) At long term: • **VAS 0-10: No diff** (strength) (1 RCT; very low; n=164)
Function			At short term: • **RMDQ 0-24: No diff** (strength) (1 RCT; low; n=191) At long term: • **RMDQ 0-24: No diff** (strength) (1 RCT; low; n=164)

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

- **Mixed population (LBP with or without sciatica)**
  - ~~**Biomechanical exercises (group) versus placebo: removed in final version due to incorrect interventions (Smith 2001: breathing, relaxation and movement audio tape vs story audio tape)**~~
    - ~~Only the outcome **psychological distress** was reported in 1 small study: a clinical benefit favouring placebo/sham was found (STAI 20-80; 1 RCT; low quality; n=26)~~
    - ~~Not reported outcomes: QoL, pain, function, responder criteria, adverse events, healthcare utilisation~~
  - **Biomechanical exercises (individual and group) versus usual care (UC)**
    - Individual biomechanical exercises versus UC: At short term, a clinically important improvement favouring individual biomechanical exercises was seen in **QoL** on all domains (RAND/SF-36; 2 RCTs; low-very low; n=57) but mental health (RAND/SF-36; 2 RCTs; very low quality; n=57) and **psychological distress** (MHI 24-142; 1 RCT; very low quality; n=54). No long term data on QoL and psychological distress were reported. No clinical difference in overall **pain** scores were seen at short term (VAS 0-10; 5 RCTs; moderate quality; n=317) and long term (VAS 0-10; 1 RCT; low quality; n=99), however 3 of the 5 subdomains showed a clinical important benefit in the individual biomechanical exercise group: pain at rest (1 RCT; moderate quality; n=30), pain during movement (1 RCT; moderate quality; n=30), pain walking (1 RCT; very low quality; n=32). No clinical differences were seen in **function** at short term (RMDQ 0-24/ODI 0-100; 5 RCTs; low; n=253) and long term (RMDQ 0-24/ODI 0-100; 2 RCTs; low quality; n=159).

- Group biomechanical exercises versus UC: A clinically important benefit for group biomechanical exercises was found for long-term pain (VAS 0-10; 1 RCT; very low quality; n=127), but not at short term (VAS 0-10; 1 RCT; very low-low quality; n=127-122), except in one study on core stability exercises (VAS 0-10; 1 RCT; moderate quality; n=40). A short term clinically important improvement in function was seen in favour of group biomechanical exercises (RMDQ 0-24; 1 RCT; low quality; n=40). No long term data on function were reported. Also at long term a decreased **NSAID use** was seen in the group of group biomechanical exercise (1 RCT; low quality; n=60). No short term data on NSAID use were reported.
- Not reported outcomes: responder criteria, adverse events

o **Biomechanical exercises (individual) versus self-management (advice to avoid bed rest and continue normal activity)**
- Compared to self-management, individual biomechanical exercises showed a clinical important benefit in long-term leg **pain** (VAS 0-10; 1 RCT; very low quality; n=77) and **function** (RMDQ 0-24; 1 RCT; very low quality; n=71). No clinical difference were found for overall pain (at short term and long term) (both VAS 0-10; 1 RCT; very low quality; n=77), for leg pain at short term (VAS 0-10; 1 RCT; very low quality; n=77) and for function at short term (RMDQ 0-24; 1 RCT; very low quality; n=77).
- Not reported outcomes: QoL, psychological distress, responder criteria, healthcare utilisation, adverse events

o **Biomechanical exercises (individual) versus active comparator (interferential therapy)**
- A clinical important short term benefit in pain (VAS 0-10; 1 RCT; moderate; n=60) was seen in patients undertaking individual biomechanical exercises compared to interferential therapy. No long term data for pain was reported.
- Not reported outcomes: QoL, function, psychological distress, responder criteria, healthcare utilisation, adverse events

o **Biomechanical exercises (group) versus active comparator (unsupervised exercise)**
- A clinically important benefit was found for long-term pain (VAS 0-10; 1 RCT; very low quality; n=141) in the group undertaking group biomechanical exercises but not at short term (VAS 0-10; 1 RCT; very low quality; n=170).
- Not reported outcomes: QoL, function, psychological distress, responder criteria, healthcare utilisation, adverse events

o Not reported comparisons in this patient group:
- Biomechanical exercises (individual) versus placebo/sham
- Biomechanical exercises (individual and group) versus active comparator (spinal manipulation)
- Biomechanical exercises (group) versus active comparator (self-management, interferential therapy)
- Biomechanical exercises (individual) versus active comparator (unsupervised exercise)

Table 9 – Clinical effectiveness of biomechanical exercise compared to placebo, usual care and active comparators in patients with low back pain with or without sciatica

Biomechanical exercises (individual and/or group sessions)						
Outcomes	**~~Group biomechanical exercise (GBME) versus placebo~~**	**Biomechanical exercise versus usual care**		**Individual biomechanical exercise (IBME) versus self-management (advice)**	**Individual biomechanical exercise (IBME) versus interferential therapy**	**Group biomechanical exercise (GBME) versus unsupervised exercise**
		Individual (IBME)	Group (GBME)			
QoL		<u>At short term:</u> • **5 of 8 domains (RAND/SF-36 0-100): CIB favouring IBME** (core stability) (2 RCTs; low-very low; n=57) <u>At long term:</u> Not reported				
Pain		<u>At short term:</u> • **Overall (VAS 0-10): No diff** (core stability, stretching, Pilates) (5 RCTs; moderate; n=317) • **Pain at rest (VAS 0-10): CIB favouring IBME** (core stability) (1 RCT; moderate; n=30)	<u>At short term:</u> • **Overall (VAS 0-10): No diff** (stretching) (1 RCT; very low; n=127) • **Evolution over time (VAS 0-10): no diff** (stretching) (1 RCT; low; n=122) • **Evolution over time (VAS 0-10): CIB favouring GBME** (core stability)	<u>At short term:</u> • **Overall (VAS 0-10): No diff** (McKenzie) (1 RCT; very low; n=77) • **Leg pain (VAS 0-10): No diff** (McKenzie) (1 RCT; very low; n=77)	<u>At short term:</u> • **VAS 0-10: CIB favouring IBME** (McKenzie) (1 RCT; moderate; n=60)	<u>At short term:</u> • **VAS 0-10: No diff** (core stability) (1 RCT; very low; n=170)

		• **Pain during movement (VAS 0-10): CIB favouring IMBE** (core stability) (1 RCT; moderate; n=30) • **Pain walking (VAS 0-10): CIB favouring IMBE** (stretching) (1 RCT; very low; n=32) At long term: • **Overall (VAS 0-10): No diff** (core stability) (1 RCT; low; n=99)	(1 RCT; moderate; n=40) At long term: • **Overall (VAS 0-10): CIB favouring GBME** (stretching) (1 RCT; very low; n=127)	At long term: • **Overall (VAS 0-10): No diff** (McKenzie) (1 RCT; very low; n=77) • **Leg pain (VAS 0-10): CIB favouring IBME** (McKenzie) (1 RCT; very low; n=77)	At long term: Not reported	At long term: • **VAS 0-10: CIB favouring GBME** (core stability) (1 RCT; very low; n=141)
Function		At short term: • **RMDQ 0-24/ODI 0-100: No diff** (stretching, core stability, Pilates) (5 RCTs; low; n=253) At long term: • **RMDQ 0-24/ODI 0-100: No diff** (Pilates, core stability)	At short term: • **RMDQ 0-24: CIB favouring GBME** (core stability) (1 RCT; low; n=40) At long term: Not reported	At short term: • **RMDQ 0-24: No diff** (McKenzie) (1 RCT; very low; n=77) At long term: • **RMDQ 0-24: CIB favouring IBME** (McKenzie) (1 RCT; very low; n=71)		

		(2 RCTs; low; n=159)				
Psychological distress	~~At short term:~~ ~~• **STAI 20-80: No diff** (Feldenkrais) (1 RCT; low; n=26)~~ ~~At long term:~~ ~~Not reported~~	At short term: • **MHI 24-142: CIB favouring IBME** (core stability) (1 RCT; very low; n=54) At long term: Not reported				
Healthcare utilisation			At short term: Not reported At long term: • **NSAID use: CIB favouring GBME** (Pilates) (1 RCT; low; n=60)			

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

In conclusion:

- **Patients with low back pain without sciatica**
  - Only comparison (with usual care) retrieved: a clinical benefit in favour of biomechanical exercises for QoL, for pain (only in individual biomechanical exercises) and function.
- **Patients with low back pain with sciatica**
  - Comparison of (individual) biomechanical exercises to placebo or usual care, showed only a clinical benefit in pain. Compared with active comparator (manipulation) only a long term benefit in the physical component of QoL was found.

- **Mixed population (LBP with or without sciatica)**
  - Comparison of (individual) biomechanical exercises to usual care, showed a short term benefit in QoL and psychological distress (both in individual biomechanical exercises), a long term benefit in pain and short term benefit in function (both in group biomechanical exercises). Comparison to active comparators (self-management, IFT, unsupervised exercises) found a clinically benefit in short term pain (compared to IFT) and long term pain (compared to unsupervised exercise), and a long term benefit in function (compared to self-management).
- **Biomechanical exercises as adjunct (see results below)**

- Several, single studies compared different modalities of active comparators in combination with biomechanical exercises, resulting in an inconsistent overview of evidence in which it is difficult to determine which combination of modalities showed the most clinical benefit. Compared to the limited evidence of biomechanical exercises as a single intervention, the combination of the latter with active comparators increased its potential clinical benefits.

Aerobic exercise

= any exercise intervention that is primarily directed at improving cardiovascular fitness and endurance

- **Patients with low back pain without sciatica**
  - **Aerobic exercises (individual and group) versus usual care (UC)**
    - Individual aerobic exercises versus UC: No clinical difference was found for **QoI** at short term (EuroQol 0.59-1; 1 RCT; low quality; n=56) and long term (EuroQol VAS 0-100; 1 RCT; low quality; n=57). Regarding **pain** severity, a clinically important improvement in pain scores was found for deep water running both at short term (VAS 0-10; 1 RCT; low quality; n=49) and at long term (VAS 0-10; 1 RCT; moderate quality; n=49). However no clinical differences were found for treadmill running (only reported at short term; VAS 0-10; 1 RCT; very low quality; n=37) and for walking (only reported at long term; VAS 0-10; 1 RCT; low quality; n=57). At short term, a clinically important benefit was found in **function** in favour of (individual) aerobic exercises (RMDQ 0-24; 2 RCTs; low quality; n=86), however no clinical difference was found in **psychological distress** (BDI 0-63; 1 RCT; very low quality; n=37). No long term data were reported for function and psychological distress.
    - Group aerobic exercises versus UC: At short term, a clinically important benefit in favour of aerobic exercises was found for physical and mental **QoL** (both SF-36 0-100; 2 RCTs; very low quality; n=109) (and 2 individual QoL domains; both SF-36 0-100; 1 RCT; very low quality; n=20) and for **pain** (McGill 0-78; 1 RCT; very low quality; n=40 and VAS 0-10; 3 RCTs; very low quality; n=119). However, at short term, no clinical differences were found for **function** (ODI 0-100; 2 RCTs; very low quality; n=106) and **psychological distress** (CESD 0-60; 1 RCT; very low quality; n=40). At long term, no clinical differences were found for pain (VAS 0-10; 1 RCT; low quality; n=83) and function (ODI 0-100; 1 RCT; very low quality; n=89). No long term data for psychological distress were reported.
    - Not reported outcomes: responder criteria, adverse events, healthcare utilisation
  - **Aerobic exercises (group) versus active comparator (group biomechanical exercise)**
    - A clinical benefit was found for **pain** in the short term (VAS 0-10; 1 RCT; low quality; n=64) but not in the long term (VAS 0-10; 1 RCT; low quality; n=64) for the group receiving aerobic exercises. No clinical difference in **function** was found both at short term (ODI 0-100; 1 RCT; low quality; n=64) and at long term (ODI 0-100; 1 RCT; low quality; n=64).
    - Not reported outcomes: QoL, responder criteria, adverse events, healthcare utilisation
  - Not reported comparisons in this patient group:
    - Aerobic exercise (individual and group) versus self-management
    - Aerobic exercise (individual) versus active comparator (biomechanical exercise)

Table 10 – Clinical effectiveness of aerobic exercise compared to usual care and active comparator in patients with low back pain without sciatica

Aerobic exercises (individual and group sessions)			
Outcomes	**Aerobic exercise (individual and group) versus usual care**		**Aerobic exercise (group) versus group biomechanical exercise (Pilates)**
	Individual (IAE)	Group (GAE)	
QoL	At short term: • **EuroQol 0.59-1: No diff** (walking) (1 RCT; low; n=56) At long term: • **EuroQol 0.59-1: No diff** (walking) (1 RCT; low; n=57)	At short term: • **Physical component (SF-36 0-100): CIB favouring GAE** (aerobics) (2 RCTs; very low; n=109) • **Mental component (SF-36 0-100): CIB favouring GAE** (aerobics) (2 RCTs; very low; n=109) • **Subdomain physical role limitation (SF-36 0-100): CIB favouring GAE** (walking) (1 RCT; very low; n=20) • **Subdomain physical functioning (SF-36 0-100): CIB favouring GAE** (walking) (1 RCT; very low; n=20) At long term: Not reported	
Pain	At short term: • **VAS 0-10: CIB favouring IAE** (deep water running) (1 RCT; low; n=49) • **VAS 0-10: No diff** (treadmill running) (1 RCT; very low; n=37) At long term: • **VAS 0-10: CIB favouring IAE**	At short term: • **McGill 0-78: CIB favouring GAE** (walking) (1 RCT; very low; n=40) • **VAS 0-10: CIB favouring GAE** (walking, aerobics) (3 RCTs; very low; n=119) At long term: • **VAS 0-10: No diff**	At short term: • **VAS 0-10: CIB favouring GAE** (stationary cycling) (1 RCT; low; n=64) At long term: • **VAS 0-10: No diff** (stationary cycling)

	(deep water running) (1 RCT; moderate; n=49) • **VAS 0-10: No diff** (walking) (RCT; low; n=57)	(aerobics) (1 RCT; low; n=83)	(1 RCT; low; n=64)
Function	At short term: • **RMDQ 0-24: CIB favouring IAE** (deep water running, treadmill running) (2 RCTs; low; n=86) At long term: Not reported	At short term: • **ODI 0-100: No diff** (aerobics) (2 RCTs; very low; n=106) At long term: • **ODI 0-100: No diff** (aerobics) (1 RCT; very low; n=89)	At short term: • **ODI 0-100: No diff** (stationary cycling) (1 RCT; low; n=64) At long term: • **ODI 0-100: No diff** (stationary cycling) (1 RCT; low; n=64)
Psychological distress	At short term: • **BDI 0-63: No diff** (treadmill running) (1 RCT; very low; n=37) At long term: Not reported	At short term: • **CESD 0-60: No diff** (walking) (1 RCT; very low; n=40) At long term: Not reported	

CIB: clinically important benefit; short term <4mo + long term 4mo-1y

- **Patients with low back pain with sciatica**
  - **No evidence was available for this patient group**
  - Not reported comparisons in this patient group:
    - Aerobic exercise (individual and group) versus usual care
    - Aerobic exercise (individual and group) versus active comparator (biomechanical exercise)
    - Aerobic exercise (individual and group) versus active comparator (self-management)

- **Mixed population (LBP with or without sciatica)**
  - **Aerobic exercises (individual) versus usual care (UC)**
    - No clinical differences were found for short term **pain** (VAS 0-10; 1 RCT; low quality; n=46) and **function** (both short term and long term; ALBPS 0-100; 1 RCT; low quality; n=46). No long term data for pain were reported.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Aerobic exercises (individual and group) versus active comparator (individual and group biomechanical exercise)**
    - Individual aerobic exercises versus individual biomechanical exercises: No clinical benefit was found in short term **function** (ODI 0-100; 1 RCT; low quality; n=52). Long term data for function were not reported.

- Group aerobic exercises versus group biomechanical exercises: No clinical difference in **pain** (VAS 0-10; 1 RCT; very low quality; n=91-83) and in **function** (RMDQ 0-24; 1 RCT; very low quality; n=91-83) were found both at short term and long term.
- Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation

o **Aerobic exercises (group) versus self-management (advice to bed rest)**
- A clinically important benefit was found in overall short term **pain** (VAS 0-10; 1 RCT; very low quality; n=18) and pain over the preceding week (VAS 0-10; 1 RCT; very low quality; n=18). No long term data for pain were reported.
- Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation

o Not reported comparisons in this patient group:
- Aerobic exercise (group) versus usual care
- Aerobic exercise (individual) versus self-management

Table 11 – Clinical effectiveness of aerobic exercise compared to usual care and active comparators in mixed population (LBP with or without sciatica)

Aerobic exercises (individual and group sessions)				
Outcomes	**Individual aerobic exercise (IAE) versus usual care**	**Aerobic exercise (individual and group) versus biomechanical exercise (individual and group) (motor control, core stability)**		**Group aerobic exercise (GAE) versus self-management (education)**
		Individual (IAE)	Group (GAE)	
Pain	At short term: • **VAS 0-10: No diff** (aerobics) (1 RCT; low; n=46) At long term: Not reported		At short term: • **VAS 0-10: No diff** (aerobics) (1 RCT; very low; n=91) At long term: • **VAS 0-10: No diff** (aerobics) (1 RCT; very low; n=83)	At short term: • **Overall pain (VAS 0-10): CIB favouring GAE** (walking) (1 RCT; very low; n=18) • **Pain over preceding week (VAS 0-10): CIB favouring GAE** (walking) (1 RCT; very low; n=18) At long term: Not reported
Function	At short term: • **ALBPS 0-100: No diff** (aerobics) (RCT; low; n=46) At long term: • **ALBPS 0-100: No diff** (aerobics) (1 RCT; low; n=46)	At short term: • **ODI 0-100: No diff** (walking) (1 RCT; low; n=52) At long term: Not reported	At short term: • **RMDQ 0-24: No diff** (aerobics) (1 RCT; very low; n=91) At long term: • **RMDQ 0-24: No diff** (aerobics) (1 RCT; very low; n=83)	

CIB: clinically important benefit; short term <4mo + long term 4mo-1y

In conclusion:

- **Patients with low back pain without sciatica**
  - Comparison with usual care revealed a clinical benefit in QoL (in group aerobic exercise), pain (both individual and group aerobic exercises) and function (in individual aerobic exercises). Only a short term pain improvement was found in favour of group aerobic exercises compared to group biomechanical exercises.
- **Patients with low back pain with sciatica**
  - No evidence was available for this patient group
- **Mixed population (LBP with or without sciatica)**
  - Comparison of (individual) aerobic exercises to usual care, showed no clinical differences. Compared to active comparators (biomechanical exercises and self-management), only a short term pain improvement was found in favour of aerobic exercises (compared to self-management).
- **Aerobic exercises as adjunct (see results below)**
  - Several, single studies compared different modalities of active comparators in combination with biomechanical exercises, resulting in an inconsistent overview of evidence in which it is difficult to determine which combination of modalities showed the most clinical benefit. Compared to the limited evidence of biomechanical exercises as a single intervention, the combination of the latter with active comparators increased its potential clinical benefits.

Mind-body exercise

= any exercise intervention that includes a combined physical, mental and spiritual focus, often with connection to metaphysical and cultural philosophies. Examples include the various forms of Yoga and Tai Chi.

- **Patients with low back pain without sciatica**
  - **Mind-body exercises (group) versus usual care (UC):**
    - A clinically important benefit in **pain** reduction in the short and the longer term was found for group mind-body exercises (both time points VAS 0-10; 1 RCT; very low; n=42).
    - Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Mind-body exercises (group) versus self-management (advice to stay active):**
    - At short term, a clinically important benefit was found in **function** (RMDQ 0-24; 2 RCTs; low quality; n=191) and **responder criteria** (improvement in function) (1 RCT; low quality; n=125) for the group mind-body exercises. At long term, no clinical difference in function (RMDQ 0-24; 2 RCTs; very low quality; n=191) could be demonstrated. Long term data on responder criteria was not reported. However, a clinically important decreased medication use (**healthcare utilisation**) was found in the group mind-body exercises (1 RCT; low quality; n=63).
    - Not reported outcomes: QoL, pain, psychological distress, adverse events
  - **Mind-body exercises (group) versus active comparator (group mixed exercises=biomechanical and aerobic exercises):**
    - No clinical difference was found for **function** both at short term (RMDQ 0-24; 2 RCTs; very low quality; n=228) and at long term (RMDQ 0-24; 2 RCTs; moderate quality; n=229). The number of patients who improved more than 30% in function (**responder criteria**) did not differ between both groups (only reported at short term) (1 RCT; low quality; n=162). Only a clinically important decreased medication use (**healthcare utilisation**) was found in the group mind-body exercises (1 RCT; low quality; n=66).
    - Not reported outcomes: QoL, pain, psychological distress, adverse events
  - Not reported comparisons in this patient group:
    - Comparisons with individual mind-body exercises
    - Mind-body exercise (individual and group) versus active comparator (individual biomechanical exercise)

Table 12 – Clinical effectiveness of mind-body exercise compared to usual care and active comparators in patients with low back pain without sciatica

Mind-body exercises (group sessions)			
Outcomes	**Group mind-body exercise (GMB) versus usual care**	**Group mind-body exercise (GMB) versus self-management (Back Book)**	**Group mind-body exercise (GMB) versus group mixed exercises (biomechanical + aerobic)**
Pain	At short term: • **VAS 0-10: CIB favouring GMB** (Lyengar yoga) (1 RCT; very low; n=42) At long term: • **VAS 0-10: CIB favouring GMB** (Lyengar yoga) (1 RCT; very low; n=42)		
Function		At short term: • **RMDQ 0-24: CIB favouring GMB** (Viniyoga) (2 RCTs; low; n=191) At long term: • **RMDQ 0-24: No diff** (Viniyoga) (2 RCTs; very low; n=191)	At short term: • **RMDQ 0-24: No diff** (Viniyoga) (2 RCTs; very low; n=228) At long term: • **RMDQ 0-24: No diff** (Viniyoga) (2 RCTs; moderate; n=229)
Responder criteria		At short term: • **>30% improvement in function: CIB favouring GMB** (Viniyoga) (1 RCT; low; n=125) At long term: Not reported	At short term: • **>30% improvement in function: no diff** (Viniyoga) (1 RCT; low; n=162) At long term: Not reported
Healthcare utilisation		At short term: Not reported At long term: • **Medication use: CIB favouring GMB** (Viniyoga) (1 RCT; low; n=63)	At short term: Not reported At long term: • **Medication use: CIB favouring GMB** (Viniyoga) (1 RCT; low; n=66)

CIB: clinically important benefit; short term <4mo + long term 4mo-1y

- **Patients with low back pain with sciatica**
  - **No evidence was available for this patient group**
  - Not reported comparisons in this patient group:
    - Mind-body exercise (individual) versus active comparator (individual biomechanical exercise)
    - Mind-body exercise (group) versus usual care
    - Mind-body exercise (group) versus active comparator (individual biomechanical exercise)
    - Mind-body exercise (group) versus active comparator (self-management)
    - Mind-body exercise (group) versus active comparator (group mixed exercise)

- **Mixed population (LBP with or without sciatica)**
  - **Mind-body exercises (individual and group) versus active comparator (individual biomechanical exercises):**
    - Individual mind-body exercise versus individual biomechanical exercise: Evidence from 1 small study showed short term clinical benefit of yoga on **pain** (VAS 0-10; 1 RCT; low quality; n=30) and **function** (RMDQ 0-23; 1 RCT; low quality; n=30), whereas a study on tai chi found no clinically important differences on short-term pain (VAS 0-10; 1 RCT; low quality; n=40) (no data on function reported). No long-term data were reported.
    - Group mind-body exercise versus individual biomechanical exercise: A clinically important improvement in **pain** was found in the group mind-body exercises at short and long term (both time points VAS 0-10; 1 RCT; moderate quality; n=60).
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Mind-body exercises (group) versus usual care (UC):**
    - Conflicting results are reported for **QoL**, the EQ-5D suggested a clinically important short-term benefit in favour of group mind-body exercises (EQ-5D 0-1; 2 RCTs; low quality; n=325) in contrary to SF-12 which detected no clinical differences between groups (both for physical component and mental component; SF-12 0-100; 2 RCTs; moderate quality; n=326). At long-term, all scales detected no clinical differences between groups (EQ-5D 0-1; 1 RCT; moderate quality; n=313 and SF-12 0-100; 1 RCT; moderate quality; n=313). Comparison between Hatha yoga (as group mind-body exercises) revealed no differences in pain severity between both groups at short term (VAS 0-10; 2 RCTs; very low quality; n=82) and at long term (VAS 0-10; 1 RCT; low quality; n=23). A similar comparison between Lyengar yoga and usual care, found no difference in **pain** at short term (VAS 0-10; 1 RCT; very low quality; n=90) but a clinically important benefit in favour of the group mind-body exercises at long term (VAS 0-10; 1 RCT; very low quality; n=90). Another study measured pain severity with the Aberdeen pain scale and found a clinically important improvement at short term (1 RCT; moderate quality; n=313) in the group mind-body exercises but not at long term (1 RCT; moderate quality; n=313). One study revealed a clinically significant higher number of patients who reported a more than 30% improvement in pain (**responder criteria**) in the group of mind-body exercises (at short term; 1 RCT; moderate quality; n=160). No clinical difference in **function** was found both at short term (RMDQ 0-24/ODI 0-100; 6 RCTs; low quality; n=516) and at long term (RMDQ 0-24/ODI 0-100; 3 RCTs; low quality; n=426). However, one study found a clinically significant higher number of patients with more than 30% improvement in function in the groups of mind-body exercises (at short term; 1 RCT; moderate quality; n=160). A benefit was seen for **psychological distress** for Hatha yoga (only reported at short term; BDI 0-63; 1 RCT; very low quality; n=16) bot no difference was found for Lyengar yoga at short term (BDI 0-63; 1 RCT; very low quality; n=90) and at long term (BDI 0-63; 1 RCT; very low quality; n=90). Regarding **healthcare utilisation**, no clinical difference were found in number of GP visits, practice nurse visits, and physiotherapy visits (all 1 RCT; very low quality; n=14). In terms of medication use, a study on viniyoga found no differences (1 RCT; very low quality; n=14) whereas another study on Hatha yoga found a clinically important benefit in favour of the mind-body exercises (1 RCT; low quality; n=30). Also a clinically important higher number of patients who reduced or stopped medication at short term (1 RCT; low quality; n=44) was found in the group of mind-body exercises. This benefit was not yet anymore seen at long term (1 RCT; very low quality; n=42).
    - Not reported outcomes: adverse events
  - Not reported comparisons in this patient group:

- Mind-body exercise (group) versus active comparator (self-management)
- Mind-body exercise (group) versus active comparator (group mixed exercise)

Table 13 – Clinical effectiveness of mind-body exercise compared to usual care and active comparators in mixed population (LBP with or without sciatica)

Mind-body exercises (individual and group sessions)			
Outcomes	**Mind-body exercise (individual and group) versus individual biomechanical exercise (core stability, stretching)**		**Group mind-body exercise (GMB) versus usual care**
	Individual (IMB)	Group (GMB)	
QoL			At short term: • **EQ-5D 0-1: CIB favouring GMB** (Viniyoga, Yoga) (2 RCTs; low; n=325) • **Physical component (SF-12 0-100): no diff** (Viniyoga, Yoga) (2 RCTs; moderate; n=326) • **Mental component (SF-12 0-100): no diff** (Viniyoga, Yoga) (2 RCTs; moderate; n=326) At long term: • **EQ-5D 0-1: No diff** (Yoga) (1 RCT; moderate; n=313) • **Physical component (SF-12 0-100): no diff** (Yoga) (1 RCT; moderate; n=313) • **Mental component (SF-12 0-100): no diff** (Yoga) (1 RCT; moderate; n=313)
Pain	At short term: • **VAS 0-10: No diff** (Tai Chi) (1 RCT; low; n=40) • **VAS 0-10: CIB favouring IMB** (Yoga) (1 RCT; low; n=30)	At short term: • **VAS 0-10: CIB favouring GMB** (Yoga) (1 RCT; moderate; n=60)	At short term: • **VAS 0-10: No diff** (Hatha Yoga) (2 RCTs; very low; n=82) • **VAS 0-10: No diff** (Lyengar Yoga) (1 RCT; very low; n=90) • **Overall pain (ABPS 0-100): CIB favouring GMB** (Yoga)

	At long term: Not reported	At long term: • **VAS 0-10: CIB favouring GMB** (Yoga) (1 RCT; moderate; n=60)	(1 RCT; moderate; n=313) At long term: • **VAS 0-10: No diff** (Hatha Yoga) (1 RCT; low; n=23) • **VAS 0-10: CIB favouring GMB** (Lyengar Yoga) (1 RCT; very low; n=90) • **Overall pain (ABPS 0-100): no diff** (Yoga) (1 RCT; moderate; n=313)
Function	At short term: • **RMDQ 0-23: CIB favouring IMB** (Yoga) (1 RCT; low; n=30) At long term: Not reported		At short term: • **RMDQ 0-24/ODI 0-100: No diff** (Yoga) (6 RCTs; low; n=516) At long term: • **RMDQ 0-24/ODI 0-100: No diff** (Yoga) (3 RCTs; low; n=426)
Psychological distress			At short term: • **BDI 0-63: CIB favouring GMB** (Hatha Yoga) (1 RCT; very low; n=16) • **BDI 0-63: No diff** (Lyengar Yoga) (1 RCT; very low; n=90) At long term: • **BDI 0-63: No diff** (Lyengar Yoga) (1 RCT; very low; n=90)
Responder criteria			At short term: • **>30% improvement in pain: CIB favouring GMB**

			(Tai Chi) (1 RCT; moderate; n=160) • **>30% improvement in function: CIB favouring GMB** (Tai Chi) (1 RCT; moderate; n=160) At long term: Not reported
Healthcare utilisation			At short term: • **GP visits: no diff** (Vinyoga) (1 RCT; very low; n=14) • **Practice nurse visits: no diff** (Vinyoga) (1 RCT; very low; n=14) • **Physiotherapist visits: no diff** (Vinyoga) (1 RCT; very low; n=14) • **Medication use -** Viniyoga**: no diff** (1 RCT; very low; n=14) • **Medication use -** Hatha Yoga**: CIB favouring GMB** (1 RCT; low; n=30) • **Reduced or stopped medication: CIB favouring GMB** (Lyengar Yoga) (1 RCT; low; n=44) At long term: • **Reduced or stopped medication: no diff** (Lyengar Yoga) (1 RCT; very low; n=42)

CIB: clinically important benefit; short term <4mo + long term 4mo-1y

In conclusion:

- **Patients with low back pain without sciatica**
  - Comparison with usual care revealed only a clinical benefit in pain (in group mind-body exercises). Compared to active comparators (self-management and group mixed exercises), a short term benefit in function (and improvement in function) (compared to self-management) and a decreased medication use (compared to self-management and group mixed exercises).

- **Patients with low back pain with sciatica**
  - No evidence was available for this patient group
- **Mixed population (LBP with or without sciatica)**
  - Comparison of (group) mind-body exercises to usual care, showed inconsistent results for QoL, pain and psychological distress. Compared to active comparator (individual biomechanical exercises), a clinical benefit in pain (in group mind-body exercises) and in short term function (in individual mind-body exercises) was found.
- **Mind-body exercises as adjunct (see results below)**
  - Several, single studies compared different modalities of active comparators in combination with biomechanical exercises, resulting in an inconsistent overview of evidence in which it is difficult to determine which combination of modalities showed the most clinical benefit. Compared to the limited evidence of biomechanical exercises as a single intervention, the combination of the latter with active comparators increased its potential clinical benefits.

Mixed exercises

= any exercise intervention that incorporates a combination of any of the previous three categories (biomechanical exercises, aerobic exercises, mind-body exercises)

- **Patients with low back pain without sciatica**
  - ~~**Mixed exercises (group) versus placebo/sham:**~~ **Machado 2007 was excluded due to incorrect intervention.**
    - ~~A clinically important benefit in **pain** (at short term: VAS 0-10; 1 RCT; very low quality; n=21 and at long term: VAS 0-10; 1 RCT; very low quality; n=27), **function** (RMDQ 0-24; 1 RCT; low quality; n=21) and **psychological distress** (BDI 0-63; 1 RCT; low quality; n=21) was found in favour of mixed exercises compared to placebo/sham. No long term data on function and psychological distress were reported.~~
    - ~~Not reported outcomes: QoL, adverse events, responder criteria, healthcare utilisation~~
  - **Mixed exercises (group) versus usual care (UC):**
    - No clinical benefit was found for short-term **pain** (VAS 0-10; 1 RCT; low quality; n=29), in 5 of the 8 domains of **QoL** (SF-36 0-100; 1 RCT; low-very low quality; n=36), **function** (RMDQ 0-24/ODI 0-100; 2 RCTs; very low quality; n=88), and **psychological distress** (HADS 0-21; 1 RCT; very low quality; n=29). A clinical benefit was found in the remaining 3 domains of QoL (SF-36 0-100; 1 RCT; low-very low quality; n=36) and in the change in pain score (VAS 0-10; 1 RCT; very low quality; n=59) in favour of mixed exercises. No long term data reported.
    - Not reported outcomes: adverse events, responder criteria, healthcare utilisation
  - **Mixed exercises (group) versus self-management (advice to stay active)**
    - No clinical benefit was found for **function** both at short term (RMDQ 0-24; 2 RCTs; moderate quality; n=125) and at long term (RMDQ 0-24; 2 RCTs; low quality; n=164), nevertheless a significant higher number of patients with 30% improvement in function (**responder criteria**) in the mixed exercise group (at short term; 1 RCT; low quality; n=125). No difference in medication use (**healthcare utilisation**) was found (only reported at long term; 1 RCT; very low quality; n=61).
    - Not reported outcomes: QoL, pain, psychological distress, adverse events
  - **NEW: Mixed exercises (group) versus cognitive therapy**
    - A clinical benefit in pain (at both time points; VAS 0-10; 1 RCT; very low quality; n=21)) and function (only short term reported; RMDQ 0-24; 1 RCT; low quality; n=21) was found in favour of group mixed exercises. No difference was retrieved in psychological distress (only reported at short term; BDI 0-63; low quality; n=21).
  - Not reported comparisons in this patient group:
    - Mixed exercise (individual) versus active comparator (unsupervised exercise)
    - Mixed exercise (individual) versus active comparator (biomechanical exercise)
    - Mixed exercise (group) versus cognitive behavioural approaches

Table 14 – Clinical effectiveness of mixed exercise compared to placebo, usual care and active comparator in patients with low back pain without sciatica

Mixed exercises (group sessions)				
Outcomes	~~**Group mixed exercise (GME) versus placebo/sham**~~	**Group mixed exercise (GME) versus usual care**	**Group mixed exercise versus self-management (Back Book)**	**NEW Group mixed exercise versus cognitive therapy**
QoL		At short term: • **3 of 8 domains (SF-36 0-100): CIB favouring GME** (aerobic (aerobics) + biomechanical (strength, stretching)) (1 RCT; low-very low; n=36) At long term: Not reported		
Pain	~~At short term:~~ ~~• **VAS 0-10: CIB favouring GME**~~ ~~(biomechanical (stretching, strength)+ aerobic (walking))~~ ~~(1 RCT; very low; n=21)~~ ~~At long term:~~ ~~• **VAS 0-10: CIB favouring GME**~~ ~~(biomechanical (stretching, strength)+ aerobic (walking))~~ ~~(1 RCT; very low; n=27)~~	At short term: • **Fixed time point (VAS 0-10): No diff** (aerobic (aerobic dance) + biomechanical (strength, stretching)) (1 RCT; low; n=29) • **Evolution over time (change score, VAS 0-10): CIB favouring GME** (aerobic (aerobics) + biomechanical (strength, stretching)) (1 RCT; very low; n=59) At long term: Not reported		At short term: • **Fixed time point (VAS 0-10): CBI favouring GME** (aerobic (walking) + biomechanical (strength, stretching)) (1 RCT; very low; n=21) At long term: • **Fixed time point (VAS 0-10): CBI favouring GME** (aerobic (walking) + biomechanical (strength, stretching)) (1 RCT; very low; n=27)
Function	~~At short term:~~ ~~• **RMDQ 0-24: CIB favouring GME**~~ ~~(biomechanical (stretching, strength)+ aerobic (walking))~~ ~~(1 RCT; low; n=21)~~	At short term: • **RMDQ 0-24/ODI 0-100: No diff** (aerobic (aerobics/aerobic dance) + biomechanical (strength, stretching)) (2 RCTs; very low; n=88)	At short term: • **RMDQ 0-24: No diff** (biomechanical (strength, stretching) + aerobic (aerobic exercises)) (2 RCTs; moderate; n=125)	At short term: • **RMDQ 0-24: CIB favouring GME** (aerobic (walking) + biomechanical (strength, stretching)) (1 RCT; low; n=21)

	~~At long term:~~ ~~Not reported~~	At long term: Not reported	At long term: • **RMDQ 0-24: No diff** (biomechanical (strength, stretching) + aerobic (aerobic exercises)) (2 RCTs; low; n=164)	At long term: Not reported
Psychological distress	~~At short term:~~ ~~• **BDI 0-63: CIB favouring GME**~~ ~~(biomechanical (stretching, strength)+ aerobic (walking))~~ ~~(1 RCT; low; n=21)~~ ~~At long term: Not reported~~	At short term: • **Anxiety score (HADS 0-21): no diff** (aerobic (aerobic dance) + biomechanical (strength, stretching)) (1 RCT; very low; n=29) • **Depression score (HADS 0-21): no diff** (aerobic (aerobic dance) + biomechanical (strength, stretching)) (1 RCT; very low; n=29) At long term: Not reported		At short term: • **BDI 0-63: no diff** (aerobic (walking) + biomechanical (strength, stretching)) (1 RCT; low; n=21) At long term:Not reported
Responder criteria			At short term: • **>30% improvement in function: CIB favouring GME** (biomechanical (strength, stretching) + aerobic (aerobic exercises)) (1 RCT; low; n=125) At long term: Not reported	
Healthcare utilisation			At short term: Not reported At long term: • **Medication use: no diff** (biomechanical (strength, stretching) + aerobic (aerobic exercises)) (1 RCT; very low; n=61)	

CIB: clinically important benefit; short term <4mo + long term 4mo-1y

- **Patients with low back pain with sciatica**
  - **NEW: Mixed exercise (individual) versus waiting list**
    - The only reported outcome showed a beneficial effect of individual mixed exercises on pain (VAS 0-10; 1 RCT; low quality; n=30) and on leg pain (VAS 0-10; 1 RCT; low quality; n=30). No long term data or other outcomes were reported.
    - Not reported outcomes: QoL, function, psychological distress, adverse events, responder criteria, healthcare utilisation
  - **Mixed exercise (group) versus usual care (UC)**
    - At short term, no clinical difference in overall **pain** (NRS 0-10; 1 RCT; very low quality; n=50) and **function** (RMDQ 0-24; 1 RCT; very low quality; n=44) were found between mixed exercises and usual care. However for pain at rest (NRS 0-10; 1 RCT; moderate quality; n=53) and on movement (NRS 0-10; 1 RCT; moderate quality; n=53) a clinically important benefit was found in favour of mixed exercises. At long term, results are more conflicting with a clinically important benefit in overall pain (NRS 0-10; 1 RCT; very low quality; n=44) favouring mixed exercises whereas function (RMDQ 0-24; 1 RCT; low quality; n=44) showed a clinically important improvement in the usual care group.
    - Not reported outcomes: QoL, psychological distress, adverse events, responder criteria, healthcare utilisation
  - Not reported comparisons in this patient group:
    - Mixed exercise (individual) versus active comparator (unsupervised exercise)
    - Mixed exercise (individual) versus active comparator (biomechanical exercise)
    - Mixed exercise (group) versus placebo/sham
    - Mixed exercise (group) versus self-management
    - Mixed exercise (group) versus cognitive behavioural approaches

- **Mixed population (LBP with or without sciatica)**
  - **Mixed exercises (individual) versus active comparator (unsupervised exercises):**
    - A clinically important benefit in short term **pain** was found in favour of mixed exercises compared to unsupervised exercises (VAS 0-10; 1 RCT; low quality; n=40). No long-term data or other outcomes reported.
    - Not reported outcomes: QoL, function, psychological distress, adverse events, responder criteria, healthcare utilisation
  - **Mixed exercises (individual) versus active comparator (biomechanical exercises):**
    - No clinical differences were found in short term **pain** (VAS 0-10; 1 RCT; moderate quality; n=63) and **function** (ODI 0-100; 1 RCT; moderate quality; n=63) between mixed exercises and biomechanical exercises. No long term data reported.
    - Not reported outcomes: QoL, psychological distress, adverse events, responder criteria, healthcare utilisation
  - **Mixed exercises (group) versus usual care (UC):**
    - At short term, a clinical benefit in favour of mixed exercises was seen for the mental component of **QoL** (SF-36 0-100; 1 RCT; moderate quality; n=38), **pain** (overall VAS 0-10; 2 RCTs; low quality; n=162; at flexion and at rest; both VAS 0-10; 1 RCT; moderate quality; n=38) and **function** (RMDQ 0-24; 2 RCTs; low quality; n=162). However at short term no clinical difference could be found for the physical component of QoL (SF-36 0-100; 1 RCT; low quality; n=38), **psychological distress** (BDI 0-63; 1 RCT; low quality; n=102) and mean difference in pain (Von Korff 0-100; 1 RCT; very low quality; n=27) and function (RMDQ 0-24; 1 RCT; low quality; n=27) from control. Not many studies reported long-term results: a clinically important benefit favouring mixed exercises was found for overall pain (VAS 0-10; 2 RCTs; very low quality; n=92), but no difference in mean difference in pain from control (Von Korff 0-100; 1 RCT; very low quality; n=27), no difference in function (RMDQ 0-24; 1 RCT; very low quality; n=52) (except mean difference in function from control RMDQ 0-24; 1 RCT; low quality; n=27).
    - Not reported outcomes: adverse events, responder criteria, healthcare utilisation
  - **Mixed exercises (group) versus cognitive behavioural approaches:**

- No clinical differences were found for **pain** (VAS 0-10; 1 RCT; low-very low quality; n=107-103), **function** (RMDQ 0-24; 1 RCT; very low quality; n=107-103), **psychological distress** (BDI 0-63; 1 RCT; very low; n=107-103) both at short term and at long term. Regarding **healthcare utilisation**, only a clinical important benefit in number of therapist sessions was found in the mixed exercise group (1 RCT; very low; n=104).
- Not reported outcomes: QoL, adverse events, responder criteria

o Not reported comparisons in this patient group:

- Mixed exercise (group) versus placebo/sham
- Mixed exercise (group) versus self-management

Table 15 – Clinical effectiveness of mixed exercise compared to usual care and active comparators in mixed population (low back pain with or without sciatica)

Mixed exercises (individual and group sessions)				
Outcomes	**Individual mixed exercise (IME) versus unsupervised exercises (biomechanical (strength, flexibility) + aerobic (not specified)**	**Individual mixed exercise (IME) versus individual biomechanical exercises (stretching, strength)**	**Group mixed exercise (GME) versus usual care**	**Group mixed exercise (GME) versus cognitive behavioural approaches (operant behavioural graded activity training and problem solving training)**
QoL			At short term: • **Physical composite score (SF-36 0-100): no diff** (aquatic program: biomechanical (strength, stretching, resistance) + aerobic) (1 RCT; low; n=38) • **Mental composite score (SF-36 0-100): CIB favouring GME** (aquatic program: biomechanical (strength, stretching, resistance) + aerobic) (1 RCT; moderate; n=38) At long term: Not reported	
Pain	At short term: • **VAS 0-10: CIB favouring IME** (biomechanical (flexibility, strength) + aerobic (not specified)) (1 RCT; low; n=40)	At short term: • **VAS 0-10: No diff** (biomechanical (stretching, strength) + aerobic (walking)) (1 RCT; moderate; n=63)	At short term: • **Evolution over time in overall pain (VAS 0-10): CIB favouring GME** (biomechanical (strength, flexibility) + aerobic (endurance, cycling)) (2 RCTs; low; n=162)	At short term: • **VAS 0-10: No diff** (biomechanical (strength) + aerobic (cycling)) (1 RCT; low; n=107)

	At long term: Not reported	At long term: Not reported	• **Pain at flexion (VAS 0-10): CIB favouring GME** (aquatic program: biomechanical (strength, stretching, resistance) + aerobic) (1 RCT; moderate; n=38) • **Pain at rest (VAS 0-10): CIB favouring GME** (aquatic program: biomechanical (strength, stretching, resistance) + aerobic) (1 RCT; moderate; n=38) • **Mean difference from control (Von Korff 0-100): no diff** (biomechanical (strength, stretching, motor relearning) + aerobic (not specified)) (1 RCT; low; n=27) At long term: • **Fixed time point overall pain (VAS 0-10): CIB favouring GME** (biomechanical (strength, flexibility)+ aerobic (endurance)) (2 RCTs; very low; n=92) • **Mean difference from control (Von Korff 0-100): no diff** (biomechanical (strength, stretching, motor relearning) + aerobic (not specified)) (1 RCT; very low; n=27)	At long term: • **VAS 0-10: No diff** (biomechanical (strength) + aerobic (cycling)) (1 RCT; very low; n=103)
Function		At short term: • **ODI 0-100: No diff** (biomechanical (stretching, strength) + aerobic (walking)) (1 RCT; moderate; n=63)	At short term: • **RMDQ 0-24: CIB favouring GME** (biomechanical (strength, flexibility) + aerobic (endurance, cycling)) (2 RCTs; low; n=162) • **Mean difference from control (RMDQ 0-24): no diff**	At short term: • **RMDQ 0-24: No diff** (biomechanical (strength) + aerobic (cycling)) (1 RCT; very low; n=107)

		At long term: Not reported	(biomechanical (strength, stretching, motor relearning) + aerobic (not specified)) (1 RCT; low; n=27) At long term: • **RMDQ 0-24: No diff** (biomechanical (strength, flexibility) + aerobic (endurance)) (1 RCT; very low; n=52) • **Mean difference from control (RMDQ 0-24): CIB favouring GME** (biomechanical (strength, stretching, motor relearning) + aerobic (not specified)) (1 RCT; low; n=27)	At long term: • **RMDQ 0-24: No diff** (biomechanical (strength) + aerobic (cycling)) (1 RCT; very low; n=103)
Psychological distress			At short term: • **BDI 0-63: No diff** (biomechanical (strength)+ aerobic (cycling) (1 RCT; low; n=102) At long term: Not reported	At short term: • **BDI 0-63: No diff** (biomechanical (strength) + aerobic (cycling)) (1 RCT; very low; n=107) At long term: • **BDI 0-63: No diff** (biomechanical (strength) + aerobic (cycling)) (1 RCT; very low; n=103)
Healthcare utilisation				At short term: Not reported At long term: • **GP visits: no diff** (biomechanical (strength) + aerobic (cycling)) (1 RCT; very low; n=104) • **Specialist care visits: no diff**

				(biomechanical (strength) + aerobic (cycling)) (1 RCT; low; n=104) • **Radiography visits: no diff** (biomechanical (strength) + aerobic (cycling)) (1 RCT; moderate; n=104) • **Occupational physician visits: no diff** (biomechanical (strength) + aerobic (cycling)) (1 RCT; moderate; n=104) • **Psychologist visits: no diff** (biomechanical (strength) + aerobic (cycling)) (1 RCT; very low; n=104) • **Therapist sessions: CIB favouring GME** (biomechanical (strength) + aerobic (cycling)) (1 RCT; very low; n=104)

CIB: clinically important benefit; short term <4mo + long term 4mo-1y

In conclusion:

- **Patients with low back pain without sciatica**
  - Comparison with sham or usual care revealed a clinical benefit in QoL (in group mixed exercise), pain and short-term function (both compared to sham) but inconsistent results for psychological distress. Compared to active comparator (self-management) only a short term improvement in function was found in favour of group mixed exercises.
- **Patients with low back pain with sciatica**
  - Comparison with usual care, showed a clinical benefit in subscales of pain in favour of mixed exercises, at long term results are conflicting with a benefit in pain in favour of mixed exercises whereas function is clinically improved in the usual care group.
- **Mixed population (LBP with or without sciatica)**
  - Comparison of (group) mixed exercises to usual care, showed a clinical benefit in pain and short term function in favour of the group mixed exercises. Compared to active comparators (unsupervised exercises, biomechanical exercises, behavioural approaches), a short term benefit in pain (compared to unsupervised exercises) and a long term decreased healthcare utilisation was found in favour of the mixed exercises.
- **Mixed exercises as adjunct (see results below)**
  - Several, single studies compared different modalities of active comparators in combination with biomechanical exercises, resulting in an inconsistent overview of evidence in which it is difficult to determine which combination of modalities showed the most clinical benefit. Compared to the limited evidence of biomechanical exercises as a single intervention, the combination of the latter with active comparators increased its potential clinical benefits.

Exercise therapy as component in a multimodal intervention

- **Patients with low back pain without sciatica**
  - **Exercise (biomechanical) + electrotherapy (TENS) versus electrotherapy (TENS):**
    - No clinical differences were found for **pain** (Borg 0-10; 1 RCT; low quality; n=44) and **function** (ODI 0-50; 1 RCT; low quality; n=44) at short term. No long term data were reported.
    - Not reported outcomes: QoL, responder criteria, psychological distress, adverse events, healthcare utilisation
  - **Exercise (biomechanical + aerobic) + electrotherapy (PENS) versus sham electrotherapy (PENS)**
    - At short term, only a clinically important benefit was found for the physical component of **QoL** favouring sham PENS (SF-36 0-100; 1 RCT; low quality; n=93). No clinical differences were found for the mental component of QoL (SF-36 0-100; 1 RCT; low quality; n=93), **pain** (McGill 0-78; 1 RCT; very low quality; n=93) and **function** (RMDQ 0-24; 1 RCT; low quality; n=93). At long term, no clinical differences were seen for QoI (both mental and physical component; SF-36 0-100; 1 RCT; low quality; n=93), pain (McGill 0-78; 1 RCT; low quality; n=93) and function (RMDQ 0-24; 1 RCT; very low quality; n=93).
    - Not reported outcomes: responder criteria, psychological distress, adverse events, healthcare utilisation
  - **Exercise (biomechanical + aerobic) + electrotherapy (PENS) versus electrotherapy (PENS)**
    - Only a clinically important benefit was found for the physical component of **QoI**, both at short term and at long term favouring the combined intervention of exercise and PENS (SF-36 0-100; 1 RCT; very low quality; n=92). No clinical differences were found for the mental component of QoL (SF-36 0-100; 1 RCT; very low quality; n=92), **pain** (McGill 0-78; 1 RCT; very low-low quality; n=92) and **function** (RMDQ 0-24; 1 RCT; low quality; n=92) (all at short term and long term).
    - Not reported outcomes: responder criteria, psychological distress, adverse events, healthcare utilisation
  - **Group exercise (biomechanical + aerobic) + self-management (education) + manual therapy (manipulation) versus individual exercise (biomechanical) + self-management (education) + manual therapy (manipulation)**
    - Only one outcome was reported: no clinical difference was found in analgesic use (**healthcare utilisation**) (at short term) (1 RCT; very low quality; n=62). No long term data was reported.
    - Not reported outcomes: QoL, pain, function, psychological distress, responder criteria, adverse events
  - **Exercise (aerobic) + psychological intervention (behavioural therapy) versus psychological intervention (behavioural therapy)**
    - Only one outcome was reported: no clinical difference was found in **pain** (at short term) (McGill 0-78; 1 RCT; very low quality; n=36). No long term data was reported.
    - Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Exercise (aerobic) + psychological intervention (cognitive behavioural therapy – CBT) + self-management (education) versus psychological intervention (cognitive behavioural therapy – CBT) + self-management (education)**
    - No clinical difference was found in **pain** (NRS 0-10; 1 RCT; very low quality; n=27) but regarding **function** a clinically important benefit was found in the combined intervention CBT + education (without the exercises) (RMDQ 0-24; 1 RCT; very low quality; n=27). No long term data were reported for pain and function.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Exercise (biomechanical – pilates) + self-management (education) versus self-management (education)**

- In the two reported outcomes, a clinically important benefit was seen in favour of the combined intervention of exercise and education for the outcome of **function** (both at short term and long term; RMDQ 0-24; 1 RCT; very low quality; n=86) and **pain** (only at short term; NRS 0-10; 1 RCT; very low quality; n=86).
- Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation

Table 16 – Clinical effectiveness of exercise as therapy adjunct compared to active comparators in patients with low back pain without sciatica

Exercise as therapy adjunct (individual and group sessions)							
Outcomes	**Individual biomechanical exercise (core stability) + TENS versus TENS**	**Individual mixed exercise (biomechanical (strength, flexibility) + aerobic (walking)) + PENS versus sham PENS**	**Individual mixed exercise (biomechanical (strength, flexibility) + aerobic (walking)) + PENS versus PENS**	**Group mixed (biomechanical aerobic) exercise (circuit) + self-management (education) + manipulation versus individual biomechanical exercise + self-management (education) + manipulation**	**Group aerobic exercise (walking) + behavioural therapy versus behavioural therapy**	**Group aerobic exercise (circuit) + cognitive behavioural therapy (CBT) + self-management (education) versus cognitive behavioural therapy (CBT) + self-management (education)**	**Individual biomechanical exercise (Pilates) + self-management (education) versus self-management (education)**
QoL		At short term: • **Physical composite score (SF-36 0-100): CIB favouring sham PENS** (1 RCT; low; n=93) • **Mental composite score (SF-36 0-100): no diff** (1 RCT; low; n=93) At long term: • **Physical composite score**	At short term: • **Physical composite score (SF-36 0-100): CIB favouring ex + PENS** (1 RCT; very low; n=92) • **Mental composite score (SF-36 0-100): no diff** (1 RCT; very low; n=92) At long term: • **Physical composite score**				

		(SF-36 0-100): no diff (1 RCT; low; n=93) • **Mental composite score (SF-36 0-100): no diff** (1 RCT; low; n=93)	**(SF-36 0-100): CIB favouring ex + PENS** (1 RCT; very low; n=92) • **Mental composite score (SF-36 0-100): no diff** (1 RCT; very low; n=92)				
Pain	At short term: • **Borg 0-10: No diff** (1 RCT; low; n=44) At long term: Not reported	At short term: • **McGill 0-78: No diff** (1 RCT; very low; n=93) At long term: • **McGill 0-78: No diff** (1 RCT; low; n=93)	At short term: • **McGill 0-78: No diff** (1 RCT; very low; n=92) At long term: • **McGill 0-78: No diff** (1 RCT; low; n=92)		At short term: • **McGill 0-78: No diff** (1 RCT; very low; n=36) At long term: Not reported	At short term: • **NRS 0-10: No diff** (1 RCT; very low; n=27) At long term: Not reported	At short term: • **NRS 0-10: CIB favouring Pilates + educ** (1 RCT; very low; n=86) At long term: • **NRS 0-10: No diff** (1 RCT; very low; n=86)
Function	At short term: • **ODI 0-50: No diff** (1 RCT; low; n=44) At long term: Not reported	At short term: • **RMDQ 0-24: No diff** (1 RCT; low; n=93) At long term: • **RMDQ 0-24: No diff** (1 RCT; very low; n=93)	At short term: • **RMDQ 0-24: No diff** (1 RCT; low; n=92) At long term: • **RMDQ 0-24: No diff** (1 RCT; low; n=92)			At short term: • **RMDQ 0-24: CIB favouring CBT + educ** (1 RCT; very low; n=27) At long term: Not reported	At short term: • **RMDQ 0-24: CIB favouring Pilates + educ** (1 RCT; very low; n=86) At long term: • **RMDQ 0-24: CIB favouring pilates + educ** (1 RCT; very low; n=86)
Healthcare utilisation				At short term: • **Analgesic use: no diff**			

				(1 RCT; very low; n=62) At long term: Not reported			

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

- **Patients with low back pain with sciatica**
  - **Exercise (biomechanical) + self-management (unsupervised exercise) versus TENS + laser + massage + self-management (unsupervised exercise)**
    - A clinically important benefit was found for short-term **pain** (Vas 0-10; 1 RCT; moderate quality; n=40) and **function** (ODI 0-100; 1 RCT; moderate quality; n=40) in favour of the combined intervention of exercise and self-management. No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
- **Mixed population (LBP with or without sciatica)**
  - **Exercise (core stability) + orthotics (orthoses) versus orthotics (orthoses):**
    - Only one outcome was reported in a single study: no clinical difference was found in terms of short-term remission of pain (**responder criteria**) (1 RCT; very low quality; n=48). No long term data was reported.
    - Not reported outcomes: QoL, pain, function, psychological distress, adverse events, healthcare utilisation
  - **Exercise (core stability) + self-management (education) versus self-management**
    - Only one outcome was reported in a single study (**responder criteria**): a clinically important higher number of patients improving at the short term on the Disability Index and on the QoL Index were found in the combined group of exercises and self-management (both 1 RCT; low quality; n=90). No long term data were reported.
    - Not reported outcomes: QoL, pain, function, psychological distress, adverse events, healthcare utilisation
  - **Exercise (?) + self-management (mixed modality-home exercise + education) + relaxation versus self-management (education):**
    - Only one outcome was reported in a single study: no clinical difference in **function** at short term and at long term (both RMDQ 0-24; 1 RCT; low quality; n=239).
    - Not reported outcomes: QoL, pain, responder criteria, psychological distress, adverse events, healthcare utilisation
  - **Exercise (biomechanical) + self-management (home exercise) versus self-management (self-care advice based on Back Book)**
    - No clinical differences were found for **QoL** (short term and long term; 15D 0-1; 1 RCT; low quality; n=83), short-term **pain** (VAS 0-100; 1 RCT; low quality; n=83), (short term and long term) **function** (RMDQ 0-18; 1 RCT; moderate-low quality; n=83). Only a clinically important benefit could be found on long term pain in the combined group of exercise and self-management (VAS 0-100; 1 RCT; low quality; n=83).
    - Not reported outcomes: responder criteria, psychological distress, adverse events, healthcare utilisation
  - **Exercise (biomechanical – core stability) + manual therapy (massage versus manual therapy (massage):**
    - At short term, a clinically important benefit in **pain** (VAS 0-10; 1 RCT; low quality; n=92) was found in favour of the combined intervention of exercise and massage, however no clinical difference was found in **function** (ODI 0-100; 1 RCT; very low quality; n=92). No long term data reported for pain and function. No clinical difference was found in number of patient with a pain free interval of at least 30 days (**responder criteria**) between both groups (only reported at long term) (1 RCT; very low quality; n=85).
    - Not reported outcomes: QoL, psychological distress, adverse events, healthcare utilisation
  - **Exercise (core stability) + manual therapy (manipulation) versus self-management (advice to stay active) + manual therapy (manipulation)**
    - At short term, a clinically important benefit was found in physical component of **QoL** (SF-12 0-100; 1 RCT; low quality; n=25) and sensory and affective **pain** (McGill 0-33/0-12; 1 RCT; very low quality; n=25) in favour of the combined intervention of exercise and manipulation. At long term, the benefit

remains in the physical component of QoL (SF-12 0-100; 1 RCT; low quality; n=25), also a benefit was found in the mental component of QoL (SF-12 0-100; 1 RCT; very low quality; n=25), but no clinical differences were anymore found in pain (McGill 0-33/0-12; 1 RCT; very low quality; n=25).
    - Not reported outcomes: function, responder criteria, psychological distress, adverse events, healthcare utilisation
- **Mixed exercises (biomechanical + aerobic) + Alexander technique versus Alexander technique:**
    - Only one outcome was reported in a single study: no clinical difference in **function** at short term (RMDQ 0-24; 1 RCT; very low quality; n=30). No long term data was reported.
    - Not reported outcomes: QoL, pain, responder criteria, psychological distress, adverse events, healthcare utilisation

Table 17 – Clinical effectiveness of exercise as therapy adjunct in mixed population (low back pain with or without sciatica)

Exercise as therapy adjunct (individual and group sessions)							
Outcomes	**Biomechanical (core stability + orthoses (cloth band with splints) versus orthoses (cloth band with splints)**	**Biomechanical exercise (core stability) + self-management (education) versus self-management (education)**	**Exercises + self-management (home exercise + education) + relaxation versus self-management (education)**	**Biomechanical exercise (graded activity program) + self-management (home exercise) versus self-management (self-care advice)**	**Biomechanical exercise (core stability) + massage versus massage**	**Biomechanical exercise (core stability) + manipulation versus self-management (advice) + manipulation**	**Mixed exercise (biomechanical (core stability, strength, stretching) + aerobic)) + Alexander technique versus Alexander technique**
QoL				At short term: • **15D 0-1: No diff** (1 RCT; low; n=83) At long term: • **15D 0-1: No diff**		At short term: • **Physical composite score (SF-12 0-100): CIB favouring ex + manip** (1 RCT; low; n=25) • **Mental composite score (SF-12 0-100): no diff** (1 RCT; very low; n=25) At long term: • **Physical composite**	

				(1 RCT; low; n=83)		**score (SF-12 0-100): CIB favouring ex + manip** (1 RCT; low; n=25) • **Mental composite score (SF-12 0-100): CIB favouring ex + manip** (1 RCT; very low; n=25	
Pain				<u>At short term:</u> • **VAS 0-10: No diff** (1 RCT; low; n=83) <u>At long term:</u> • **VAS 0-10: CIB favouring ex + self-man** (1 RCT; low; n=83)	<u>At short term:</u> • **VAS 0-10: CIB favouring ex + massage** (1 RCT; low; n=92) <u>At long term:</u> Not reported	<u>At short term:</u> • **Sensory pain (Mc Gill 0-33): CIB favouring ex + manip** (1 RCT; very low; n=25) • **Affective pain (Mc Gill 0-12): CIB favouring ex + manip** (1 RCT; very low; n=25) <u>At long term:</u> • **Sensory pain (Mc Gill 0-33): no diff** (1 RCT; very low; n=25) • **Affective pain (Mc Gill 0-12): no diff** (1 RCT; very low; n=25)	

Function			At short term: • **RMDQ 0-24: No diff** (1 RCT; low; n=239) At long term: • **RMDQ 0-24: No diff** (1 RCT; low; n=239)	At short term: • **RMDQ 0-18: No diff** (1 RCT; moderate; n=83) At long term: • **RMDQ 0-18: No diff** (1 RCT; low; n=83)	At short term: • **ODI 0-100: No diff** (1 RCT; very low; n=92) At long term: Not reported		At short term: • **RMDQ 0-24: No diff** (1 RCT; very low; n=30) At long term: Not reported
Responder criteria	At short term: • **Remission of pain: no diff** (1 RCT; very low; n=48) At long term: Not reported	At short term: • **Number improving on Disability Index: CIB favouring ex + educ** (1 RCT; low; n=90) • **Number improving on QoL Index: CIB favouring ex + educ** (1 RCT; low; n=90) At long term: Not reported			At short term: Not reported At long term: • **Pain free interval of >30 days: no diff** (1 RCT; very low; n=85)		

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

Overall conclusion on exercise as therapy adjunct: (quote NICE) The evidence (ranging from very low to moderate quality) showed that there was no clinical difference nor nearly all outcomes and nearly all combinations of non-invasive interventions that had exercise therapy as an adjunct, with a few exceptions.

Economic evidence

- **Mind-body exercise**
  - No studies found on individual mind-body exercises in people with low back pain or sciatica

- One cost-utility analysis: group mind-body exercise + usual care cost effective compared to usual care alone for mixed population (ICER: £13 606 per QALY gained)

- **Aerobic exercise**
  - No studies found on individual or group aerobic exercises in people with low back pain or sciatica
- **Biomechanical exercise**
  - No studies found on individual or group biomechanical exercises in people with low back pain or sciatica
  - One cost-utility analysis: biomechanical exercise was dominated (more effective and less costly) by a 3 element MBR programme (physical, psychological and educational) for mixed population
- **Mixed modality**
  - One cost-utility analysis: group mixed modality exercise (biomechanical + aerobic) was dominated (more costly and less effective) by cognitive behavioural approaches in mixed population
  - No studies found on individual mixed modality exercises in people with low back pain or sciatica
  - One cost-utility analysis in low back pain without sciatica:
    - Combination of manual therapy and self-management most cost-effective compared to combination of biomechanical, mixed modality manual therapy and self-management, biomechanical exercise in combination with self-management, and self-management alone (ICER: £ 8700 per QALY gained when compared to combination of self-management, biomechanical exercise and manual therapy). Combination of biomechanical exercise and self-management was dominated by combination of biomechanical exercise, manual therapy and self-management.
    - If manual therapy (manipulation) is not available, combination of biomechanical exercise and self-management was cost-effective compared to self-management alone (ICER £ 8300 per QALY gained)
  - One cost-consequence analysis: mixed modality manual therapy in combination with self-management and biomechanical exercise in people with low back pain or sciatica: no statistically significant increase in costs or outcomes compared to self-management.

NICE GDG considerations (March 2016)

- **Relative values of different outcomes**
  - Most critical outcome was health-related QoL with pain severity, function and psychological distress as individually critical outcomes as well as components of QoL measure.
  - Adverse events and healthcare utilisation were considered important for decision-making
  - Responder criteria, as defined as >30% improvement in pain or function, was not considered as a critical outcome
- **Trade-off between clinical benefits and harms**
  - NEW: The GDG discussed the necessity of a body of evidence to show specific intervention effects, that is, over and above any contextual or placebo effects. It was therefore agreed that if placebo or sham-controlled evidence is available, this should inform decision making in preference to contextual effects. However, if there was a lack of placebo or sham-controlled evidence, evidence against usual care will be given priority when decision making. Although some trials were identified that had sham exercise as a comparator, on consideration of these, the GDG agreed none met the protocol criteria for appropriate sham interventions for this review. Some shams were interventions being considered elsewhere within the guideline, and are considered under the relevant comparators, whereas others were comparing different forms of exercise and have been excluded. There was consequently no evidence available for exercise compared to placebo/sham.
  - Some benefit for all exercise types compared to ~~sham~~, usual care or other active comparators, but no clear evidence for one type being superior to another and benefits were seen inconsistently across critical outcomes
  - GDG agreed on known benefits to general health and wellbeing from exercise whilst data on adverse events was very limited there was no evidence of harm and exercise, conducted appropriately, should be safe.
  - ~~Only two studies compared exercise to sham with benefits in favour of exercise.~~

- GDG agreed that aerobic exercise has many additional health benefits and therefore, would not discourage anyone from partaking in such exercise programmes, but were not able to support a recommendation for aerobic exercise alone.
- For mind-body, individual biomechanical and mixed exercises: inconsistent evidence
- GDG agreed on evidence of clinically important effects for critical outcomes but difficult to clearly determine which form of exercise was most beneficial
- Effect of exercise compared to usual care or self-management could be due to imbalance of therapeutic attention
- **In summary**: The GDG agreed that there was insufficient evidence that one form of exercise was superior to another and a recommendation for a specific exercise modality was not supported from the current evidence base. However they agreed that the evidence compared to usual care did show that exercise is likely to be of value, although with some uncertainty about the effect size. In the absence of a feasible sham control, the GDG agreed that this was sufficient evidence for a recommendation to consider exercise should be made for people with low back pain with or without sciatica.

- **Trade-off between net clinical effects and costs**
  - GDG agreed on uncertainty about cost effectiveness of exercise programmes. Costs will largely depend on number of sessions provided and if delivered in group or individually.
  - Evidence not strong enough for strong recommendation with regards to optimal type, dose or duration of any exercise programme.
  - Despite uncertainties it was likely that the benefits of exercise to people with a specific episode or flare-up with or without sciatica would justify the costs
  - Given the additional costs and uncertainties regarding the benefits of individual exercise, it was considered appropriate to recommend group exercise
- **Quality of evidence**
  - Ranging from moderate to very low
  - Contextual factors, such as therapist' attention, might explain, at least in part, the observed effects to the likelihood of overestimating the effect
  - The GDG agreed that the pooling of studies with widely differing interventions, despite strengthening the body of evidence, would make it difficult to draw a conclusion about what type of exercise to offer, and to which populations.
  - The economic evidence was assessed as partially applicable with potentially serious limitations
- **Other considerations**
  - The recommendation to consider offering exercise in a group environment was based on the likely cost savings of that approach and the lack of evidence for the superior efficacy of individually delivered exercise. However GDG discussed on various instances where group exercises may not be suitable or acceptable, the GDG recognised the need for clinicians to be sensitive to this (e.g. cultural, psychological or functional ability).
  - The GDG found it difficult to tease out which type of exercise modality was effective and the frequency and duration of the exercise to be given. The GDG agreed that it would be useful to recommend an intervention that the person with back pain would be likely to participate in and that promotes self-management.
  - This review was unable to inform on the intensity of exercise programme, and the GDG agreed it was important to consider tailoring the programme to the individual, including taking into account an intensity that was feasible for the individual to be able to undertake and sustain. It was noted that the majority of exercise considered in this review was delivered by clinical providers.

NICE 2016 recommendation 7

7. "Consider a group exercise programme (biomechanical, aerobic, mind-body or a combination of approaches) within the NHS for people with a specific episode or flare-up of low back pain with or without sciatica. Take people's specific needs, capabilities and preferences into account when choosing the type of exercise."

Belgian GDG considerations mentioned in the Lime survey at the beginning of June 2016

Agreement with the content of the NICE recommendation 7: 13 Yes, 2 No, 0 no opinion, 0 out of competence, 0 no answer, 1 not completed

- **Comments from those who do not agree:**

- I do not like the subgroup called "biomechanical"... It groups very very different concepts. Therefore, I do not think one should make conclusions when grouping them. Pour la recommandation en Fr, certains lecteurs risquent de ne pas comprendre le "dans le cadre du NHS"; par ailleurs, le "épisode spécifique" pourrait prêter à confusion, le terme "spécifique" étant plus souvent utilisé pour faire référence à une rachialgie non-mécanique.
- Er bestaat geen wetenschappelijke evidentie dat groepstherapie betere functionele resultaten geeft dan individuele behandelingen. Het wordt binnen groepstherapie héél moeilijk (lees: onmogelijk) om rekening te houden met de specifieke behoeften en voorkeuren en mogelijkheden van individuele personen - deze aanbeveling spreekt zichzelf derhalve wat tegen.

- **Other comments:**
  - In de vertaling de nationale gezondheidsdienst laten wegvallen, want niet relevant in de Belgische setting
  - Ik ben akkoord dat een oefenprogramma in groepsverband overwogen kan worden. Ik betwijfel echter of een oefenprogramma in groep voor het merendeel van de LRP patiënten die een oefenprogramma doorlopen, een betere outcome zou geven in vergelijking met individuele oefenprogramma's - individuele oefenprogramma's eventueel in combinatie met thuisoefenprogramma ('self-management'). Dit gelet op gerichte persoonlijke feedback die gegeven kan worden in individuele programma's. Persoonlijke feedback niet enkel op het oefenprogramma zelf, maar ook bijvoorbeeld het maken van een rechtstreekse koppeling aan fear-avoidance gedrag, malcognities, etc. welke eventueel aanwezig kunnen zijn.
  - I am not really convinced it should be a group exercise programme. Because non-specific low back pain is a heterogenous group, with different needs, patients should either be treated individual or in group but with at least an individualized approach. A patient with low back pain should get a treatment according the specific disturbed body functions, his needs, goals and expectations.
  - Vérifier la traduction Fr (aérobic-> aérobie, NHS-> INAMI)

Strength of the recommendation 7: According to NICE formulation, it is a <u>weak</u> recommendation

GRADE Factors (NICE=black, GDG preference for strong recommendation=red, GDG preferences for weak recommendation=orange)	
Balance between desirable and undesirable effects	• Evidence of clinically important effects for critical outcomes, but insufficient evidence that one form of exercise was superior to another • Evidence on group sessions is not superior to evidence on individual sessions
Quality of evidence	• Moderate to very low • High number of studies showing good results (even of low quality) • Clinical important and quality of evidence • Quality of evidence
Values and preferences	• Known benefits to general health and wellbeing from exercises • Aerobic exercise has many additional health benefits and therefore, would not discourage anyone from partaking in such exercise programmes, but no support for a specific recommendation for aerobic exercises. • Non-specific effects occurring in exercise groups due to contextual factors • Individualized approach needed • Specification of type of exercise is not necessary due to lack of superior evidence of one type of exercise therapy
Costs (resource allocation)	• Uncertainty about the cost effectiveness of exercise programmes, largely depending on the number of sessions and in group or individually but the benefits of exercise are likely and therefore appropriate to recommend group exercise. • costs

Agreement with the strength of the recommendation 7: 5 strong, 6 weak, 1 no opinion, 1 no answer, 3 not completed

- **Comments for a weak recommendation**
  - Quality of evidence, costs
- **Comments for a strong recommendation**
  - Given the high number of studies showing good results, even if of low quality, I think that there must be a strong recommendation.
  - According the clinical importance and the quality of evidence I can agree with the strong recommendation. Personally I would advise a more individualized approach (cfr.supra "I am not really convinced it should be a group exercise programme….")

Belgian GDG comments during the GDG meeting on the 29th June 2016

- **Changes in formulation:**
  - Remove "group" because:
    - evidence on group sessions is not superior to individual sessions
    - individual approach is needed
    - cost reduction in group sessions as mentioned by NICE is not considered as important by Belgian GDG
  - remove "with a specific episode or flare-up" because:
    - unclear link between evidence and formulation of NICE recommendation
    - chronic patients can also benefit from exercise therapy
  - proposition to replace "biomechanical, aerobic, mind-body" by "specific exercises"
    - specification of type of exercises seemed unnecessary due to the lack of superior effect of one type of exercise
    - leaves more open to the clinicians to adapt the treatment plan to the individual needs of the patient
  - remove "within the NHS" because
    - not valid for the Belgian situation
    - unclear why payment system should be mentioned, in Belgium already nomenclature codes available for exercise therapy in patients with LBP
- **Comments concerning strength of recommendation**
  - in the lime survey more GDG members have chosen for weak strength, so recommendation remains weak
- **Other comments**
  - Will individualized therapy lead to a more passive approach? Discussion within the GDG group but consensus on the fact that exercise therapy requires an active participation of the LBP patient.
  - NICE 2009 recommendation on exercise therapy:
    - advise people with low back pain that staying physically active is likely to be beneficial
    - advise people with low back pain to exercise
    - consider offering a structured exercise programme tailored to the person:
      - this should comprise up to a maximum of 8 sessions over a period of up to 12 weeks
      - offer a group supervised exercise programme, in a group of up to 10 people
      - a one-to-one supervised exercise programme may be offered if a group programme is not suitable for a particular person
    - Exercise programmes may include the following elements:
      - Aerobic activity
      - Movement instruction
      - Muscle strengthening
      - Postural control
      - Stretching

- A new formulation of the NICE recommendation is proposed
- 7. "Consider an exercise programme (specific exercises or a combination of approaches) for people with low back pain with or without sciatica. Take people's specific needs, capabilities and preferences into account when choosing the type of exercise."

Stakeholders' comments and replies from NICE team on draft of March 2016

Evidence

- Acupuncture Association of Chartered Physiotherapists: It assumes AP to be acting only on "contextual mechanisms"- but so are most of the other therapies that are still recommended including exercise
  Reply NICE: When revisiting the exercise review, the GDG agreed neither of the sham comparisons were true exercise shams and therefore excluded this evidence from the review. As a result, the recommendation formed for the exercise review was focussed on the evidence against usual care.
- Acupuncture Now foundation: data misinterpretation: the values used in the plot are different to those in the original study, and different to those extracted in Appendix H, p146. Albert 2012 reports the following: Exercise group VAS: 1.5 (SD=2.1). Sham exercise group VAS: 2.3 (SD=2.7). Thus, the mean difference is -0.80 [-1.52, -0.07]. So the effect of exercise over sham is not clinically significant.
  Reply NICE: On revisiting the 'sham exercise' evidence, the GDG agreed that none of the included sham interventions were true forms of 'sham exercise'. Therefore, the revised guideline no longer has any evidence for exercise versus sham including the Albert 2012 study, as this was subsequently excluded due to the arm previously labelled as sham comprising of another form of exercise, which does not meet the protocol.
- Acupuncture Now foundation: there is a data error in Goren 2010. The study is testing Exercise + Ultrasound vs Usual Care. The usual care group did not receive ultrasound and thus, this study should be reported in combination therapy, not in exercise vs usual care.
  Reply NICE: We have checked the data and there are no errors in the data extracted from Goren 2010. This trial has 3 arms; exercise plus ultrasound, exercise plus sham ultrasound and usual care. The 2 arms extracted from Goren 2010 for inclusion in the exercise chapter were the exercise plus sham ultrasound and usual care. The comparison between exercise plus ultrasound versus usual care has not been included in the exercise review, it has been included however in the electrotherapy review under the combination of interventions section (chapter 14).
- Acupuncture Now foundation*:* The incorrect results of group aerobics versus usual care were extracted for VAS. The results shown are for the Resistance Training arm, but they should be for aerobics. So it should be Group 1: 4.8. SD. 0.8. This means that the results in Appendix K, p76, Figure 282 are incorrect. Using the correct data, group aerobic exercise does not outperform usual care.
  Reply NICE: The data extraction, forest plots, evidence tables and evidence statements have been corrected using the correct mean and SD for the aerobic arm; we apologise for the error. The amended mean difference is -0.10, which changes the analysis from clinically significant favouring aerobic exercise (mean difference of -1.13) to no clinically important difference between aerobic exercise and usual care.
- Arthritis Research UK: Two examples are the strong preference expressed for offering group-based exercise (which is not systematically superior in clinical effect or universally accepted by patients in comparison to individual exercise) and the advice against offering acupuncture (which a best-quality evidence synthesis individual-patient-data meta-analysis from a 2014 JAMA publication supported for chronic pain generally). These concerns from our group point to an apparent inconsistency in the criteria applied to the evidence base for different recommendations in the draft guidance. We would therefore welcome more explicit explanations of why similar levels of evidence for different interventions led to different recommendations. **Reply NICE**: The evidence review for exercise considered group and individual programmes separately, however, no difference between group and individual exercise in terms of benefit was observed. Although there was limited cost effectiveness evidence for individual exercise, group mind body exercise was shown to be cost effective compared to usual care. Furthermore, although group mixed exercise was more costly and less effective compared to cognitive behaviour approaches, the GDG considered that group mixed exercise may be cost effective compared to usual care. Therefore, after reviewing the clinical and cost effectiveness evidence, the GDG concluded that group exercise would incur fewer costs than individual exercise and consequently recommended group exercise. The GDG are aware that some people may not be able to fully engage with group exercise, and emphasise in the recommendation that people's specific needs, capabilities and preferences should be taken into account when choosing the type of exercise. Although the GDG agreed to ensure consistency

across reviews by giving placebo/sham evidence priority across reviews, for some interventions sham/placebo comparisons were either not possible to conduct or not available This is reflected in the exercise review. Unlike acupuncture, where a sham intervention is possible (whether penetrating or non-penetrating), the GDG agreed it is much harder to achieve this for exercise. On revisiting the 'sham exercise' evidence that was included in the draft guidance, the GDG agreed that none of the included sham interventions could be considered as true forms of 'sham exercise' (one was a psychological therapy and the other was an alternate form of exercise), therefore these have now moved to another comparison or excluded as appropriate according to the review protocol. Therefore, the revised guideline will no longer have any evidence for exercise versus sham. Consequently, the GDG have had to base their decision on the evidence against usual care in the absence of a reliable sham (following standard methodology).

- Arthritis Research UK: It is unclear why a definite priority has been given to group-based exercise interventions, in the absence of evidence that they are systematically superior in clinical effect to individual interventions. We understand there may be economic advantages to group delivery of exercise, however the GDG do not provide economic evidence on the comparison between group and individual exercise or an economic model on this. Furthermore some individuals prefer group-based treatments, but it also evident that others do not like group treatments and do not engage with them, there is variable take-up of group sessions and often limited availability. Given the above, we therefore suggest that supervised exercise be recommended for all patients with LBP and that this can be either delivered in groups or individual treatment sessions. There is evidence in favour of individualisation of exercise – the guideline recommends 'tailoring' (see pg 307). This suggests the recommendation should be for 'supervised exercise that incorporates individualisation and progression of exercises'. Is the UK BEAM trial missing from the evidence for exercise (it is in the cost effectiveness analyses)?

  Reply NICE: The GDG found no difference between group and individual exercise in terms of clinical evidence. There was no economic analysis of group exercise directly compared with individual exercise, as there was no evidence for this comparison, however each type of exercise intervention was analysed where cost effectiveness data was available. Although there was limited cost effectiveness evidence for individual exercise, group mind body exercise was shown to be cost effective compared to usual care. Furthermore, although group mixed exercise was more costly and less effective compared to cognitive behaviour approaches, the GDG considered that group mixed exercise may be cost effective compared to usual care. Therefore, after reviewing the cost effectiveness evidence, the GDG concluded that group exercise would incur fewer costs than individual exercise and consequently recommended group exercise. The GDG are aware that some patients may not fully engage with group exercise, however do state in the recommendation that people's specific needs, capabilities and preferences should be taken into account when choosing the type of exercise, in order to promote engagement. We apologise that the UK BEAM trial was not previously fully extracted, and is now included in chapters 9 and 12.

- British Acupuncture Council: The issue is why relaxation controls are excluded for exercise but sham needling is allowed for acupuncture, given that both contain elements of the specific intervention

  Reply NICE: The GDG considered that given the differences between exercise and relaxation, relaxation could not be considered a sham control for exercise as it would be clear to the participants that they were not receiving any form of exercise.

- National Council for Osteopathic Research: Exercise Implementation comment. The GDG recommend group exercise programmes. In reality clinicians individually prescribe bespoke exercise programmes, therefore the implications of implementing this recommendation is far reaching, especially if it is to be paid for and organised via the NHS and in an NHS setting. Little consideration has been given to patient choice in either group or individual exercise, even though studies have shown this is importance for compliance [Chown M, Whittamore L, Rush M, Allan S, Scott D, Archer M. A prospective study of patients with chronic back pain randomised to group exercise, physiotherapy or osteopathy. Physiother. 2008;94:21–28]. Exercise Evidence comment. The evidence does not support the recommendation for group exercise over individual exercise programmes. There are no real difference in effectiveness between individual or group. Should this be supervised exercise? The recommendation to have exercise as the mandatory component in the multi-modal delivery of non-invasive interventions does not seem to be fully considered due to the high drop-out rate consistently reported in the studies included. If the GDG make this recommendation in the hope of economies of scale (page 305 one line only yet this is a major recommendation) we suggest that some modelling is considered to assess the consequences of the costs of the high drop-out rate on the other components suggested in the multi-modal model recommended. This is not clear and we are unable to access the full economic analysis due to software issues. The short version says 'consider' a group exercise programme but recommend later as the key component of multi-modal package. Suggestion: Reconsider the strength of the recommendation for group exercise and consider supervised exercise instead for both individuals and groups.

Reply NICE: Whilst we recognise that there are some individuals who would prefer individual exercise, and that currently clinicians may prescribe individual exercise, we were unable to recommend it as an option based on the economic analysis. Whilst there was no difference between individual and group exercise in the clinical evidence, the GDG concluded that group exercise is likely to incur fewer costs compared to individual exercise, and therefore a recommendation was made for group exercise. The recommendation does however emphasise that people's specific needs, preferences and capabilities are to be taken into account when choosing the type of exercise. Furthermore, all patient treatment decisions would be discussed with the patient. Please see the introduction on page 4 of the short version about patient decisions, and the linked 'Your Care' web page. All exercise included in the exercise review is supervised exercise. Unsupervised exercise has been considered as self-management and can be found in the self-management review in Chapter 8. Exercise is included as the mandatory component in the multimodal treatment package as the evidence on which the recommendation is based all involved a treatment package where exercise was one of the components. The GDG reconsidered the strength of the recommendation for both group and individual exercise, and concluded that there is no evidence to show that exercise therapies delivered individually are cost effective, therefore decided that the recommendation should not change.

- Society for Back Pain Research: inconsistency: Supervised exercise is to be" considered", but it has larger effect size than self-management which is to be "provided", Based on the evidence exercise should be in Box 1, it is not clear why this is the only recommendation that advises "NHS", it is not clear why this is the only recommendation related to "specific episode" it is not clear why this is the only recommendation related to "flare ups". No evidence of cost effectiveness for groups is provided. The GDG have not considered the following: many therapy services are small with no facility for groups, it is known that there is a high dropout rate from groups. It may be cheaper to deliver, but may reduce effectiveness and long term compliance. Group sessions can only delivered at certain times and finding a set time to suit individual patients is not possible. Some patients do not/cannot engage in groups. Key papers which do not appear to have been included: Hurley et al, 2015: walking versus group exercise and standard physiotherapy. This paper includes an economic analysis and shows that walking is a more cost effective option. Other key walking paper that are missing are listed below (Eadie et a;, 2013; Krein et al, 2013)
  Reply NICE: The wording of the recommendation refers to the provision of exercise programmes within the NHS. The recommendation of such programmes to be offered in the context of a specific episode or flare-up is based on a clinical and cost-effectiveness basis. These are detailed in section 9.6 (Recommendations and link to evidence). The importance of keeping active with normal activities outside specific episodes or flare-ups is addressed by the self-management recommendation, please see section 8.6 for details. Two economic evaluations of group exercise were included in the review: one comparing group-mind-body exercise to usual care, and one comparing group mixed modality exercise to cognitive behavioural approaches, and a 2 element MBR programme (combination of mixed modality exercise and cognitive behavioural approaches). Group mind body exercise was shown to be cost effective compared to usual care, and although group mixed exercise was more costly and less effective compared to cognitive behaviour approaches, the GDG considered that group mixed exercise may be cost effective compared to usual care. This is explained in more detail in the 'Trade-off between net clinical effects and costs' section of the LETR alongside GDG considerations of the evidence. The GDG acknowledge that individually delivered exercise programmes may be preferable in some circumstances and that adherence is a key consideration for exercise programmes. However, the economic evidence suggested that group exercise could be cost effective for the NHS, whereas individual exercise therapy would be more costly. Furthermore, there was a lack of evidence from the review clearly demonstrating individually delivered exercise to be superior to group exercise. Therefore it was agreed that individual exercise could not be specifically recommended, but was emphasised in the recommendation that the specific needs, preferences and capabilities of the individual should be taken into account. The Hurley 2015 paper was considered, however excluded from the exercise review as it was considered a MBR intervention. However, it was also excluded from this review as the population included postpartum back pain, which is not covered by the scope. Krein 2013 was also excluded from the review as the comparator arm was considered inappropriate due to being an 'enhanced usual care' intervention where participants received a pedometer, as in the active group, but did not receive goals and reminders an in the active group. Therefore this did not fit into the protocol. Eadie 2013 has now been extracted and fully added to the evidence report. The results show some benefit for group exercise, which further supports the exercise recommendation made.
- Warwick Clinical Trials Unit: It is difficult to judge the effect sizes for exercise against usual care because of the larger number of different comparators and outcomes. However, if we look at group mind-body exercise, a comparator for which there are several relevant studies and cost utility data from within a trial, the VAS at 4 months does not show a benefit (Appendix K figure 303; data not pooled for one year), the standardised mean difference for the RMDQ/ODI is 0.34 (0.17 to 0.52) at four months and 0.30 (0.11 to 0.50) at one year (Appendix K figure 307). Expressing these results as SMDs makes interpretation harder. Using the baseline data for the standard deviation of the RMDQ from the Tilbrook study (the largest study contributing to this analysis) the point estimates equate to around 1.5 and 1.3 RMDQ points respectively.

This does not suggest that either of the GDG's pre-specified minimally important difference in SMD of 0.5, or 2 points on the RMDQ, has been achieved and no explanation has been given as to why the GDG chose a lower threshold to conclude that exercise should be considered as an effective intervention.
Reply NICE: Although the group mind-body exercise versus usual care comparisons does not reach clinical significance for pain or function, several of the other comparisons, including individual and group biomechanical exercise and group mixed exercise, reach clinical significant for pain, function and quality of life. Therefore, the GDG agreed that there was enough evidence showing a benefit of exercise compared to usual care to warrant a recommendation for exercise.

- Extended Scope Practitioners Professional Network: Although we welcome the use of group exercise as a helpful and cost-effective way to manage back pain, many patients for various reasons including personal preference, capabilities and needs are unable to participate in a group setting. We feel it would be appropriate to add individual exercise into this recommendation. **Reply NICE**: Whilst we recognise that there are some individuals who would prefer individual exercise, we were unable to recommend it as an option as group exercise was demonstrated to be cost effective and likely to be more cost effective than individually delivered programmes. However, the recommendation emphasises that people's specific needs, preferences and capabilities are to be taken into account when choosing the type of exercise.
- Faculty of Sport and Exercise Medicine: Other considerations section: potential for future consideration / research to further investigate sub classification systems for patients with non specific low back pain with or without sciatica and trialling specific exercise therapy according to the sub classification.
  Reply NICE: Unfortunately, the GDG are unable to make research recommendations on topics that have not been reviewed in the guideline. As sub classification systems were not addressed in this review, the GDG are unable to make a research recommendation on this topic.
- Chartered Society of Physiotherapy***:*** Whilst we welcome a recommendation focused on exercise, this recommendation highlights some inconsistencies in how the GDG has approached the evidence. We are unsure as to why the recommendation is only a "consider" recommendation rather than an "offer" when the evidence suggests that supervised exercise is more effective than self-management and unsupervised exercise in reducing pain, improving function, and decreasing healthcare utilisation. This is inconsistent with the strength of recommendation given for self-management, and we would recommend that recommendations about exercise are "offer" instead of "consider".
  Reply NICE: A consider recommendation was made for exercise as although there was evidence of an effect, there was not strong consistent high quality evidence providing certainty of the effect. This is as per guidance in the NICE manual for strength of recommendations**.**
- Chartered Society of Physiotherapy: We are also unclear as to why there is a focus on group-based exercise interventions, when there is no evidence in the review to suggest that this is superior to individual exercise interventions. The impact of higher cost associated with individual exercise is used as a reason for this decision, yet this is not based on economic evidence or economic modelling. Physiotherapists also report concerns over group exercise with regards to DNA rates. In light of this, we would suggest altering the recommendation to "*offer* supervised exercise that incorporates individualisation and progression of exercises". This can be delivered in a group or individual basis, depending on the needs of the individual.
  Reply NICE: The GDG found no difference between group and individual exercise in terms of clinical evidence. Although there was limited cost effectiveness evidence for individual exercise, group mind body exercise was shown to be cost effective compared to usual care. Furthermore, although group mixed exercise was more costly and less effective compared to cognitive behaviour approaches, the GDG considered that group mixed exercise may be cost effective compared to usual care. Therefore, after reviewing the cost effectiveness evidence, they concluded that group exercise would incur fewer costs than individual exercise and consequently recommended group exercise.
- Warwick Clinical Trials Unit: The UK BEAM trial has been included as evidence in the combination manual therapy adjunct (Table 158), but not in the exercise therapy adjunct. First, it is not clear why manual therapy as an adjunct has been considered, but exercise therapy as an adjunct has not (this is inconsistent). Moreover, it is not clear why one arm of the UK BEAM has been deemed suitable (combined exercise and manipulation), whilst the exercise arm has not. In all three arms, the interventions were adjuncts to best usual care. In the questions on exercise the UK BEAM trial is listed neither in included nor excluded studies. Given the size and quality of UK BEAM, including it under these questions may have changed conclusions and so why it was omitted needs to be clear.
  Reply NICE: The exercise adjunct arms of the UK BEAM trial have now been added to the exercise review.
- Royal College of Chiropractors: The GDG apparently based its decision to recommend *group* exercise rather than *individual* exercise on cost. We question whether the basis of this decision is made sufficiently clear to health professionals and members of the public, particularly in the summary (short version) document. Individual exercise prescription, both supervised and self-supported, is commonly provided as part of the package of care given by chiropractors, and other practitioners who deliver manual therapy, and so it may be unnecessary for patients seeing these practitioners privately or within the NHS to be prescribed separate group exercise classes. The full

exercise recommendation highlights the importance of taking people's specific needs, capabilities and preferences into account when choosing the type of exercise. We suggest that it will be challenging to deliver this in a group exercise situation and that individual exercise prescription provides a better prospect of delivering the required patient support.

Reply NICE: Whilst we recognise that there are some individuals who would prefer individual exercise, we were unable to recommend it as an option as it was not demonstrated to be cost effective. However, the recommendation emphasises that people's specific needs, preferences and capabilities are to be taken into account when choosing the type of exercise. The short version of the guideline is designed for clinicians to refer to the recommendations. The rationale behind the recommendations can be found in section 9.6 of the full guideline.

- Institute of Osteopathy: The recommendation is for group exercise programmes, while stating a need to take into account specific preference and capabilities (page 4, short version). Most clinicians provide specific bespoken exercises programmes, to take into account of specific presentations and capabilities, as recommended by the guidance (page 4). The experience of clinicians is that there is greater compliance by patients with bespoke programmes, compared the high drop-out rates that are commonly seen in group classes as reported in the studies. According to our researchers the review of the evidence does not support the use of group exercise over individual bespoke programmes. Therefore, the implementation of a group exercise programmes could have significant cost implications if organised and implemented in an NHS setting, while seeing high drop-out rates and not meeting the specific needs of the patients as required. We also suggest the clarification of the implementation of exercise as part of the multi-modal package to acknowledge the role manual therapist as qualified in delivering bespoke exercise programmes. (See comment 7 on the implementation of multi-modal care.)

  Reply NICE: The evidence showed no difference between individual and group exercise in terms of clinical outcomes, however, as group exercise is more cost effective, this was recommended rather than individual exercise. The GDG are aware some patients may not fully engage with group exercise, however state in the recommendation that people's specific needs, capabilities and preferences should be taken into account when choosing the type of exercise.
- United Chiropractic Association**:** This recommendation, particularly the group aspect of this programme, will be a challenging change in practice because of a concern over foreseeable waiting times. We are concerned that this recommendation must take into account a timely and appropriate implementation based on the patient's history, examination and assessment of the nature of their particular cause of the NSLBP and Sciatica presentation. If this clinical due diligence cannot be accomplished within the NHS due to waitlist, then allied healthcare alternatives delivered in a timely manner should be considered to avoid unnecessary chronicity.

  Reply NICE: NICE guidelines are created to improve the standard of care, based on evidence. Difficulties with implementation do not warrant not striving for the highest standard of care. NICE guidelines only cover settings in which NHS funded care is received, therefore we are unable to make recommendation concerning other healthcare alternatives.
- Yoga Studio International*:* Yoga, by its very nature is not ipsefacto a form of 'exercise' but an holistic practice involving body, mind and spirit (breath) and it is the combination of these that makes it a uniquely suitable practice for people with both LBP and Sciatic pain. Yoga Therapy as distinct from general yoga classes should be considered as a major NHS asset in the treatment of LBP with or without Sciatic pain. In order to facilitate this more properly trained therapist will be required.

  Reply NICE: For the purposes of this review yoga was classified as a form of 'mind-body' exercise. Yoga classes and yoga therapy were not considered as distinct.
- Pain concern: Why should exercise classes be "within" the NHS?. A small but growing number of leisure centre staff are trained in long term conditions. There are teachers trained by the Yoga for Healthy Lower Backs Institute who train teachers to follow an evidence based approach

  Reply NICE: NICE guidelines are produced for the NHS and only cover settings in which NHS funded care is provided.
- Royal College of General Practitioners: Health care professional doing initial assessment can usefully teach simple mobilisation techniques such as McKenzie exercises or dynamic stretches. They can also apply simple manipulation if they are skilled in this. This will particularly be the case if the initial assessment is done by a physiotherapist (as should probably be the case most often). (DA)

  Reply NICE: For many of the interventions included in the guideline, levels of training may differ according to the expertise of the practitioner, however this cannot be assessed within the systematic review and it has been assumed that unless otherwise stated, that the people delivering the interventions are trained to do so. Professionals delivering interventions should be appropriately trained to do so.

- British Council for Yoga Therapy: We are concerned that this recommendation is not specific in its guidance. The term mind-body exercise could be construed to mean a number of different techniques and specific mention of the relevant mind-body group exercise programmes that NICE are recommending, such as Yoga, would be helpful.
  Reply NICE: The protocol for the exercise review outlines examples of relevant mind-body programmes.

NICE 2016 first version of recommendation: 1 clinical recommendation (March 2016)

8. Consider a group exercise programme (biomechanical, aerobic, mind-body or a combination of approaches) within the NHS for people with a specific episode or flare-up of low back pain with or without sciatica. Take people's specific needs, preferences and capabilities into account when choosing the type of exercise.

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

No comments

KCE 2017 final recommendations on exercise therapies (February 2017)

7. Consider an exercise programme (specific exercises or a combination of approaches) for people with low back pain with or without radicular pain. Take patient's specific needs, capabilities and preferences into account when choosing the type of exercise programme.

(weak recommendation based on moderate to very low quality evidence from RCTs)

7.6. Postural therapies

Postural therapies in patients with low back pain ± radicular pain

NICE search question

"What is the clinical and cost effectiveness of postural therapies in the management of non-specific low back pain and sciatica?"

Introduction based on the draft version of NICE guideline (March 2016)

- Postural therapies aim to prevent or reduce low back pain by focusing on the correction of postures that are theorised to be suboptimal and place excessive or damaging loads upon the spine. Postural therapy also focuses on exercises and practice at adopting the postures and movements that are considered healthy**.**
- There are various disciplines of postural therapy. The **Alexander technique** is a specific approach that involves tailored education, movement and breathing retraining over a 12 number of treatment sessions with an instructor, supplemented by practice with a focus on reducing muscle tension and spinal load.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with non-specific low back pain • People aged 16 or above with sciatica
Intervention(s)	Postural therapies: • Postural education/exercise • Alexander technique
Comparison(s)	• Placebo/Sham/Attention control • Usual care/waiting list • To each other • Any other non-invasive interventions in the guideline • Combination of interventions: any combination of the non-invasive interventions in the guideline
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (> 30% improvement in pain or function) • Adverse events: morbidity • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

Single and combined interventions are presented separately

- **Single intervention**: Two randomised trials were identified comparing Alexander technique lessons (6, 10 or 24 lessons) with usual care, massage or mixed exercises. The population included was people 18-65 year old with a recurrent episode of non-specific low back pain, scoring 4 or more on the Roland Morris disability scale (RMDQ) at time of recruitment. A further search for cohort studies was conducted, but without providing additional studies. Thus, evidence on postural therapies as single intervention concerned only Alexander technique lessons.

  Programme of Alexander technique lessons versus usual care, exercise prescription or massage

  - **Patients with recurrent LBP without sciatica, scoring ≥4 on the RMDQ scale:**
    - Potential clinical important benefit in **quality of life (SF-36) at long term** with 6 lessons of Alexander technique for all 3 comparisons (usual care, massage or exercise prescription) but no difference for pain, function, primary care contacts and prescriptions (moderate to low quality; n = 118, 109 or 122).
    - When the number of Alexander technique lessons was increased to 24, improvements were seen for **quality of life, pain and function** for all 3 comparisons (low to moderate quality; n = 121, 112 or 125). No difference for primary care contacts and prescriptions.
    - No evidence was available to assess the clinical benefit of Alexander technique in terms of psychological distress.
  - **Mixed population (recurrent LBP with or without sciatica), scoring ≥4 on the RMDQ scale**:
    - Potential clinically important benefit in **function (RMDQ 0-24) at long term**, but not in short term with 10 lessons of the Alexander technique compared to usual care (1 study; low to very low quality; n = 28). No difference in term of pain severity at any time points. No other outcomes measured.
    - Compared to mixed exercise combining stretching, strengthening and aerobic exercises, there was no difference with 10 lessons of the Alexander technique for the single measured outcome: function at short term (1 study; very low quality; n = 29).

  Alexander technique (24 lessons) versus Alexander technique (6 lessons)

  - **Patients with recurrent LBP without sciatica, scoring ≥4 on the RDS:**
    - Clinically important benefit with 24 lessons for the **physical domain of quality of life (SF-36) and for function (RMDQ) at long term (>4 months-1 year)** (1 study, low quality; n = 119).
    - No clinically important difference for the mental health domain of quality of life, pain intensity, primary care contacts and prescriptions (moderate to low quality; n = 119).
    - No evidence for other outcomes at short term nor for psychological distress at any points of time.

- **Combined interventions:** Two studies looking at combinations of non-invasive interventions (with postural therapy as the adjunct) were included. One concerned a combination of 10 lessons of Alexander technique and mixed group exercise (stretching, strengthening and aerobic); the other focused on postural therapy added to a multidisciplinary biopsychosocial rehabilitation (MBR) programme i.e. physical, psychological and education components.

  Combination of 10 lessons of Alexander technique and mixed group exercise compared with usual care or with mixed exercise alone

  - **Mixed population (recurrent LBP with or without sciatica), scoring ≥4 on the RMDQ scale**:
    - Compared with usual care, potential clinically important benefit for **long term function** in favour of the combination Alexander technique and mixed group exercise. However, no difference for short term function or pain at any time points (1 study; low and very low quality; n = 28).
    - Compared to group mixed exercise, no difference for the single measured outcome: short term function (1 study; very low quality; n = 29).

  Programmes combining postural therapy (head posture corrective exercise program) with 3 elements of a multidisciplinary biopsychosocial rehabilitation (MBR) i.e. physical, psychological and education components versus 3 elements MBR

  - **Patients with LBP and sciatica**
    - No clinically important difference in back pain, leg pain or function (ODI 0-100) at short term (1 study; moderate quality; n=154).

Economic evaluation

- **One economic evaluation was identified that included Alexander technique lessons as a comparator.**
  - This cost-utility analysis (partially applicable; potentially serious limitations) concerned people with low back pain (without sciatica). Compared to usual care, Alexander technique lessons were cost effective (both alone and as an adjunct to an exercise prescription). There was some uncertainty (depending on concurrent treatment) but **24 lessons is probably the most cost effective option (over 6 lessons**).
  - When considered amongst a selection of active treatments, the combination of Alexander technique (24 lessons) with unsupervised exercise (exercise prescription) was the most effective (highest QALYs) and most cost effective option from usual care, unsupervised exercise (exercise prescription), soft tissue techniques (massage), exercise prescription + massage, Alexander technique lessons (6 lessons), exercise prescription + Alexander technique lessons (6 lessons).
- No relevant economic evaluations were identified relating to Alexander technique in people with sciatica.

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:** The most critical outcomes for decision-making agreed by the GDG for this review question were health-related quality of life, pain severity, function and psychological distress**.** Within adverse events, it was acknowledged that the Alexander technique and other postural therapies are recognised as safe interventions in general, and therefore morbidity was a less relevant outcome in this case. The GDG agreed that mortality was not relevant as an outcome for this review and so was not included within the review protocol.
- **Trade-off between clinical benefits and harms**
  - **Postural education:** Given that no RCT or observational study evidence was identified relating to the effectiveness of postural education/exercise, the GDG agreed a recommendation should not be made.
  - **Alexander technique:**
    - When compared with usual care in people with low back pain (without sciatica), a programme of 6 Alexander technique lessons showed improvement in quality of life. This was accompanied by only a very small reduction in pain and improvement in function as well as a small increase in primary care contacts and a reduction in prescription use. However, these differences were considered too small to be clinically important.
    - When 24 Alexander technique lessons were provided, an improvement in physical quality of life, pain and function was demonstrated in people without sciatica. This was agreed by the GDG to be clinically important and was accompanied by a very small increase in healthcare utilisation. The GDG considered the benefits of a longer course of treatment to outweigh the harms.
    - When 10 lessons of Alexander technique was provided in the overall population (with or without sciatica), a clinically important benefit of long term function was demonstrated compared to usual care. However, no other clinically important benefits were demonstrated. The GDG noted that this evidence was from a feasibility trial with a small number of participants
  - **Active interventions**:
    - When compared with provision of an exercise prescription, the programme of 24 lessons of Alexander technique in population without sciatica showed an improvement in quality of life, pain and function at the longer term follow-up, which was considered by the GDG to be clinically important and to outweigh the very small increase in prescriptions associated. The same conclusion occurred when 24 lessons of Alexander technique was compared with massage sessions (6 weeks).
    - In the overall population, no benefit for short term function was found for 10 lessons of Alexander technique compared to mixed exercise, however no other outcomes were measured. Although no evidence was reported in the included study on occurrence of adverse events, the GDG highlighted that the Alexander technique was a low risk treatment for patients, and serious adverse events were unlikely.
  - **Combinations of interventions**:
    - In the **mixed** population **(±sciatica)**, 10 lessons of Alexander technique combined with mixed exercise showed a clinically important benefit of long term function compared with usual care. However, no benefits were found for pain. When Alexander technique and mixed exercise were compared with mixed exercise, no clinically important benefit was observed.

- In people with sciatica, postural lessons combined with a package of treatment including physical, psychological and educational components, showed no clinically important additional benefit.

The GDG agreed that the evidence reviewed was promising in terms of potential quality of life for people with low back pain, however the evidence in favour of the Alexander technique was taken from a single study. The GDG agreed that further research was warranted to test this further.

- **Trade-off between net clinical effects and costs:**
  - **Postural education:** No economic evaluation found
  - **Alexander technique:** One cost-utility analysis based on the ATEAM RCT suggested that Alexander technique lessons may be cost effective for the NHS. However, the GDG concluded that the evidence of cost-effectiveness was only relevant if they were confident in the evidence for effectiveness of the Alexander technique from the ATEAM RCT and this was not the case. While there is evidence of effectiveness for the Alexander technique, this was based only on a single trial and since recommending the intervention would lead to a significant change in practice, **the GDG decided more evidence was required before making a recommendation.**
- **Quality of evidence:**
  - ranged from moderate to very low quality due to high risk of bias (absence of a description of usual care, high rate of missing data (>20%), differential rate in missing data between groups and difficulties surrounding the issue of adequate blinding with such interventions) and in some cases significant imprecision in the effect estimate.
  - Limited information about the other care, particularly doctor-led exercise prescription received; this meant it is not possible to tell if it is the Alexander technique itself or simply the contact with a therapist that is causing any effects seen in the first trial. All the data reported from this trial were longer-term follow-up data (> 4 months - 1 year), and none of the outcomes were measured at ≤4 months. It was recognised that the nature of the intervention itself may preclude designing an adequate placebo-controlled study, however, it was agreed that concurrence of results in more than one pragmatic trial with clear descriptions of comparator interventions and intention to treat analyses would give greater confidence to the GDG in recommending the intervention than the single trial currently available.
  - Further, given that a second study did not support these results, and the fact that all evidence came group single studies of a small sample size, it was decided that no recommendation would be given for postural therapies. The economic analysis was judged to be partially applicable with potentially serious limitations. The latter largely due to the limitations in the reporting of uncertainty within the analysis. However, the available information does suggest that the conclusion is probably reasonable robust.
- **Other considerations**
  - Overall the GDG concluded that while the evidence for the Alexander technique was promising they were not sufficiently confident in the effectiveness of the intervention to recommend a significant change in practice. Given the potential benefit demonstrated for the Alexander technique in the evidence reviewed, the GDG considered making a research recommendation on this therapy to be conducted in order to re-evaluate its use in the future. It was however noted that following completion of the ASPEN feasibility trial (included in this review), it is likely that a larger trial will follow and therefore a research recommendation was not prioritised for this topic.

No NICE 2016 recommendation on this topic

Belgian GDG considerations mentioned in the Lime survey at the beginning of June 2016

Agreement with the absence of recommendation in this topic: 13 Yes, 0 No, 2 no opinion, 0 out of competence, 0 no answer, 1 not completed

- **Comments:**
  - Alexander technieken zijn niet geïntegreerd in de opleding kinesitherapie - ergotherapie. Er zijn volgens mij ook weinig goed methodologische studies over deze technieken
  - Why do they cite only the Alexander technique? Why not the 'Global Postural Reeducation' for example: http://www.ncbi.nlm.nih.gov/pubmed/21162726 If not discussed here, I suppose that the Pilates exercises (which could be also considered as "postural exercises") will be reported in another section (because there are several scientific studies and reviews on the topic)

- Because postural control seems important in low back pain mainly on the long term and in the prevention of relapse, re-evaluation in future should be recommended.
- One problem of these techniques is that they are very dependent on the caregiver.

- **Cochrane review on Pilates 2015**: **http://www.cochrane.org/CD010265/BACK_pilates-for-low-back-pain**

Belgian GDG comments during the GDG meeting on the 29th June 2016

No comment

- **Conclusion: Agreement with the absence of recommendation on this topic**

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30th November 2016)

- Society of Teachers of the Alexander Technique: Parts of the statement above are highly problematic, namely:
  - *'A second study did not support these results'*: The second study in question was a small, methodological feasibility study (ASPEN) whose design specifically stated that it was not sufficiently statistically powered to be able to show clinical benefit. Thus, in the Methods section of the ASPEN publication it states: 'no formal sample size calculation was appropriate' and 'the analysis of effectiveness was underpowered, we performed an intention-to-treat analysis of covariance to estimate the main effects of the interventions'. The results state 'As expected given the very limited power, most outcomes did not reach significance at the 5% level and so the lack of significance should be interpreted very cautiously...(changes) were nearly always in a beneficial direction, suggesting that type 1 errors are unlikely. The estimates suggest that clinically important improvements were probably occurring'. The study concluded 'The exploratory analysis of clinical outcomes suggests that the estimates of treatment effects are likely to be clinically important....in particular 10 Alexander technique lessons appeared to provide the same order of benefit as 24 Alexander technique lessons did in the ATEAM trial. As a secondary point, ASPEN was only a 6-month study (unlike the 1-year ATEAM trial); since **Alexander lessons are not a treatment for back pain but a method for improving movement coordination and postural support, through self-management it would be anticipated that effectiveness would not diminish over time but may actually improve** (as seen in ATEAM). Elsewhere in the report the GDG do acknowledge that ASPEN was **only a feasibility study** but this has not prevented the above unsupported conclusion being drawn.
  - *All evidence came (from) group single studies of a small sample size:* This point is debatable as, for some reason, all the data that the GDG has considered from the ATEAM trial come from the analyses of individual groups. The main analysis of the study (with its larger group sizes) does not appear to have been considered, namely 6 Alexander lessons plus/minus exercise versus usual care and 24 Alexander lessons plus/minus exercise versus usual care. The ATEAM trial randomised nearly 600 individuals followed up for a year and thus represents the first substantial randomised controlled trial evidence for the effectiveness of Alexander lessons for people with chronic back pain. We agree that more evidence is needed to confirm the findings of ATEAM and address key gaps in the evidence.
  - *'Based on limited evidence':* We acknowledge that the evidence for the effectiveness of Alexander lessons for people with low back pain is currently relatively limited but do not agree that the evidence base consists of a single trial only (ATEAM trial). Since the time when the literature searching for the draft guidelines was conducted, the ATLAS trial has been published. This large randomised controlled pragmatic trial also shows clinically meaningful benefit of Alexander Technique lessons in primary care patients who have chronic pain associated with the spine and its musculature, in this case at the level of the neck. The ATLAS trial demonstrated significant long term (1 year) reductions in chronic neck pain and associated disability following 20 Alexander lessons (N=517). Since the ATLAS trial provides robust evidence of the effectiveness of Alexander lessons for people with pain associated with the spine and its musculature, it can be considered as strongly supportive of the ATEAM trial findings. Further supportive data come from a small randomised controlled trial that does not appear to have been considered in the current NICE review. This was a small (N=91) randomised controlled trial that reported significant benefit in pain severity and disability following Alexander Technique lessons for patients with chronic non-specific low back pain. The trial has not been published in a peer-review journal and would be considered to be of very low quality, so can only be considered as preliminary supporting evidence. A study report is available and the methodology and findings have also been described in a systematic review.
  - *'as this is a usual care comparison it is not possible to tell if it is the technique itself or simply the contact with a therapist that is causing any effects seen'*. Firstly, as mentioned, a comparator group of massage was included to control for non-specific effects of contact and individual attention. Secondly, as the GDG

acknowledges, clinical outcomes were significantly superior in the Alexander lesson groups compared with the massage group. Thirdly, the endpoint for the primary outcome measure was at 1 year, several months after the intervention had ceased, so it would be surprising if non-specific benefit persisted to this point. Fourthly, it is important to take into account that pragmatic trials to estimate the effectiveness and cost-effectiveness of interventions are the primary source of evidence needed: the key piece of evidence for any intervention is the estimate of the total effect of the intervention (i.e. the combined specific and non-specific elements of an intervention) since these are the benefits that patients experience.

- Alexander technique cannot be considered as postural therapy.
- Pain frequency has not been considered as an outcome measure.
- We recognise the aim of Alexander lessons to be *'focusing on the correction of postures'* which is the definition of postural therapy given in the draft guidelines. The Alexander Technique is a taught practical educational approach for improving coordination of postural support, movement, breathing and control of response; Alexander lessons can lead to therapeutic and self-development-related benefits.

Reply NICE: The GDG are aware of the nature and length of the ASPEN study and took this into account when weighing up the evidence and making recommendations. We have now included the Alexander (6 lessons) + exercise prescription, and Alexander (24 lessons) + exercise prescription versus usual care in the combination section of the postural review. Although both combination arms showed a clinically important benefit on pain, function and quality of life, the GDG agreed it was not sufficient to make a recommendation for the Alexander technique due to the fact that all evidence favouring the Alexander technique still came from just a single study. The GDG have considered the two further studies mentioned however, unfortunately they are not includable in this review; the ATLAS trial consisted of a population with neck pain, rather than low back pain, and therefore is beyond the scope of the guideline. Additionally, the Vickers trial was unpublished at the time the systematic review was undertaken. Regarding massage as an attention control, all of the interventions included in the review were discussed and agreed by the GDG; therefore massage was considered an active intervention, as this is an intervention that is being considered within the manual therapies review in this guideline, rather than an attention control. Therefore, the statements regarding difficulties surrounding the issue of adequate blinding and lack of sham or attention control have not been changed. The overall quality rating of the outcomes for the ATEAM and ASPEN trials have not changed in the review and therefore the GDG's conclusion remains unchanged. For the purpose of this review, Alexander technique was appropriately classified as postural therapy. The priority outcomes were defined in the scope of the guideline, with pain severity specifief, rather than frequency.

While the GDG recognises the complex nature of the Alexander Technique, and the description provided by STAT, it was felt that due to the focus of the technique being on postural movements and support, the categorisation of the technique as 'postural therapy' was appropriate. We acknowledge that falling under the broad heading of 'postural therapy' may be an over-simplification, but each comparison was labelled to state the technique used and the GDG were made aware of the components of each trial, and these were stated in detail in the evidence tables as described by the included studies. Since the Alexander technique requires attendance at lessons where people are provided with guidance and supervision from teachers, this does not fit into our definition of self-management, in the same way that that being asked to walk more would be considered self-management as it isn't monitored or taught and therefore wouldn't be classified as aerobic exercise in the exercise review. The GDG are aware that the two interventions included in the review (alexander technique and head posture corrective exercises) are distinct, but feel that both fall under the overarching heading of postural therapy, in the same way that yoga and aerobic exercise are distinct but both fall under exercise.

NO NICE final recommendations on postural therapy (November 2016)

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

The Alexander technique is considered as different from postural therapy.

"The Alexander Technique is a way of learning to move mindfully through life. The Alexander process shines a light on inefficient habits of movement and patterns of accumulated tension, which interferes with our innate ability to move easily and according to how we are designed. It's a simple yet powerful approach that offers the opportunity to take charge of one's own learning and healing process, because it's not a series of passive treatments but an active exploration that changes the way one thinks and responds in activity. It produces a skill set that can be applied in every situation. Lessons leave one feeling lighter, freer, and more grounded."

"The Alexander Technique is a method that works to change (movement) habits in our everyday activities. It is a simple and practical method for improving ease and freedom of movement, balance, support and coordination. The technique teaches the use of the appropriate amount of effort for a particular activity, giving you more energy for all your

activities. It is not a series of treatments or exercises, but rather a reeducation of the mind and body. The Alexander Technique is a method which helps a person discover a new balance in the body by releasing unnecessary tension. It can be applied to sitting, lying down, standing, walking, lifting, and other daily activities..."

NO KCE 2017 final recommendations on Alexander technique and on postural therapy (February 2017)

7.7. Orthotics and appliances

Orthotics and appliances in patients with low back pain ± radicular pain

NICE search question

"What is the clinical and cost effectiveness of orthotics and appliances in the management of low back pain and sciatica?"

Introduction based on the draft version of NICE guideline (March 2016)

- Orthotics and specialist footwear may be used for a number of reasons to treat or prevent back pain (correction of proposed leg length or foot posture abnormalities, with the goal of normalising or altering lower limb, pelvis and trunk mechanics and load, training and enhancing balance and proprioception or reducing the lumbar lordosis). There is a broad range of products, and the materials used vary, with soft, semi-rigid and rigid orthotics available.
- There is also a wide range of lumbar corset, belts and supports available, which are considered as appliances or devices. They vary widely in design, materials, the degree of rigidity and the area to which they are designed to provide support. The devices are commonly used with the aim of providing support to or reducing the load on the lower back and/or pelvic joints. They can also be used to attempt to correct deformity, limit motion or provide a type of massage or heat to the area.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with non-specific low back pain • People aged 16 or above with sciatica
Intervention(s)	• Orthopaedic shoes • Belts/corsets
Comparison(s)	• Placebo/sham/attention control • Usual care/waiting list • To each other • Any other non-invasive interventions in the guideline • Combination of interventions: any combination of the non-invasive interventions in the guideline
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (> 30% improvement in pain or function) • Adverse events: morbidity • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

- Twelve randomised controlled trials and one cohort study were included in the review for single interventions; one study looking at combinations of non-invasive interventions (with orthotics as the adjunct) was also included in this review: foot orthotics versus placebo/sham/usual care (3 RCTs and 1 cohort study), corsets and belts versus usual care (4 RCTs), analgesics (1 RCT), massage (2 RCTs) or manual therapy (3 RCTs).
- Five Cochrane reviews were identified but could not be included in the review due to methodological issues (e.g. combined data from RCTs with observational studies). The studies included in these reviews were individually assessed and included if they matched the review protocol.

Belts/Corsets

- **Low back pain population (without sciatica)**: Very low quality evidence from single studies (n = 38, 90, 190 and 456) reporting on the short term (less or equal to 4 months) use of lumbar corsets compared with usual care, manipulation or paracetamol, demonstrated no clinically important benefit for function or pain severity.
- However, compared with massage, 1 study demonstrated that the short-term use of lumbosacral belts had a clinically important benefit on function (very low quality; n =27), although no clinically important benefit for improving pain severity compared with massage was observed in another single study (low quality; n = 57).
- Low quality evidence from 1 very short term study (2 weeks; n=127) comparing both inextensible and extensible corsets with standard care showed no clinically important benefit for improving function for corsets in general and extensible corsets, however when focusing on inextensible corsets a small clinical benefit was observed. However there is serious imprecision associated with this result. No benefit was observed for any corset type with respect to improvement in pain severity.
- No evidence was available to assess the clinical benefit of belts/corsets in terms of quality of life, nor in the population of **people with sciatica**. No comparison with sham or placebo was available.

Foot orthotics

- **Low back pain population (with sciatica):** When compared with placebo insoles, evidence from 1 study (n = 51) demonstrated a clinical benefit of wearing customised insoles on pain severity (moderate quality) and function (low quality). There was also low quality evidence from 1 study (n = 48) to suggest the use of foot orthotics has a clinically important benefit on pain severity when compared to usual care; however, no clinically important difference in function was observed (very low quality). No evidence was available to assess the clinical benefit of foot orthotics in terms of quality or life or psychological distress. No comparison with sham was available.
- **Low back pain population (without sciatica):** There was no clinically important benefit observed with rocker sole shoes when compared with flat sole shoes for function, pain, anxiety or depression at either short or longer term (low to moderate quality; 1 study; n = 100). Additionally, low quality evidence from the same study suggested a clinically important benefit favouring the flat sole shoes, rather than rocker sole shoes, for health-related quality of life in both the short and longer term. One non-randomised study also found no clinical benefit of foot orthotics compared with usual care for function (very low quality; n = 48).

Combinations – orthotics

- **Low back pain population (with or without sciatica):** When compared with electrotherapy and mixed modality manual therapy, evidence from 1 study (n 20 = 58) demonstrated a clinical benefit of using orthotics (corsets) as an adjunct on pain and function (low quality) at less or equal to 4 months. No other relevant outcome measures were reported

Economic literature

- No relevant economic evaluations were identified.
- For the consideration of cost effectiveness, not only unit costs of the orthotics but also additional costs, e.g. appointment for fitting, needs to be taken into account.

NICE GDG considerations on orthotics and appliances (March 2016)

- **Relative values of different outcomes:** The most critical outcomes for this review question were pain severity, function, psychological distress and health-related quality of life. No evidence was found for responder criteria (for pain and function), healthcare utilisation and adverse events. Mortality was not considered a relevant outcome for this review.
- **Trade-off between clinical benefits and harms:**
  - **Belts/Corsets:** The GDG agreed there was insufficient evidence to support a positive recommendation for the use of belts or corsets as a treatment for LBP. The only benefit observed was for lumbosacral belts when compared to massage in terms of function but not pain. The evidence for the use of corsets when given as part of a combined treatment with electrotherapy, massage and traction did indicate some benefit for pain and function but this evidence was all from single small studies, and no evidence was found for their use in people with sciatica. The evidence identified was agreed as sufficient to recommend that belts and corsets should not be used for the management of low back pain with or without sciatica.
  - **Foot orthotics:** Some evidence of benefit was found from the use of customised insoles compared to placebo in improving pain and function for people with LBP and sciatica. However, this evidence was from a small single study. There was evidence to suggest the use of foot orthotics may have a clinically important benefit on pain severity when compared to usual care in patients with LBP and sciatica, however the evidence was of low quality and from a single study and no clinically important difference in function was observed. When rocker sole shoes were compared with flat sole shoes no benefit was observed favouring rocker sole shoes for any of the reported outcomes in either the short or long term follow-up. It was noted that health-related quality of life was in fact, worse in the rocker sole group at both the short and longer term time points. The GDG therefore agreed that there was no good evidence that foot orthotics or rocker soles were of benefit to people with low back pain with or without sciatica, and recommended against their use.
- **Trade-off between net clinical effects and costs:** No economic evaluations identified; orthotics are currently often purchased by the patient. However, if prescribed by the NHS, there will be a cost associated with the orthotics themselves and potentially healthcare professional time if a referral is made to a podiatrist, orthotics or similar. If orthotics are effective, upfront costs may be offset by downstream cost savings due to reduced healthcare utilisation or may be justified due to the benefits to the patient. Given the lack of sufficient evidence of clinical benefit for belt/corset, intervention costs were not considered justified. Although some indications of possible benefit were seen for foot orthotics, overall the GDG concluded that it was insufficient to support a conclusion of clinical benefit and thus also insufficient to justify intervention costs.
- **Quality of evidence:** The quality of evidence in this review ranged from moderate to very low. All the studies included in this review were assessed as having serious or very serious risk of bias (e.g. difficulty of adequate blinding with such interventions). There was also a lack of detail provided about the care that the 2 study groups received apart from the intervention, and therefore, it was not possible in some cases to assess whether the care in the 2 groups was comparable (risk of overestimating effects on subjective outcomes such as pain and function). The attempt to achieve blinding by the use of a placebo foot insole in one study was considered insufficient due to the explicit visual differences between the placebo and customised foot insoles. There was also possible error in outcome reporting when comparing foot orthotics to placebo (pain severity appears to be reported on a scale of 0-10, but reported as a scale of 0-100).
- **Other considerations:** The GDG agreed that a research recommendation was not a priority for this intervention.

NICE 2016 recommendations on orthotics: 3 clinical recommendations (draft March 2016)

8. Do not offer belts or corsets for managing non-specific low back pain with or without sciatica.
9. Do not offer foot orthotics for managing non-specific low back pain with or without sciatica.
10. Do not offer rocker sole shoes for managing non-specific low back pain with or without sciatica..

Belgian GDG considerations on orthotics and appliances mentioned in the Lime survey at the beginning of June 2016

Agreement with the content of the NICE recommendation 8: 13 Yes, 1 No, 0 no opinion, 1 out of competence, 1 no answer, 3 not completed

- **Comments from the one respondent who does not agree:**
  - in patients with multilevel discopathy (perhaps this is not more aspecific LBP) not better with physical therapy , pain killers and infiltration techniques, a distraction corset may be helpful in lowering pressure on the discs also for older people with multilevel spondylatrosis, a corset may be helpful for pain control

- **Other comments:**
  - I never reviewed the literature on this topic. However, I would go in line with NICE.

Strength of the recommendation 8: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	Only benefit observed was for lumbosacral belts when compared to massage in terms of function but not pain and the evidence for the use of corsets when given as part of a combined treatment with electrotherapy, massage and traction did indicate some benefit for pain and function but this evidence was all from single small studies.
Quality of evidence	Low to very low
Values and preferences	
Costs (resource allocation)	Orthotics often purchased by the patient. Given the lack of sufficient evidence of clinical benefit for belt/corset, intervention costs were not considered justified by NICE 2016.

Agreement with the strength of the NICE recommendation 8: 8 strong, 2 weak, 1 no opinion, 3 no answer, 5 not completed

- **Comments for a strong recommendation**
  - Balance between clinical benefits and harms. Reduce costs.
  - Given the insufficient evidence of clinical benefit, the potential harms and the costs, I think it should be a strong recommendation.
  - Quality of evidence is very low. Costs
- **Comments for a weak recommendation**
  - Weak because quality of evidence is low to very low; otherwise, I would have state "strong"
  - May depend of the representations of the patient. May have a place if light and cheap in patient that can then accept an optimal treatment.

Agreement with the content of the NICE recommendation 9: 11 Yes, 1 No, 1 no opinion, 2 out of competence, 1 no answer, 3 not completed

- **Comments from the one respondent who does not agree:**
  - Voetorthesen kunnen eventueel wel nodig zijn bij aspecifieke lage rugpijn
- **Other comments: /**

Strength of the recommendation 9: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	Some evidence of benefit but from small single study
Quality of evidence	Moderate to very low quality
Values and preferences	
Costs (resource allocation)	Orthotics often purchased by the patient. Although some indications of possible benefit were seen for foot orthotics, overall the NICE 2016 GDG concluded that it was insufficient to support a conclusion of clinical benefit and thus also insufficient to justify intervention costs.

Agreement with the strength of the NICE recommendation 9: 7 strong, 1 weak, 0 no opinion, 4 no answer, 7 not completed

- **Comments for a strong recommendation**
  - Costly and inefficient.

- Balance between benefits and harms
- cfr. Supra (Given the insufficient evidence of clinical benefit, the potential harms and the costs, I think it should be a strong recommendation)
- Weak evidence and costs

- **Comments for a weak recommendation**
  - Evidence: low quality

Agreement with the content of the NICE recommendation 10: 12 Yes, 0 No, 1 no opinion, 2 out of competence, 1 no answer, 3 not completed

No comments

Strength of the recommendation 10: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	No benefit and worse health-related quality of life in the rocker sole group compared to flat sole shoes at both the short and longer term time points. The GDG therefore agreed that there was no good evidence that rocker soles were of benefit to people with low back pain with or without sciatica, and recommended against their use
Quality of evidence	Low to very low quality
Values and preferences	
Costs (resource allocation)	Orthotics often purchased by the patient. Insufficient evidence to justify intervention costs.

Agreement with the strength of the NICE recommendation 10: 6 strong, 3 weak, 0 no opinion, 4 no answer, 6 not completed

- **Comments for a strong recommendation**
  - Costs
  - cfr. Supra (Given the insufficient evidence of clinical benefit, the potential harms and the costs, I think it should be a strong recommendation)
  - Weak evidence/costs
- **Comments for a weak recommendation**
  - Quality of evidence: low
  - Some are cheap and may have a place in case of associated knee or foot problem.

Belgian GDG comments on orthotics and appliances during the GDG meeting on the 16th June 2016:

No comments

Conclusion: recommendation NICE 2016 unchanged

Synthesis of stakeholders' comments and replies from NICE team on draft for public consultation (March 2016)

- British Association of Prosthetists and Orthotists (BAPO): do not agree with recommendations 8, 9, and 10 (against providing belts, corsets, insoles and rocker sole shoes). BAPO would highlight that whilst evidence level is low, the majority of the studies considered did show positive outcomes using these devices. BAPO recognises that prescription of these items is currently a common modality with clinicians generally prescribing such items where professional expertise indicates that prescription may aid the patient to self-manage the condition in acute stages principally to encourage participation in an active lifestyle and aid the return to work (particularly if manual/labour intensive). These goals are greatly supported by this draft guidance. To this end, BAPO would like to see the recommendations amended to the following: '**Do not routinely offer belts/corsets/insoles/rocker sole shoes without identifying that these devices may aid self-management, return to work or maintenance of an active lifestyle. Clinicians should discourage long term reliance upon these devices."** The amended statement highlights that these devices are not to be used for every patient but considered for on a case for case basis as a short term solution to symptoms. NICE do not suggest further research in the area. As evidence levels are low, BAPO would like to see recommendation for further research to support clinicians in identifying those who may best benefit from these orthoses.

Reply NICE: As summarised on pages 344-346, the majority of evidence was not in favour for the use of orthotics and appliances. Of the 8 studies included for belts/corsets, short-term benefit was only seen in limited outcomes from 3 small studies; belts/corsets compared to massage, inextensible corsets compared to standard care (with serious imprecision), and corsets used in combination with manual therapy. Similarly, there was limited evidence in support of foot orthotics from the 4 studies included, with 2 small studies showing benefit of insoles in a total of 3 outcomes, and no benefit seen for rocker sole shoes. The GDG therefore felt confident in recommending against the use of orthotics and appliances for the management of low back pain with or without sciatica. The GDG also felt there was sufficient evidence included in this review; therefore a research recommendation was not required.

- The United Chiropractic Association is concerned that the recommendation of sacroiliac belts/ foot orthotics be considered as an ancillary support if the correct use of said items assists in improving the functional stability and integrity of the spine and its adjacent structures.
  Reply NICE: The GDG agreed that there was no evidence suggesting foot orthotics/ sacroiliac belts were of benefit to people with low back pain with or without sciatica, and recommended against their use. The GDG were therefore unable to recommend their use as an ancillary support.
- South West Yorkshire Partnership NHS Foundation Trust*:* if a patient has a biomechanical cause for their LBP foot orthotics can be helpful in addressing this.
  Reply NICE: The GDG found no evidence that foot orthotics were of benefit to people with low back pain with or without sciatica, and therefore recommended against their use.
- Acupuncture Association of Chartered Physiotherapists*:* mentioned that "With reference to orthotics NICE are now in the ridiculous position of being able to offer insoles for knee OA (even with age related changes) but not Spinal OA despite the presence of forces throughout the kinetic chain".
  Reply NICE: The GDG found no evidence that foot orthotics or rocker soles were of benefit to people with low back pain with or without sciatica, and therefore recommended against their use for this population.

NICE change in the final version of the guideline :

- Evidence on Cochrane reviews added.
- No change in evidence nor in formulation of the recommendations

NICE final recommendations on imaging (November 2016)

9. Do not offer belts or corsets for managing low back pain with or without sciatica.
10. Do not offer foot orthotics for managing low back pain with or without sciatica.
11. Do not offer rocker sole shoes for managing low back pain with or without sciatica.

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

- No comments

KCE 2017 final recommendations on orthotics and appliances (February 2017)

9. Do not offer belts or corsets for managing low back pain with or without radicular pain
10. Do not offer foot orthotics for managing low back pain with or without radicular pain.
11. Do not offer rocker sole shoes for managing low back pain with or without radicular pain.

Strong recommendation

7.8. Manual therapies

Manual therapy in patients with low back pain ± radicular pain:

NICE search question

"What is the clinical and cost-effectiveness of manual therapies in the management of non-specific low back pain and sciatica?"

Introduction based on the draft version of NICE guideline (March 2016)

Manual therapy interventions use passive or active assisted movements, usually delivered by the hands of the practitioner. Typically, they aim to act on the neuromusculoskeletal system focussing on joints and soft tissues to improve mobility and function, and to decrease pain. Techniques include:

- **Spinal manipulation:** a gapping motion of a synovial joint within a spinal segment in response to a force of typically short duration
- **Spinal mobilisation:** joint movement within the normal range of movement
- **Soft tissue techniques:** manual manipulation/mobilisation of soft tissues

Mobilisation and soft tissue techniques are performed by a wide variety of practitioners; whereas manipulation is usually performed by chiropractors or osteopaths, and by doctors or physiotherapists who have undergone additional training in manipulation. Manual therapists often combine a range of techniques in their approach and may also include exercise interventions and advice about self-management.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with non-specific low back pain • People aged 16 or above with sciatica
Intervention(s)	• Soft tissue technique • Traction • Manipulation/mobilisation (including Spinal Manipulation Therapy (SMT) • Maitland technique), mixed modality manual therapy (soft tissue technique +/- traction +/- manipulation/mobilisation)
Comparison(s)	• Placebo/sham/attention control • Usual care/waiting list • To each other • Any other non-invasive interventions in the guideline • Combination of interventions (any combination of the non-invasive interventions in the guideline
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (> 30% improvement in pain or function) • Adverse events: morbidity, mortality

	• Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

- 48 RCTs on single interventions, 18 RCTs on combined interventions
- *New in the final version of NICE 2016*: Seven Cochrane reviews were identified on manual therapies but could not be included for the following reasons:
  - the review was withdrawn from publication (Assendelft 2013);
  - the review excluded spinal manipulation interventions if not in combination with other interventions, and included comparator interventions that were not considered in this guideline, for example nutritional advice (Walker 2010);
  - the review included intra-class comparison and applied no language restrictions to the included studies (Clarke 2007, Furlan 2008, Wegner 2013);
  - the stratification of people with low back pain, low back pain with or without sciatica and sciatica did not match the guideline stratification were not included (Rubinstein 2012, Rubinstein 2011).

  The studies included in these Cochrane reviews were individually assessed and included if they matched the review protocol.

Soft tissue techniques

Evidence for soft-tissue techniques was exclusively from a population of low back pain without sciatica.

- **Patients with low back pain without sciatica**
  - **Soft tissue techniques (massage) versus sham:**
    - **Pain** measured with the VAS demonstrated a borderline clinically important reduction at short term (VAS 0-10; 2 RCTs; very low quality; n=72) favouring massage, however using the McGill Pain scale no benefit was anymore found (McGill 0-78; 3 RCTs; very low quality; n=146). Also no clinical difference in **function** was found (Quebec Disability Score 0-100; 3 RCTs; low quality; n=146). No long term data were reported for pain and function.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Soft tissue techniques (massage) versus usual care:**
    - No clinical difference was found for **QoL** and **pain** (both at short term and long term) (SF-36 0-100; 2 RCTs; very low-low quality; n=473-474, Von Korff 0-10; 1 RCT; moderate quality; n=223-231). Only a clinically important benefit in **function** was found at short term (RMDQ 0-24; 2 RCTs; very low quality; n=473) favouring massage, but this was not sustained at long term (RMDQ 0-24; 2 RCTs; very low quality; n=474).
    - Not reported outcomes: psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Soft tissue techniques (massage) versus acupuncture :**
    - No clinical difference was found for **function**, both at short term and long term (RMDQ 0-24; 1 RCT; very low-low quality; n=166).
    - Not reported outcomes: QoL, pain, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Soft tissue techniques (massage) versus self-management (education):**
    - At short term, a clinically important improvement in **function** was found (RMDQ 0-24; 1 RCT; very low quality; n=160) after massage, but this was not sustained at long term (RMDQ 0-24; 1 RCT; low quality; n=159).
    - Not reported outcomes: QoL, pain, psychological distress, responder criteria, adverse events, healthcare utilisation

Table 18 – Clinical effectiveness of soft tissue techniques compared to sham, usual care and active comparators in patients with low back pain without sciatica

Soft tissue techniques (massage)				
Outcomes	**Massage versus sham**	**Massage versus usual care**	**Massage versus acupuncture**	**Massage versus self-management (education)**
QoL		At short term: • **Physical composite score (SF-36 0-100): no diff** (2 RCTs; very low; n=473) • **Mental composite score (SF-36 0-100): no diff** (2 RCTs; very low; n=473) At long term: • **Physical composite score (SF-36 0-100): no diff** (2 RCTs; low; n=474) • **Mental composite score (SF-36 0-100): no diff** (2 RCTs; low; n=474)		
Pain	At short term: • **VAS 0-10: CIB favouring massage** (2 RCTs; very low; n=72) • **McGill 0-78: No diff** (3 RCTs; very low; n=146) At long term: Not reported	At short term: • **Von Korff 0-10: No diff** (1 RCT; moderate; n=223) At long term: • **Von Korff 0-10: No diff** (1 RCT; moderate; n=231)		
Function	At short term: • **Quebec Disability Score 0-100: No diff** (3 RCTs; low; n=146) At long term: Not reported	At short term: • **RMDQ 0-24: CIB favouring massage** (2 RCTs; very low; n=473) At long term: • **RMDQ 0-24: No diff** (2 RCTs; very low; n=474)	At short term: • **RMDQ 0-24: No diff** (1 RCT; very low; n=166) At long term: • **RMDQ 0-24: No diff** (1 RCT; low; n=166)	At short term: • **RMDQ 0-24: CIB favouring massage** (1 RCT; very low; n=160) At long term: • **RMDQ 0-24: No diff** (1 RCT; low; n=159)

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

- **Patients with low back pain with sciatica**
  - **No evidence found for this patient group**
  - Not reported comparisons:
    - Soft tissue techniques versus sham
    - Soft tissue techniques versus usual care
    - Soft tissue techniques versus acupuncture
    - Soft tissue techniques versus self-management

- **Mixed population (low back pain with or without sciatica)**
  - **No evidence found for this patient group**
  - Not reported comparisons:
    - Soft tissue techniques versus sham
    - Soft tissue techniques versus usual care
    - Soft tissue techniques versus acupuncture
    - Soft tissue techniques versus self-management

In conclusion:

- Studies which compared soft-tissue techniques as a **single intervention** to sham, usual care or active comparators in a population of low back pain without sciatica reported no consistent results on a potential clinical benefit. Compared to sham, conflicting results were found for pain (due to different scales) but no clinical difference in function. In the comparison with usual care and active comparators (acupuncture and self-management), only a short term clinical benefit on function was found in favour of massage (compared to usual care or self-management).
- Studies on soft-tissue techniques in **multimodal interventions** reported: (see results on manual therapy adjunct)
  - No consistent results were found in patients with low back pain with sciatica: the combination of soft-tissue techniques (muscle energy techniques), exercise and self-management revealed a clinical benefit in pain and function (at short term) (in favour of manual therapy) compared to standard treatment (TENS+ laser + massage) combined with self-management, whereas no clinical differences in pain and function were found compared to self-management combined with exercise.
  - In a population of low back pain without sciatica, only a long term benefit was seen in the physical component of QoL (SF-36 0-100). No clinical differences in the other reported outcomes (pain, function, healthcare utilisation).
  - No studies were found in a mixed population (with or without sciatica).

Traction

- **Patients with low back pain without sciatica**
  - **Traction versus sham:**
    - A single study reported only one outcome: no clinical difference was found in short-term **pain** between traction and sham (VAS 0-10; 1 RCT; moderate; n=60). No long term data were reported.
    - Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation
  - Not reported comparisons:
    - Traction versus usual care
    - Traction versus biomechanical exercises

- **Patients with low back pain with sciatica**
  - **Traction versus usual care (UC)**
    - Two studies were retrieved in this patient group, one study on the efficacy of weight-bath traction and one study on mechanical traction. In the study on weight-bath traction: a clinically important short-term benefit was reported on all domains of **QoL** (SF-36; 1 RCT; very low quality; n=36) and **pain** (VAS 0-10; 1 RCT; very low quality; n=36), both in favour of traction. However no clinical difference was found for **function** (ODI 0-100; 1 RCT; very low quality; n=36). In the study on mechanical traction, no clinical differences were found for **function** (ODI 0-100; 1 RCT; very low quality; n=64) and **pain** (VAS 0-10; 1 RCT; very low quality; n=64) (QoL not reported). No long term data were reported in both studies.
    - Not reported outcomes: psychological distress, responder criteria, adverse events, healthcare utilisation
  - Not reported comparisons:
    - Traction versus sham
    - Traction versus biomechanical exercises
  - KCE comment: the study on weight-bath traction (Olah 2008) concerned a population lumbar pain caused by lumbar discopathy (demonstrated by MRI) radiating to the lower extremities and the study on mechanical traction (Fritz 2008) focused on patients with symptoms of pain and/or numbness, signs of nerve root compression but without red flags indicative of non-mechanical LBP.
- **Mixed population (low back pain with or without sciatica)**
  - **Traction versus sham**
    - A clinically important reduction in **pain** at short term was demonstrated in patients who received inversion traction (only outcome reported on inversion traction) (VAS 0-10; 1 RCT; moderate quality; n=29), but not among those who received mechanical traction (at short and long term) (VAS 0-10; 1 RCT; moderate-high quality; n=150-148). No clinical difference was found in **function** after mechanical traction at both time points (RMDQ 0-24; 1 RCT; moderate-high quality; n=150-148). Use of other medical treatments (**healthcare utilisation**) was increased in the mechanical traction group in the short term (1 RCT; moderate quality; n=150), but this between group difference was not sustained at long term (1 RCT; low quality; n=148).
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events
  - **Traction versus usual care (UC)**
    - No clinical difference found in **pain** and **function** at short term (VAS 0-10; 1 RCT; very low quality; n=39 and ODI 0-100; 1 RCT; very low quality; n=39). No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Traction versus biomechanical exercises**
    - Only one long-term outcome (**healthcare utilisation**) was reported in a single study: a lower number of visits to other healthcare practitioners was seen in those receiving traction (1 RCT; moderate quality; n=191)
    - Not reported outcomes: QoL, pain, function, psychological distress, responder criteria, adverse events

Table 19 – Clinical effectiveness of traction compared to sham, usual care and active comparators in mixed population (low back pain with or without sciatica)

Traction			
Outcomes	**Traction versus sham**	**Traction versus usual care**	**Traction versus biomechanical exercise**
Pain	At short term: • **Mechanical traction (VAS 0-10): no diff** (1 RCT; moderate; n=150) • **Inversion traction (VAS 0-10): CIB favouring traction** (1 RCT; moderate; n=29) At long term: • **Mechanical traction (VAS 0-10): no diff** (VAS 0-10; 1 RCT; high; n=148)	At short term: • **VAS 0-10: No diff** (1 RCT; very low; n=39) At long term: Not reported	
Function	At short term: • **Mechanical traction (RMDQ 0-24): no diff** (RMDQ 0-24; 1 RCT; moderate; n=150) At long term: • **Mechanical traction (RMDQ 0-24): no diff** (RMDQ 0-24; 1 RCT; high; n=148)	At short term: • **ODI 0-100: No diff** (1 RCT; very low; n=39) At long term: Not reported	
Healthcare utilisation	At short term: • **Mechanical traction: other medical treatments sought: CIB favouring sham** (1 RCT; moderate; n=150) At long term: • **Mechanical traction: other medical treatments sought: no diff** (1 RCT; low; n=148)		At short term: Not reported At long term: • **Visits to other healthcare practitioners: CIB favouring traction** (1 RCT; moderate; n=191)

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

In conclusion:

- **Traction as single intervention:**
  - Compared to sham, no clinical differences in pain and function were found in a population of low back pain without sciatica (only short term pain reported) and in a mixed population (after mechanical traction). Only an increased healthcare utilisation (use of other medical treatments) was seen in the (mixed) group who received mechanical traction.

- In a population of low back pain with sciatica, the weight-bath traction induced a clinical improvement in QoL and pain compared to usual care, whereas the mechanical traction induced no clinical difference in pain. After either type of traction, no improvement in function could be found. In the mixed population no differences were found in pain and function.
- Compared to the group who received biomechanical exercises, a decreased healthcare utilisation (number of visits to other healthcare practitioners) was found in the (mixed) group who received traction.

- **Traction as adjunct** (see results in multimodal intervention)
  - No benefit (in pain, function and healthcare utilisation) was seen when traction was combined in a mixed population with infra-red therapy and biomechanical exercise (stretching) except for a reduction in medication use both in short and long term compared to infra-red therapy and exercise alone.

Manipulation/mobilisation

- **Patients with low back pain without sciatica**
  - **Manipulation/mobilisation versus sham**
    - No clinical differences were found for **pain** (VAS 0-10; 5-2 RCTs; moderate quality; n=533-229), **function** (ODI 0-100; 4-1 RCTs; low-moderate quality; n=374-63 and Von Korff 0-100; 1 RCT; moderate quality; n=174-166) and **QoL** (except of the SF-36 physical composite at short term, SF-36/SF-12 0-100; 1 RCT; moderate quality; n=174) (Euroqol Health State 0-100; 1 RCT; moderate-high quality; n=174-166 and SF-36/SF-12 0-100; 1 RCT; very low-low-moderate-high quality; n=136-174-166), at short term and at long term.
    - Not reported outcomes: psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Manipulation/mobilisation versus usual care (UC)**
    - At short term, a clinical important benefit in **pain** reduction was seen in the group who received manipulation (NRS 0-10; 1 RCT; low quality; n=72). Also a higher number of patients with more than 30 or 50% pain reduction (**responder criteria**) was noticed in this patient group (1 RCT; low quality; n=72). However at long term, no clinical difference in pain was anymore seen (NRS 0-10; 1 RCT; low quality; n=72). Nevertheless the lack of clinical difference in overall score on **function** (both at short term and long term; ODI 0-100; 2 RCTs-1RCT; very low quality; n=197-72), a clinically significant higher number of patients with 30% or 50% increase in function were noticed in the group who received manipulation (1 RCT; low quality; n=72).
    - Not reported outcomes: QoL, psychological distress, adverse events, healthcare utilisation
  - **Manipulation/mobilisation versus soft tissue techniques (massage)**
    - No clinical differences were found at short term and long term in **pain** (VAS 0-10; 2 RCTs; low-very low quality; n=191-87) and **function** (RMDQ 0-24; 1 RCT; very low quality; n=94-88).
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Manipulation/mobilisation versus orthotics (belts/corsets)**
    - Only one outcome was reported in a single study: no clinical difference was found in short-term **pain** (VAS 0-10; 1 RCT; very low quality; n=90). No long-term data was reported.
    - Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Manipulation/mobilisation versus electrotherapy (ultrasound)**
    - A single study reported a clinical benefit in **pain** in favour of manipulation, both at short term and long term (VAS 0-10; 1 RCT; very low quality; n=112-73), however no clinical difference was found for **function**, at both time points (ODI 0-100; 1 RCT; very low quality; n=112-73).
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Manipulation/mobilisation versus NSAIDs**
    - No clinical difference was found in short term **pain** (VAS 0-10; 1 RCT; moderate quality; n=115) and **function** (RMDQ 0-24; 1 RCT; moderate quality; n=115). No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - Not reported comparisons:

- Manipulation/mobilisation versus exercise
- Manipulation/mobilisation versus interferential therapy
- Manipulation/mobilisation versus self-management
- Manipulation/mobilisation versus combined intervention of exercise + education

Table 20 – Clinical effectiveness of manipulation/mobilisation compared to sham, usual care and active comparators in patients with low back pain without sciatica

Manipulation/mobilisation						
Outcomes	**Manipulation/mobilisation versus sham**	**Manipulation/mobilisation versus usual care (UC)**	**Manipulation/mobilisation versus massage**	**Manipulation/mobilisation versus belts/corsets**	**Manipulation/mobilisation versus ultrasound**	**Manipulation/mobilisation versus NSAIDs**
QoL	<u>At short term:</u> • **EuroQol Health State 0-100: No diff** (1 RCT; moderate; n=174) • **Physical composite score (SF-36/SF-12 0-100): CIB favouring manip** (1 RCT; moderate; n=174) • **Mental composite score (SF-36/SF-12 0-100): no diff** (1 RCT; moderate; n=174) • **Subdomains (SF-36/SF-12 0-100): no diff** (1 RCT; very low-low; n=136) <u>At long term:</u> • **EuroQol Health State 0-100: No diff** (1 RCT; high; n=166) • **Physical composite score (SF-36/SF-12 0-100): no diff**					

	(1 RCT; high; n=166) • **Mental composite score (SF-36/SF-12 0-100): no diff** (1 RCT; high; n=166)					
Pain	At short term: • **VAS 0-10: No diff** (5 RCTs; moderate; n=533) At long term: • **VAS 0-10: No diff** (2 RCTs; high; n=229)	At short term: • **NRS 0-10: CIB favouring manip** (1 RCT; low; n=72) At long term: • **NRS 0-10: no diff** (1 RCT; low; n=72)	At short term: • **VAS 0-10: No diff** (2 RCTs; low; n=191) At long term: • **VAS 0-10: No diff** (2 RCTs; very low; n=87)	At short term: • **VAS 0-10: No diff** (1 RCT; very low; n=90) At long term: Not reported	At short term: • **VAS 0-10: CIB favouring manip** (1 RCT; very low; n=112) At long term: • **VAS 0-10: CIB favouring manip** (1 RCT; very low; n=73)	At short term: • **VAS 0-10: No diff** (1 RCT; moderate; n=115) At long term: Not reported
Function	At short term: • **ODI 0-100: No diff** (4 RCTs; low; n=374) • **Von Korff 0-100: No diff** (1 RCT; moderate; n=174) At long term: • **ODI 0-100: No diff** (1 RCT; moderate; n=63) • **Von Korff 0-100: No diff** (1 RCT; moderate; n=166)	At short term: • **ODI 0-100: No diff** (2 RCTs; very low; n=197) At long term: • **ODI 0-100: No diff** (1 RCT; very low; n=72)	At short term: • **RMDQ 0-24: No diff** (1 RCT; very low; n=94) At long term: • **RMDQ 0-24: No diff** (1 RCT; very low; n=88)		At short term: • **ODI 0-100: No diff** (1 RCT; very low; n=112) At long term: • **ODI 0-100: No diff** (1 RCT; very low; n=73)	At short term: • **RMDQ 0-24: No diff** (1 RCT; moderate; n=115) At long term: Not reported
Respon-der criteria		At short term: • **>30% reduction in pain: CIB favouring manip** (1 RCT; low; n=72)				

		• **>50% reduction in pain: CIB favouring manip** (1 RCT; low; n=72) • **>30% increase in function: CIB favouring manip** (1 RCT; low; n=72) • **>50% increase in function: CIB favouring manip** (1 RCT; low; n=72) <u>At long term:</u> Not reported				

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

- **Patients with low back pain with sciatica**
  - **Manipulation versus sham**
    - A single study showed long term clinical benefit of spinal manipulation for **QoL** in the majority of the domains (except for general health domain in favour of sham and no differences in the role physical and bodily pain domains) (SF-36 0-100; moderate-high quality; n=98). Also a clinical benefit of spinal manipulation was found in terms of **responder criteria** (>30% improvement in (local back and radiating) pain) in the long term (1 RCT; low quality; n=98).
    - Not reported outcomes: pain, function, psychological distress, adverse events, healthcare utilisation
  - **Manipulation/mobilisation versus usual care (UC)**
    - Only one study of very low quality (1 RCT; very low quality; n=192) was found on the comparison of manipulation versus usual care in patients with LBP and sciatica: no clinical difference at short term and long term was found in **pain** (VAS 0-10), **QoL** (SF-36) (except physical component at short term) and **adverse events** (only at short term reported, number of patients with >1 adverse events). A clinical benefit for **function** (RMDQ 0-24) at short term in favour of manipulation was seen, but not anymore at long term.
    - Not reported outcomes: psychological distress, responder criteria, healthcare utilisation
  - Not reported comparisons:
    - Manipulation/mobilisation versus soft tissue techniques (massage)
    - Manipulation/mobilisation versus orthotics (belts)
    - Manipulation/mobilisation versus exercise
    - Manipulation/mobilisation versus interferential therapy
    - Manipulation/mobilisation versus ultrasound
    - Manipulation/mobilisation versus self-management
    - Manipulation/mobilisation versus NSAIDs
    - Manipulation/mobilisation versus combined intervention of exercise + education

- **Mixed population (low back pain with or without sciatica)**
  - **Manipulation/mobilisation versus usual care**
    - The retrieved studies compared different modalities of manipulation/mobilisation with usual care: one study on spinal adjusting mobilisation, one study on high velocity thrust and one study on traction gap manipulation. The study on spinal adjusting mobilisation found no clinical difference in **pain** (at short term and long term) (VAS 0-10; 1 RCT; moderate quality; n=681) and on short-term **function** (RMDQ 0-24; 1 RCT; low quality; n=339) (no long-term data reported). However a lower number of healthcare visits (**healthcare utilisation**) were found in the group who received usual care (at short term and at long term) (1 RCT; moderate-low quality; n=338-330). The study on high velocity thrust found no clinical difference in short-term **pain** (no long-term data reported) (VAS 0-10; 1 RCT; very low quality; n=240), in **function** (short term and long term) (RMDQ 0-24; 1 RCT; very low quality; n=145-240) and **adverse events** (1 RCT; very low quality; n=145). Only a clinically important benefit in short-term **QoL** was found (no long term data reported) (SF-36 physical functioning 0-100; 1 RCT; very low quality; n=240). The study on traction gap manipulation reported only one outcome: a clinically important short-term benefit in **function** was found in favour of manipulation (RMDQ 0-24; 1 RCT; low quality; n=29). No long term data were reported.
    - Not reported outcomes: psychological distress
  - **Manipulation/mobilisation versus exercise (biomechanical)**
    - Only one study was found which reported a short term clinical benefit in **pain** (VAS 0-10; 1 RCT; very low quality; n=24) and **function** (RMDQ 0-24; 1 RCT; very low quality; n=24). No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
    - KCE comment: In this study from Ferreira 2010, it was unclear if neurological deficit was included or excluded (primary study not available)
  - **Manipulation/mobilisation versus interferential therapy (IFT)**
    - **QoL** measured with the EQ-5D revealed no clinical difference both at short term and at long term (EQ-5D 0-1; 1 RCT; low quality; n=128). However, the SF-36 showed some conflicting results (SF-36 0-100; 1 RCT; low quality; n=128): at short term, a clinical benefit was seen in 2 of the 8 domains (physical and social function) in favour of manipulation and in 1 domain (emotional role limitation) in favour of IFT. At long term, similar results were seen (SF-36 0-100; 1 RCT; very low quality; n=107): a clinical benefit in 2 domains (social function and mental health) in favour of manipulation and in 1 domain (bodily pain) in favour of IFT. No clinical differences were found in **pain** (VAS 0-10; 1 RCT; low-very low quality; n=128-107) and **function** (RMDQ 0-24; 1 RCT; very low-low quality; n=128), both at short term and long term.
    - Not reported outcomes: psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Manipulation/mobilisation versus self-management (education, advice, reassurance)**
    - A single study reported no clinical difference in short term **pain** (VAS 0-10; 1 RCT; high quality; n=86) and **function** (ODI 0-100; 1 RCT; moderate quality; n=77). No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Manipulation/mobilisation versus NSAIDs**
    - A single study reported no clinical difference in short term **pain** (VAS 0-10; 1 RCT; moderate quality; n=96) and **function** (ODI 0-100; 2 RCTs; moderate quality; n=171). No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Manipulation/mobilisation versus combined intervention of (biomechanical) exercise + education**
    - A clinical benefit was found in short term **pain** (VAS 0-10; 1 RCT; very low quality; n=23) and **function** (RMDQ 0-24; 1 RCT; very low quality; n=23) in favour of manipulation. No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
    - KCE comment: In this study from Ferreira 2010, it was unclear if neurological deficit was included or excluded (primary study not available)
  - Not reported comparisons:
    - Manipulation/mobilisation versus sham

- Manipulation/mobilisation versus soft tissue techniques (massage)
- Manipulation/mobilisation versus orthotics (belts)
- Manipulation/mobilisation versus ultrasound

Table 21 – Clinical effectiveness of manipulation/mobilisation compared to usual care and active comparators in mixed population (low back pain with or without sciatica)

Manipulation/mobilisation						
Outcomes	**Manipulation/mobilisation versus usual care (UC)**	**Manipulation/mobilisation versus individual biomechanical exercise (motor control)**	**Manipulation/mobilisation versus interferential therapy (IFT)**	**Manipulation/mobilisation versus self-management (education, advice, reassurance)**	**Manipulation/mobilisation versus NSAIDs**	**Manipulation/mobilisation versus combined intervention of exercise + education (biopsychosocial model program)**
QoL	At short term: • **SF-26 physical functioning 0-100: CIB favouring manip (high velocity thrust)** (1 RCT; very low; n=240) At long term: Not reported		At short term: • **EQ-5D 0-1: No diff** (1 RCT; low; n=128) • **2/8 domains SF-36 0-100: CIB favouring manip** (1 RCT; low; n=128) • **1/8 domains SF-36 0-100: CIB favouring IFT** (1 RCT; low; n=128) At long term: • **EQ-5D 0-1: No diff** (1 RCT; low; n=128) • **2/8 domains SF-36 0-100: CIB favouring manip** (1 RCT; very low; n=107) • **1/8 domains SF-36 0-100: CIB favouring IFT** (1 RCT; very low; n=107)			

Pain	At short term: • **VAS 0-10: No diff** (2 RCTs; very low; n=921) At long term: • **VAS 0-10: No diff (Spinal adjusting-mobilisation)** (1 RCT; moderate; n=681)	At short term: • **VAS 0-10: CIB favouring manip** (1 RCT; very low; n=24) At long term: Not reported	At short term: • **VAS 0-10: No diff** (1 RCT; low; n=128) At long term: • **VAS 0-10: No diff** (1 RCT; very low; n=107)	At short term: • **VAS 0-10: No diff** (1 RCT; high; n=86) At long term: Not reported	At short term: • **VAS 0-10: No diff** (1 RCT; moderate; n=96) At long term: Not reported	At short term: • **VAS 0-10: CIB favouring manip** (1 RCT; very low; n=23) At long term: Not reported
Function	At short term: • **RMDQ 0-24: No diff (high velocity thrust)** (1 RCT; very low; n=145) • **RMDQ 0-24: No diff (Spinal adjusting-mobilisation)** (1 RCT; low; n=339) • **RMDQ 0-24: CIB favouring manip (Traction gap manipulation)** (1 RCT; low; n=29) At long term: • **RMDQ 0-24: No diff high velocity thrust)** (1 RCT; very low; n=240)	At short term: • **RMDQ 0-24: CIB favouring manip** (1 RCT; very low; n=24) At long term: Not reported	At short term: • **RMDQ 0-24: no diff** (1 RCT; very low; n=128) At long term: • **RMDQ 0-24: no diff** (1 RCT; low; n=128)	At short term: • **ODI 0-100: no diff** (1 RCT; moderate; n=77) At long term: Not reported	At short term: • **RMDQ 0-24: no diff** (2 RCTs; moderate; n=171) At long term: Not reported	At short term: • **RMDQ 0-24: CIB favouring manip** (1 RCT; very low; n=23) At long term: Not reported
Health-care utilisa-tion	At short term: • **(Spinal adjusting-mobilisation) Number of healthcare visits: CIB favouring UC**					

	(1 RCT; moderate; n=338) At long term: • **(Spinal adjusting-mobilisation) Number of healthcare visits: CIB favouring UC** (1 RCT; low; n=330)					
Adverse events	At short term: • **No diff (high velocity thrust)** (1 RCT; very low; n=145) At long term: Not reported					

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

In conclusion:

- **Manipulation/mobilisation as single intervention**
  - Compared to sham, no differences were found in pain, function and QoL in a population of low back pain without sciatica. However, in a population with sciatica, a clinical benefit was found in QoL and in responder criteria (>30% improvement in pain).
  - Compared to usual care, the clinical benefit depended on the manipulation modality but overall could be stated that the retrieved evidence was not consistent in favour or against manipulation in mixed population. Only an increased number of healthcare visits were found in patients who received manipulation/mobilisation.

- **Patients with low back pain without sciatica**
  - Comparison with sham, revealed only a short term clinical benefit on the physical component of QoL in favour of manipulation/mobilisation. Comparison with usual care found a short term pain improvement and a higher number of patients who reported a 30 or 50% improvement in pain and function in favour of manipulation/mobilisation. Comparison with active comparators (massage, belts/corsets, US, NSAIDs) showed only a clinical benefit in pain (compared to US).
- **Patients with low back pain with sciatica**
  - Comparison with usual care, only a clinical short-term benefit in function was found in favour of manipulation/mobilisation.
- **Mixed population (low back pain with or without sciatica)**
  - Compared to usual care, the clinical benefit depended on the manipulation modality but overall could be stated that the retrieved evidence was not consistent in favour or against manipulation. Only an increased number of healthcare visits were found in patients who received manipulation/mobilisation. Comparison with active comparators (exercise, IFT, self-management, NSAIDs, combined intervention of exercise + education) showed inconsistent results for QoL and only a short term clinical benefit in pain and function in favour of manipulation compared to the combined intervention of exercise + education.
- **Manipulation/mobilisation as adjunct**

- Several, single studies compared different modalities of active comparators in combination with manual therapy, resulting in an inconsistent overview of evidence in which it is difficult to determine which combination of modalities showed the most clinical benefit. Compared to the limited evidence of manipulation/mobilisation as a single intervention, the combination of the latter with active comparators increased its potential clinical benefits.

Mixed modality manual therapy

- **Patients with low back pain without sciatica**
  - **Mixed modality manual therapy versus usual care**
    - Only one outcome was reported in a single study: a clinically important benefit was found for **pain** in favour of the mixed modality (Melzak pain score 0-5; 1 RCT; very low quality; n=18). No long term data was reported.
    - Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Mixed modality manual therapy versus sham**
    - Only one outcome was reported in a single study: a clinically important benefit was found for **responder criteria** (>30% improvement in pain) in favour of the mixed modality (1 RCT; moderate quality; n=445). No long term data was reported.
    - Not reported outcomes: QoL, pain, function, psychological distress, adverse events, healthcare utilisation
  - **Mixed modality manual therapy versus manipulation/mobilisation**
    - No clinical differences were found for **pain** (VAS 0-10; 1 RCT; very low-low quality; n=93-89) and **function** (RMDQ 0-24; 1 RCT; very low-low quality; n=93-89), at short term and long term.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Mixed modality manual therapy versus soft tissue technique (massage)**
    - Only a short term benefit in **function** was found, but not at long term (RMDQ 0-24; 1 RCT; very low quality; n=97-95). For **pain**, no clinical differences were found at both time points (VAS 0-10; 1 RCT; very low quality; n=97-96).
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Mixed modality manual therapy versus traction**
    - A single study reported only one outcome: a clinically important benefit in short term **pain** in favour of the mixed modality (VAS 0-10; 1 RCT; very low quality; n=60). No long term data was reported.
    - Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Mixed modality manual therapy versus biomechanical exercise**
    - A single study reported only one outcome: a clinically important benefit in short term **pain** in favour of the mixed modality (Melzak pain score 0-5; 1 RCT; very low quality; n=18). No long term data was reported.
    - Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation

Table 22 – Clinical effectiveness of mixed modality manual therapy compared to usual care, sham and active comparators in patients with low back pain without sciatica

Mixed modality manual therapy						
Outcomes	**Mixed modality manual therapy (manipulation, mobilisation, traction) versus usual care (UC)**	**Mixed modality manual therapy (manipulation, massage) versus sham**	**Mixed modality manual therapy (manipulation, massage) versus manipulation/mobilisation**	**Mixed modality manual therapy (manipulation, massage) versus massage (myofascial techniques)**	**Mixed modality manual therapy (massage, traction) versus traction**	**Mixed modality manual therapy (manipulation, mobilisation, massage) versus biomechanical exercise (core stability)**
Pain	At short term: • **Melzak pain score 0-5: CIB favouring mixed mod** (1 RCT; very low; n=18) At long term: Not reported		At short term: • **VAS 0-10: No diff** (1 RCT; very low; n=93) At long term: • **VAS 0-10: No diff** (1 RCT; low; n=89)	At short term: • **VAS 0-10: No diff** (1 RCT; very low; n=97) At long term: • **VAS 0-10: No diff** (1 RCT; very low; n=96)	At short term: • **VAS 0-10: CIB favouring mixed mod** (1 RCT; very low; n=60) At long term: Not reported	At short term: • **Melzak pain score 0-5: CIB favouring mixed mod** (1 RCT; very low; n=18) At long term: Not reported
Function			At short term: • **RMDQ 0-24: No diff** (1 RCT; very low; n=93) At long term: • **RMDQ 0-24: No diff** (1 RCT; low; n=89)	At short term: • **RMDQ 0-24: CIB favouring mixed mod** (1 RCT; very low; n=97) At long term: • **RMDQ 0-24: No diff** (1 RCT; very low; n=95)		
Responder criteria		At short term: • **>30% improvement in pain: CIB**				

		favouring mixed mod (1 RCT; moderate; n=445) <u>At long term:</u> Not reported				

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

- **Patients with low back pain with sciatica**
  - **No evidence found for this patient group**
  - Not reported comparisons:
    - Mixed modality manual therapy versus usual care
    - Mixed modality manual therapy versus sham
    - Mixed modality manual therapy versus manipulation/mobilisation
    - Mixed modality manual therapy versus massage
    - Mixed modality manual therapy versus traction
    - Mixed modality manual therapy versus (biomechanical) exercise
- **Mixed population (low back pain with or without sciatica)**
  - **Mixed modality manual therapy versus sham**
    - No clinical differences in **pain** (NRS 0-10; 1 RCT; moderate-low; n=29) and **function** (ODI 0-100; 1 RCT; moderate; n=29) were reported, both at short term and long term.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
    - <u>KCE comment: this study (Cambron 2014) concerned patients diagnosed with neurogenic claudication or chronic nerve root compression.</u>
  - Not reported comparisons:
    - Mixed modality manual therapy versus usual care
    - Mixed modality manual therapy versus manipulation/mobilisation
    - Mixed modality manual therapy versus massage
    - Mixed modality manual therapy versus traction
    - Mixed modality manual therapy versus (biomechanical) exercise

In conclusion:

- **Patients with low back pain without sciatica**
  - Comparison with sham and usual care, showed a clinically important benefit in pain (compared to usual care) and in improvement in pain (compared to sham). Comparison with active comparators (manipulation/mobilisation, massage, traction, biomechanical exercise) showed a short term improvement in pain in favour of the mixed modality (compared to traction and biomechanical exercise) and a short term improvement in function (compared to massage).
- **Patients with low back pain with sciatica**
  - No evidence found for this patient group
- **Mixed population (low back pain with or without sciatica)**
  - One comparison was retrieved (sham): no clinical differences in pain and function were found.
- **Mixed modality as adjunct**

- Several, single studies compared different modalities of active comparators in combination with manual therapy, resulting in an inconsistent overview of evidence in which it is difficult to determine which combination of modalities showed the most clinical benefit. Compared to the limited evidence of mixed modality as a single intervention, the combination of the latter with active comparators increased its potential clinical benefits.

Manual therapy as component in a multimodal intervention (manual therapy adjunct)

- **Patients with low back pain without sciatica**
  - In total, 10 different comparisons were found which can be grouped in 4 categories:
    - **Combined intervention with manual therapy (massage) + self-management (exercise prescription) versus postural therapy (Alexander technique 6 or 24 lessons)** (2 RCTs; moderate-low quality)
      - Only a long-term benefit in the physical component of **QoL** was observed in the postural therapy group (24 lessons Alexander technique). No clinical difference in **pain**, **function**, and **healthcare utilisation** in both studies (6 or 24 lessons of Alexander technique). Only long term data was reported.
      - Not reported outcomes: psychological distress, responder criteria, adverse events
    - **Combined intervention with manual therapy (manipulation) versus (biomechanical/aerobic) exercises** (6 RCTs, see Table 23)
      - The combination of manipulation and biomechanical exercises, revealed a clinically important benefit in short-term **pain** (reported in 2 studies of very low quality). In only one of the four studies a clinical short-term benefit on **function** was found. The combination of manipulation and aerobic exercises (2 RCTs, very low quality) revealed no clinical difference in **pain** and **function** (only short term data were reported).
      - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
    - **Combined intervention with manual therapy (manipulation) + (biomechanical) exercise versus manual therapy (manipulation) + (aerobic) exercise)** (1 RCT; very low quality)
      - No clinical difference in short term **pain** and **function**. No long term data were reported.
      - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
    - **Combined intervention with manual therapy (manipulation + massage) versus sham** (1 RCT, moderate-high quality)
      - No clinical difference in short term **pain** and **function**. No long term data were reported.
      - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation

Table 23 – Clinical effectiveness of manual therapy (manipulation) as component in a multimodal intervention compared to exercises in patients with low back pain without sciatica

Manual therapy as component in a multimodal intervention						
Outcomes	**Manipulation + biomechanical exercises (McKenzie) versus biomechanical exercise (core stability)**	**Manipulation + biomechanical exercises (McKenzie) versus biomechanical exercise (stretching)**	**Manipulation + biomechanical exercises (stretching) versus aerobic exercise (walking)**	**Manipulation + biomechanical exercises (stretching) versus biomechanical exercise (core stability)**	**Manipulation + aerobic exercises versus aerobic exercise**	**Manipulation + aerobic exercises versus biomechanical exercise**
Pain			At short term: • **VAS 0-10: CIB favouring combined intervention** (1 RCT; very low; n=39) At long term: Not reported	At short term: • **VAS 0-10: CIB favouring combined intervention** (1 RCT; very low; n=39) At long term: Not reported	At short term: • **VAS 0-10: No diff** (1 RCT; very low; n=33) At long term: Not reported	At short term: • **VAS 0-10: No diff** (1 RCT; very low; n=33) At long term: Not reported
Function	At short term: • **ODI 0-100: No diff** (1 RCT; low; n=86) At long term: • **ODI 0-100: No diff** (1 RCT; low; n=86)	At short term: • **ODI 0-100: No diff** (1 RCT; low; n=77) At long term: • **ODI 0-100: No diff** (1 RCT; low; n=77)	At short term: • **Quebec Back pain Disability scale 0-100: CIB favouring combined intervention** (1 RCT; very low; n=39) At long term: Not reported	At short term: • **Quebec Back pain Disability scale 0-100: No diff** (1 RCT; very low; n=39) At long term: Not reported	At short term: • **Quebec Back pain Disability scale 0-100: CIB favouring combined intervention** (1 RCT; very low; n=33) At long term: Not reported	At short term: • **Quebec Back pain Disability scale 0-100: No diff** (1 RCT; very low; n=33) At long term: Not reported

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

- **Patients with low back pain with sciatica**
  - Three (similar) comparisons were found:
    - Manual therapy (manipulation) + self-management (education) + exercise (aerobic) versus self-management (education) + exercise (aerobic + McKenzie) (1 RCT; very low quality; n=25): no clinical difference in **pain** (VAS 0-10) and **function** (ODI O-100) both at short term. No long term data were reported.

- Manual therapy (soft tissue technique – muscle energy technique) + self-management (unsupervised exercise) + biomechanical exercise (McKenzie) versus self-management (unsupervised exercise) + biomechanical exercise (McKenzie) (1 RCT; very low quality; n=40): no clinical difference in **pain** (VAS 0-10) and **function** (ODI 0-100), both at short term. No long term data were reported.
- Manual therapy (soft tissue technique – muscle energy technique) + self-management (unsupervised exercise) + biomechanical exercise (McKenzie) versus self-management (unsupervised exercise) + standard treatment (TENS+laser+massage) (1 RCT; very low quality; n=40): a clinical benefit in **pain** (VAS 0-10) and **function** (ODI 0-100) in favour of manual therapy + exercise + self-management.
- Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation

o Overall conclusion: Only in the comparison with the standard treatment + self-management, a clinically important benefit in short term **pain** and **function** could be found in the group who received the combined manual therapy intervention. No long term data were reported.

o KCE comment: one study from Schenk 2003 concerned patients with radiculopathy, lumbar disc derangement and the other study from Szulc 2015 focused on patients with confirmed protrusion or bulging in the lumbosacral spine.

- **Mixed population (low back pain with or without sciatica)**
  - In total, 12 different comparisons were found which can be grouped in 3 categories:
    - **Combined intervention with manual therapy (manipulation) versus usual care/active comparator** (8 RCTs, see Table 24)
      - Three of the 8 studies reported results on **QoL** and demonstrated an overall clinical benefit of the addition of manual therapy in a combined intervention. Only one of the 6 studies which reported **pain**, found a clinical benefit in favour of manipulation. The results for **function** are less consistent: in 4 of the 6 studies a short term benefit was found in favour of manipulation, however at long term only 2 of the 5 studies reported this benefit. In the majority of the studies (5/8) results for both time points were not reported, which hampers the overall conclusion of the potential effect of manipulation on functioning of the patient. Regarding **healthcare utilisation**, only a long term benefit was found for medication use in favour of manipulation.
      - Not reported outcomes: psychological distress, responder criteria, adverse events

    - **Combined intervention with manual therapy (traction) + infra-red + biomechanical exercise (stretching) versus active comparator (infra-red + biomechanical exercise-stretching)** (1 RCT; very low- low quality)
      - No clinical difference in short term and long term pain, function and healthcare utilisation (medication use).
      - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events
    - **Combined intervention with mixed modality manual therapy versus active comparator** (3 RCTs, see Table 25)
      - Overall could be stated that no clinical difference was found for short term and long term **pain**, **function** and **healthcare utilisation**. Nevertheless the lack of difference in function, a significant higher number of patients reported more than 30% improvement in function after the mixed modality intervention (**responder criteria**) (in 2 of 3 studies). The results for **QoL** are less consistent: in the combination of mixed modality with self-management, only a clinical benefit was seen in the physical component of SF-36 at short term. In the combination of mixed modality with exercise and self-management, a clinical benefit was seen in the physical component of SF-36 at both time points and in QoL measured by the EQ-5D in favour of the mixed modality.
      - Not reported outcomes: psychological distress, adverse events

Table 24 – Clinical effectiveness of manual therapy (manipulation) as component in a multimodal intervention in mixed population (low back pain with or without sciatica)

Manual therapy as component in a multimodal intervention								
Outcomes	**Manipulation + self-management (home exercise) versus self-management (home exercise) + exercise (mixed)**	**Manipulation + exercise (endurance) + self-management (education, advice) versus exercise (endurance) + self-management (education, advice)**	**Manipulation + self-management (advice) + NSAIDs versus usual care**	**Manipulation + biomechanical exercise () + self-management (education, advice, reassurance) versus self-management (education, advice, reassurance)**	**Manipulation + exercise (core stability) versus exercise (core stability)**	**Manipulation + exercise (trunk strengthening) versus NSAID + exercise (trunk strengthening)**	**Manipulation + exercise (trunk stretching) versus NSAID + exercise (trunk strengthening)**	**Manipulation + electrotherapy (IFT) versus electrotherapy (IFT)**
QoL			At short term: • **Bodily pain (SF-36 0-100): no diff** (1 RCT; low; n=72) • **Physical function (Sf-36 0-100): CIB favouring manip** (1 RCT; moderate; n=72) At long term: • **Bodily pain (SF-36 0-100): CIB favouring manip**	At short term: Not reported At long term: • **15D 0-1: No diff** (1 RCT; low; n=130)				At short term: • **EQ-5D 0-1: No diff** (1 RCT; moderate; n=131) • **3/8 domains SF-36 0-100: CIB favouring manip** (1 RCT; moderate-very low; n=131) At long term: • **EQ-5D 0-1: CIB favouring manip** (1 RCT; low; n=106) • **8/8 domains Sf-36 0-100: CIB favouring manip**

			(1 RCT; moderate; n=71) • **Physical function (Sf-36 0-100): CIB favouring UC** (1 RCT; low; n=12)					(1 RCT; low-very low; n=106)
Pain	At short term: • **VAS 0-10: CIB favouring manip** (1 RCT; moderate; n=48) At long term: • **VAS 0-10: CIB favouring manip** (1 RCT; moderate; n=49)	At short term: • **VAS 0-10: No diff** (1 RCT; very low; n=64) At long term: Not reported		At short term: Not reported At long term: • **VAS 0-10: No diff** (1 RCT; very low; n=196)		At short term: • **11 box scale 0-10: No diff** (1 RCT; very low; n=96) At long term: Not reported	At short term: • **11 box scale 0-10: No diff** (1 RCT; very low; n=76) At long term: Not reported	At short term: • **VAS 0-10: No diff** (1 RCT; moderate; n=131) • **McGill 0-78: No diff** (1 RCT; moderate; n=131) At long term: • **VAS 0-10: No diff** (1 RCT; moderate; n=106) • **McGill 0-78: No diff** (1 RCT; moderate; n=106)
Function	At short term: • **ODI 0-100: CIB favouring manip** (1 RCT; moderate; n=48) At long term:	At short term: • **ODI 0-100: No diff** (1 RCT; low; n=64) At long term: Not reported	At short term: • **RMDQ 0-24: CIB favouring manip** (1 RCT; moderate; n=72) At long term:	At short term: Not reported At long term:	At short term: Not reported At long term:	At short term: • **RMDQ 0-24: CIB favouring manip** (1 RCT; very low; n=96) At long term: Not reported	At short term: • **RMDQ 0-24: CIB favouring manip** (1 RCT; very low; n=76) At long term: Not reported	At short term: • **RMDQ 0-24: No diff** (1 RCT; low; n=131) At long term:

	• **ODI 0-100: No diff** (1 RCT; moderate; n=49)		• **RMDQ 0-24: CIB favouring manip** (1 RCT; moderate; n=71)	• **ODI 0-100: No diff** (1 RCT; very low; n=196)	• **ODI 0-100: CIB favouring manip** (1 RCT; low; n=92)			• **RMDQ 0-24: No diff** (1 RCT; low; n=106)
Healthcare utilisation				At short term: Not reported At long term: • **Visits to physicians: no diff** (1 RCT; low; n=196) • **Visits to physiotherapy or other therapies: no diff** (1 RCT; very low; n=196)	At short term: Not reported At long term: • **Medication use: CIB favouring manip** (1 RCT; very low; n=92)			

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

Table 25 – Clinical effectiveness of manual therapy (mixed modality) as component of a multimodal intervention in mixed population (low back pain with or without sciatica)

Mixed modality			
Outcomes	**Mixed modality (manipulation package)+ self-management (advice) versus self-management (advice)**	**Mixed modality (manipulation package) + biomechanical exercise (core stability) + self-management (advice) versus self-management (advice)**	**Mixed modality (manipulation, massage) + biomechanical exercise (McKenzie) + self-management (education) versus biomechanical exercise (McKenzie) + self-management (education)**
QoL	At short term: • **Physical composite score SF-36 0-100: CIB favouring manip** (1 RCT; low; n=486) • **Mental composite score SF-36 0-100: no diff** (1 RCT; low; n=486) • **EQ-5D 0-1: No diff** (1 RCT; low; n=688) At long term: • **Physical composite score SF-36 0-100: no diff** (1 RCT; low; n=473) • **Mental composite score SF-36 0-100: no diff** (1 RCT; very low; n=473) • **Q-5D 0-1: No diff** (1 RCT; low; n=688)	At short term: • **Physical composite score SF-36 0-100: CIB favouring manip** (1 RCT; low; n=458) • **Mental composite score SF-36 0-100: no diff** (1 RCT; low; n= 458) • **EQ-5D 0-1: CIB favouring mixed mod** (1 RCT; low; n=648) At long term: • **Physical composite score SF-36 0-100: CIB favouring manip** (1 RCT; low; n=442) • **Mental composite score SF-36 0-100: no diff** (1 RCT; very low; n=442) • **EQ-5D 0-1: CIB favouring mixed mod** (1 RCT; low; n=648)	
Pain	At short term: • **Modified Von Korff 0-100: No diff** (1 RCT; low; n=514) At long term: • **Modified Von Korff 0-100: No diff** (1 RCT; low; n=499)	At short term: • **Modified Von Korff 0-100: No diff** (1 RCT; low; n=485) At long term: • **Modified Von Korff 0-100: No diff** (1 RCT; low; n=480)	At short term: • **VAS 0-60 Back and leg pain: No diff** (1 RCT; moderate; n=329) At long term: • **VAS 0-60 Back and leg pain: No diff** (1 RCT; moderate; n=324)
Function	At short term: • **RMDQ 0-24: No diff** (1 RCT; low; n=543)	At short term: • **RMDQ 0-24: No diff** (1 RCT; low; n=514)	At short term: • **RMDQ 0-24: No diff** (1 RCT; moderate; n=329)

	• **Modified Von Korff scale 0-100: No diff** (1 RCT; low; n=514) At long term: • **RMDQ 0-24: No diff** (1 RCT; low; n=521) • **Modified Von Korff scale 0-100: No diff** (1 RCT; low; n=514)	• **Modified Von Korff scale 0-100: No diff** (1 RCT; low; n=485) At long term: • **RMDQ 0-24: No diff** (1 RCT; low; n=505) • **Modified Von Korff scale 0-100: No diff** (1 RCT; low; n=481)	At long term: • **RMDQ 0-24: No diff** (1 RCT; moderate; n=324)
Responder criteria	At short term: • **>30% improvement in function: CIB favouring mixed mod** (1 RCT; low; n=480) At long term: • **>30% improvement in function: CIB favouring mixed mod** (1 RCT; very low; n=480)	At short term: • **>30% improvement in function: CIB favouring mixed mod** (1 RCT; low; n=480) At long term: • **>30% improvement in function: CIB favouring mixed mod** (1 RCT; very low; n=480)	At short term: • **Success (decrease 5 points or absolute score below 5 points on RMDQ): CIB favouring ex + self-man** (1 RCT; moderate; n=329) At long term: • **Success (decrease 5 points or absolute score below 5 points on RMDQ): no diff** (1 RCT; moderate; n=324)
Healthcare utilisation			At short term: • **Contact with healthcare in previous 2 months: No diff** (1 RCT; low; n=330) At long term: • **Contact with healthcare in previous 2 months: No diff** (1 RCT; moderate; n=325)

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

Economic evidence

- **Patients with low back pain without sciatica**
  - One cost-utility analysis (Hollinghurst 2008) found that massage + usual care was not cost effective but was cost effective when used as an adjunct to unsupervised exercise. Also the combination of Alexander technique (24 lessons) with unsupervised exercise was most effective and most cost effective option from usual care and active comparators
  - One cost-utility analysis (Vavrek 2014) found that manipulation (12 sessions) was cost effective compared to sham manipulation (ICER £14 800 per QALY gained)
  - One cost-consequence analysis (Beam 2004) found that the combination of mixed modality with self-management and exercise did not show any statistically significant increase in costs or outcomes

- One cost-utility analysis (Niemisto 2003/2005) found that mixed modality + self-management was cost effective compared to combination of mixed modality, exercise and self-management, self-management + exercise or self-management alone (ICER £8700 per QALY gained)
- One cost-utility analysis (Critchley 2007) found that manual therapy + self-management was dominated by a 3 element MBR programme (physical, psychological, educational).
- No relevant economic evaluations were identified relating to traction

- **Patients with low back pain with sciatica**
  - No relevant economic evaluations were identified

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:** The most critical outcomes for decision-making agreed by the GDG for this review question.
  - Most critical outcome was health-related QoL with pain severity, function and psychological distress as individually critical outcomes as well as components of QoL measure.
  - Important outcomes: adverse events and healthcare utilisation
  - Responder criteria, as defined as >30% improvement in pain or function, was not considered as a critical outcome
- **Trade-off between clinical benefits and harms**

***New in the final version*:** The GDG discussed the necessity of a body of evidence to show specific intervention effects, that is, over and above any contextual or placebo effects. It was therefore agreed that if placebo or sham-controlled evidence is available, this should inform decision making in preference to contextual effects. However, if there was a lack of placebo or sham-controlled evidence, evidence against usual care will be given priority when decision making.

  - **Single interventions:**
    - **Evidence:** There was **mixed evidence** for the effectiveness of manual therapy modalities, particularly with function outcomes not correlating with quality of life outcomes. It was also difficult to assess evidence from a wide variety of interventions for traction, and for manipulation/mobilisation.
      Comparison to sham: The GDG discussed that there was some albeit limited evidence of benefit of soft tissue techniques, spinal manipulation and mixed modality manual therapies compared to sham treatments in terms of improving pain or quality of life. Where these benefits were observed in the short term follow up they were somewhat inconsistent, and were not maintained in the longer term.
      Comparison to usual care: Evidence compared to usual care was conflicting and did not consistently show benefit when manual therapy was offered as a single treatment. However, when offered in combination with self-management and exercise, evidence from a large multicentre study demonstrated benefits in terms of quality of life and in terms of responder criteria for function. The GDG agreed the benefits seen by the package of therapy including mixed modality manual therapy was supportive of the evidence observed from evidence of mixed modality manual therapy from smaller trials in the review. For the critical outcomes where manual therapy was a single intervention, there was little effect seen beyond four months. One mixed modality trial in combination with other treatments did report positive outcomes for quality of life in both short and longer term and similarly for responder analysis for functional improvement. The GDG discussed whether the **passive nature of manual therapies** might explain why effects were not usually seen beyond four months.
    - **Adverse events**: Adverse events were **common, minor and transient**, consisting mainly of muscle soreness for a few days following treatment. No serious events attributable to manual therapy were reported by the studies reviewed. The GDG were aware of ~~case reports and estimates of~~ **possible serious but very rare adverse events that may be related to spinal manipulation** and took this into account when making a recommendation.
    - **Traction:** The GDG discussed that when considered alongside the body of evidence for soft-tissue techniques, manipulation/mobilisation or mixed modality manual therapies, there was very limited evidence of benefit for traction as a single therapy. Some benefit was observed in people with low back pain and sciatica when compared to usual care, but the GDG did not consider this as sufficient evidence of effect as it was from a small single study (n=36) and the evidence was rated as very low quality. Further benefits were seen from a group who received weight-bath traction when compared to usual care (separated from a group receiving mechanical traction). However, it was discussed that all of the participants in this trial were inpatients admitted due to sciatica and therefore were unlikely to be representative of the broader population with sciatica. Furthermore, there was also an indication

from one study in people with low back pain with or without sciatica that healthcare utilisation was increased in the group that received traction compared to sham treatment in the short term. Although when compared to biomechanical exercise the converse was true, the GDG noted that this healthcare utilisation data should be interpreted with care as it did not include the resource use associated with provision of the intervention itself. **Therefore the GDG agreed that traction should not be offered for low back pain or sciatica**.

- **Combination of interventions:** The majority of the evidence for combinations of interventions was from a mixed population of those with low back pain with or without sciatica. The GDG noted ~~a general trend for~~ that evidence suggested manual therapy was possibly potentiated when provided in combination with exercise in terms of providing benefit in pain and function for people with low back pain. However, it was noted that the evidence for this was limited and mostly came from single studies. The evidence for these combined interventions was challenging to unravel, because the combinations themselves and the comparator groups differed widely in terms of the intervention that they comprised. The studies used any one (or a combination) of a number of different modalities/types of manual therapy. The interventions were also often given in combination with other interventions, which differed in each trial, and were also compared to single or combinations of various different interventions. It was therefore very difficult to pick out which type of adjunct and combination of interventions was most effective. However, there was some inconsistent evidence of clinical benefit (in terms of pain, function, quality of life or responder criteria) when the intervention contained mixed modality manual therapy or a spinal manipulation component. The large multicentre study in particular showed that mixed modality manual therapy demonstrated clinical benefit for quality of life (SF-36 physical and EQ-5D) as well as for responder criteria (improvement in RMDQ function) in both the short and longer term. The GDG noted that the responder evidence for mixed manual therapy came from post-hoc analyses of 2 trials. In addition one of these trials demonstrated benefit in terms of responder analysis for pain, but not for function, whereas the other trial only presented the (positive) results of responder analysis for function; demonstrating a lack of consistency across important outcomes. Post hoc analyses present a further risk of bias. The GDG felt that, for these reasons, the evidence from the responder analyses should be considered with caution.
- **Summary:** Overall the GDG concluded that there was **mixed evidence** for the effectiveness of manual therapy modalities.
  For **soft-tissue techniques**, the evidence was based on massage. Considering that a comparison with usual care should result in a greater effect estimate than the specific effect of the intervention (as demonstrated in placebo comparisons), the GDG felt that the absence of a clinically important improvement in quality of life and pain in this comparison indicated sufficient evidence of absence of effect to recommend against the use of soft tissue techniques (massage) on its own. Similarly, based on the ~~lack of~~ limited clinical benefit seen for **mobilisation/manipulation**, the GDG felt this form of manual therapy could not be recommended for low back pain or sciatica as an independent intervention.
  The GDG concluded that soft-tissue techniques (e.g. massage) and manipulation/mobilisation should only be considered **as part of ~~multimodal~~ treatment packages**, where benefits were observed and seen to be maintained in the longer term. ~~Due to the~~ The GDG were aware of possible risk of adverse events, and due to the conflicting nature of the evidence, the GDG agreed that this recommendation should be **to consider** manual therapy as part of ~~multimodal~~ treatment package, rather than to offer manual therapy alone as a sole intervention to all people with low back pain with or without sciatica. The GDG did not feel that manual therapy should be a mandatory component of a ~~multimodal~~ treatment package, but that it is one optional modality that might be considered alongside exercise.

- **Trade-off between net clinical effects and costs**
  - **Soft tissue techniques:** One relevant economic evaluation was included that considered soft tissue techniques (massage) in a population with low back pain without sciatica. This was based on the RCT reported by Little et al. included in the clinical review. This within-trial analysis found that, compared to usual care, soft tissue techniques (massage) was found not to be cost effective when given alone (it had lower QALYs and higher costs), but was cost effective when used as an adjunct to self-management (unsupervised exercise - exercise prescription). Given the wide use of self-management in low back pain these results suggest uncertainty in the cost effectiveness of massage. In addition, when considered amongst a selection of active treatments, the combination of Alexander technique (24 lessons) with unsupervised exercise (exercise prescription) was found to be the most cost effective option from usual care, unsupervised exercise (exercise prescription), soft tissue techniques (massage), exercise prescription with massage, Alexander technique lessons (6 lessons), exercise prescription and Alexander technique lessons (6 lessons), Alexander technique (24 lessons), exercise prescription with Alexander technique lessons (24 lessons). Given the uncertainty around cost effectiveness from this study and the overall lack of evidence relating to soft tissue techniques from the clinical review, the GDG concluded there was **insufficient evidence to conclude that it would be cost effective** for the NHS.

- **Traction: No economic evaluations** were identified from the published literature. Use of traction will be associated with costs relating to the equipment and personnel time required to deliver the therapy. If effective, upfront costs may be offset by downstream cost savings due to reduced healthcare utilisation or may be justified due to the benefits to the patient. Although some indications of possible benefit were seen for traction in a sciatica population, overall the GDG concluded that it was insufficient to support a conclusion of evidence of clinical benefit and thus also insufficient to justify intervention costs.
- **Manipulation/mobilisation:** One relevant economic evaluation was included that considered manipulation/mobilisation in a population with low back pain without sciatica. This was based on the RCT reported by Haas et al. 2014 included in the clinical review. This within-trial analysis suggests, based on unadjusted data, that manipulation (12 sessions) may be cost-effective (£14,800 per QALY gained). It used a sham comparator but note that the cost of providing the sham is appropriately not included in this calculation. However, the authors also undertook a regression analysis to adjust costs and QALYs and in this analysis the QALY gain was reduced – this is not fully reported but appears that it may be as low as no difference – this would potentially reduce the cost effectiveness estimate. However, also of note the sham comparator would be expected to underestimate treatment benefits compared to a usual care comparator and this may improve cost effectiveness. Uncertainty around cost effectiveness was not reported. The adjusted costs analysis reported the difference as not statistically significant however this analysis excluded the intervention costs. QALY differences were also reported as not statistically significant. The study limitations include the setting which is the USA – this has low applicability to the UK due to the differences in the health care systems which can translate to differences in resource use and costs. Overall, while this study suggests that manipulation could potentially be cost effective but there are a large number of uncertainties in this evidence. One study by Niemisto et al (2003) compared manual therapy as part of a combination manual therapy, self-management, and biomechanical exercise with self-management alone. The authors reported no difference in health-related quality of life at 2 years between the two interventions and the increase in costs with the combination intervention was £25 after 1 year and £56 after 2 years. However this increase was reported as not statistically significant. Therefore it was not possible to make any definite conclusions from this study.
- **Mixed modality manual therapy:** In the UK BEAM analysis, the self-management and mixed modality manual therapy arm had most QALYs and the most costs. Sub-analysis showed that with mixed modality manual therapy unavailable it would be cost-effective to add exercise and vice versa. This study was deemed to have minor limitations. Another UK study showed that mixed manual therapy plus self-management is more cost effective than biomechanical exercise alone; however when all the comparisons evaluated in the study were considered, a three-element MBR programme with physical, psychological and education components was the cheapest and more effective option.
- **Summary:** The GDG considered the uncertainty in the economic evidence and felt that manual therapy may not be cost effective as a standalone intervention; however, the GDG considered that cost effectiveness might be more likely if manual therapy is provided as part of a ~~multimodal~~ treatment package including exercise with or without psychological therapy.

- **Quality of evidence**
  - Ranged from very low to high, mainly downgraded for imprecision of the effect estimate and the risk of bias due to unclear allocation concealment and lack of blinding.
  - The GDG noted that a large trial (UK Beam trial, n=1334) included in the combinations evidence was helpful in informing the manual therapy recommendation, because this large study showed clinical benefit of mixed modality manual therapy. However, the GDG did note that the evidence from this study was mostly rated as low quality (due to high drop-out rates and lack of blinding) and that the clinical benefit for function came from a post hoc analysis of the data.
  - The responder analyses for pain and function from two large trials of manual therapy informed the GDG's recommendation. The trials had evidence varying from medium to very low quality, and with some uncertainty about the magnitude of the differences between the groups. The GDG were aware of the limitations of responder analyses: responder analyses have reduced power to detect differences compared to analyses on the original scales, that there is a natural recovery rate observed in both intervention and comparator arms and 'responders' have not necessarily improved due to the intervention, and that the distribution functions of the dependent variables are similar in both groups. The GDG considered that the cut-offs chosen for the responder analyses reflected clinically important differences in the mean responses between the groups but were mindful that some patients may have had worse outcomes in both the intervention group and comparator groups. As well as the concerns of responder criteria, the GDG further noted that 2 of these were post-hoc analyses which raised further concerns about the reliability of this analysis. The GDG discussed that the post hoc nature of the responder analyses in these 2 trials introduces a risk of bias due to the potential for data mining. The GDG reflected their concerns about responder analyses in the strength of their recommendation and chose to advise 'consider' manual therapies as part of a ~~multimodal package of care~~ treatment package. The GDG were aware of the difficulties with providing adequate patient blinding to

manual therapy treatments as sham or placebo interventions may have contextual or primary therapeutic effects, which may reduce the differences between groups. Conversely, subjects may be able to detect if they are receiving sham treatment and this may amplify a true difference between groups because subjects in the sham group may be adversely affected psychologically.

- **Other considerations**
  - For recommendations on exercise therapies, psychological interventions, and multidisciplinary biopsychosocial rehabilitation, please see chapters 9, 15 and 17, respectively.
  - It was noted that the evidence was mixed as to whether it related to people with low back pain only, low back pain and sciatica, or mixed populations with or without sciatica, with the exception of soft-tissue therapies offered in isolation where evidence was only identified for people without sciatica.
  - The GDG agreed that there was sufficient evidence to assume the effects for a combination of therapies would apply equally to those with low back pain with or without sciatica and therefore recommended these should be considered for either condition.

NICE 2016 recommendations on manual therapy (March 2016)

11. Do not offer traction for managing non-specific low back pain with or without sciatica.

12. Consider manipulation, mobilisation or soft tissue techniques (for example massage) for managing non-specific low back pain with or without sciatica, but only as part of multimodal treatment packages.»

Belgian GDG considerations mentioned in the Lime survey at the beginning of June 2016

NICE draft recommendation11. Do not offer traction for managing non-specific low back pain with or without sciatica

Agreement with the content of the NICE recommendation 11 on traction: 15 Yes, 0 No, 0 no opinion, 0 out of competence, 0 no answer, 1 not completed

- **Comments:**
  - The section on "mixed modality manual therapy" is not clear, it should be described what are the components of the therapy.
  - According to me, the section related to "Economic evaluation" is the wrong one (it is related to imaging and not manual therapies). I am ok with the terms "manual therapies" to reflect techniques delivered by the hands of the practitioner. However, according to me, it is different from "manual therapy" which was officially defined by the IFOMPT (International Federation of Orthopaedic Manipulative Physical Therapists) and which do not include only hands-on techniques (it also include education, exercises, etc.). Therefore "manual therapies" and "manual therapy" should not be used interchangeably as it is done.

Strength of recommendation 11 on traction: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	Very limited evidence of benefit for traction as a single intervention
Low to high quality, downgrading mainly due to imprecision of effect and/or high risk of bias.	Low to high quality, downgrading mainly due to imprecision of effect and/or high risk of bias.
Values and preferences	No info provided
Costs (resource allocation)	No economic evaluation relating to traction

Agreement with the strength of the NICE recommendation 11: 10 strong, 2 weak, 0 no opinion, 3 no answer, 1 not completed

- **Comments for a weak recommendation:**
  - Because there is currently no strong evidence against traction I think it should be a weak recommendation.
- **Comments for a strong recommendation:** /

NICE draft recommendation12. Consider manipulation, mobilisation or soft tissue techniques (for example massage) for managing non-specific low back pain with or without sciatica, but only as part of multimodal treatment packages.

Agreement with the content of the NICE recommendation on 12 manipulation: 13 Yes, 1 No, 1 no opinion, 0 out of competence, 0 no answer, 1 not completed

- **Comments from the one who does not agree:**
  - I agree with the recommendation, but if the following statement is added: ... but only as part of multimodal treatment packages and never replacing active treatment strategies.
- **Other comments**:
  - It is recommended to differentiate the response between manipulation therapy and massage.
  - According to me, one should distinguish between the (sub)acute and the chronic patients. For chronic patients, OK for me. What is meant by "multimodal"? Do they mean "multidisciplinary"? If yes, still ok for me for patients with chronic pain. For acute patients, I would agree with this recommendation if "multimodal" suggests that the therapist also needs to provide education and exercices to the patient.
  - Because patients with low back pain and/or sciatica need an individual approach in function of the needs, manual therapy can be useful for some, but mostly also other strategies will be necessary. Therefore I totally agree that manual therapy can be considered, but as part of a broader package.
  - If manual therapy is used, it is essential that it is fully integrated in the multimodal treatment strategy. The manual therapist must be member of the treatment team and fully adhere to the treatment approach (rationale that must be given to the patient). A "miraculous" osteopath working completely on his own with a completely different "mechanical" rationale must be absolutely avoided.

Strength of recommendation 12 on manipulation: According to NICE formulation, it is a weak recommendation

GRADE Factors	
Balance between desirable and undesirable effects	There was mixed evidence for the effectiveness of manual therapy modalities, particularly with function outcomes not correlating with quality of life outcomes. It was also difficult to assess evidence from a wide variety of interventions for traction, and for manipulation/mobilisation. No serious events attributable to manual therapy reported but common minor and transient adverse events (mainly muscle soreness for a few days following treatment). The NICE GDG were aware of case reports and estimates of serious but very rare adverse events that may be related to spinal manipulation and took this into account when making a recommendation. Due to the possible risk of adverse events and conflicting nature of the evidence, manual therapy should be considered as part of multimodal package, rather than a sole intervention to all people with low back pain with or without sciatica. There was sufficient evidence to assume the effects for a combination of therapies would apply equally to those with low back pain with or without sciatica and therefore recommended these should be considered for either condition.

Quality of evidence	Range from very low to high quality, downgrading mainly due to imprecision of effect and/or high risk of bias. One large trial (UK Beam trial, n=1334) showing clinical benefit of mixed modality manual therapy. Concerns about responder analyses (low quality of studies, effect of natural recovery rate, post-hoc analyses), and weak strength of the recommendation: "consider" manual therapies as part of a multimodal package.
Values and preferences	Due to the possible risk of adverse events and conflicting nature of the evidence, this recommendation should be to consider manual therapy as part of multimodal package, rather than to offer manual therapy alone as a sole intervention to all people with low back pain with or without sciatica. Manual therapy should not be a mandatory component of a multimodal treatment package, but that it is one optional modality that might be considered. There was sufficient evidence to assume the effects for a combination of therapies would apply equally to those with low back pain with or without sciatica and therefore recommended these should be considered for either condition. *NICE 2009:* - *Do not offer traction* - *Consider offering a course of manual therapy, including spinal manipulation, comprising up to a maximum of nine sessions over a period of up to 12 weeks*
Costs (resource allocation)	The uncertainty in the economic evidence and manual therapy may not be cost effective as a standalone intervention but might be more likely if manual therapy is provided as part of a multi-modal package.

Agreement with the strength of the NICE recommendation 12: 5 strong, 5 weak, 1 no opinion, 2 no answer, 3 not completed

- **Comments for a strong recommendation**
  - Strong, because the recommendation is to consider it as part of a broader approach. This matches with literature findings and my own comments (cfr. supra)
- **Comments for a weak recommendation:** /

Belgian GDG comments during the GDG meeting on the 29th June 2016

NICE draft recommendation11. Do not offer traction for managing non-specific low back pain with or without sciatica

- **Changes in formulation**
  - Agreement in GDG meeting on formulation of recommendation
- **Comments concerning strength of recommendation**
  - Majority of GDG members chose for a strong recommendation
- **Conclusion: recommendation NICE 2016 unchanged**

NICE draft recommendation12. Consider manipulation, mobilisation or soft tissue techniques (for example massage) for managing non-specific low back pain with or without sciatica, but only as part of multimodal treatment packages.

- **Changes in formulation**
  - "(e.g. massage)" should be removed: soft-tissue techniques involves much more than only massage
  - "with or without sciatica" should be removed: The GDG members mentioned the potential harms of manipulation in patients with radicular pain. Due to the confusion on the definition of non-specific low back pain with sciatica, the GDG preferred to remove this part of the sentence. If radicular pain is included in the definition, the GDG prefer to formulate a seperate recommendation on the potential harmful effects of manipulation. This will be looked further in detail by the KCE researchers.

- A differentiation should be made between manual therapy and massage. This will be looked in detail by the KCE researchers.
- Addition of "integrated" in the multimodal treatment packages: this emphasises the need of an integrated approach in which the manual therapists (including osteopaths and chiropractors) work in in line with the other care disciplines and to avoid parallel care approaches.
- Confusion possible with definition of manual therapy: IFOMT defined manual therapy more broad as an integrated approach combined with exercises and education. NICE, however, considered manual therapy mainly as the manual actions performed by the practitioner. In the results section on combined interventions, also the results of the combinations with manual therapy are reported and taken into account in the formulation of the recommendation. In the Belgian recommendation, the definition of manual therapy will be added as a footnote.

- **Comments concerning strength of recommendation:** the majority of GDG members choose for a weak recommendation.
- **Conclusion:** new formulation of recommendation **"Consider an exercise programme (specific exercises or a combination of approaches) for people with low back pain with or without radicular pain. Take people's specific needs, capabilities and preferences into account when choosing the type of exercise".**

Additional information from Belgian GDG members

In Belgium, it would be better to mention manual techniques instead of manual therapy (that can be performed by different health providers such as osteo, chiro, manual therapists, manual physicians, etc.)

L'IFOMPT, acknowledged by WCPT and WHO provided the following definition:"Orthopaedic Manual Therapy is a specialised area of physiotherapy / physical therapy for the management of neuro-musculoskeletal conditions, based on clinical reasoning, using highly specific treatment approaches including manual techniques and therapeutic exercises.

Orthopaedic Manual Therapy also encompasses, and is driven by, the available scientific and clinical evidence and the biopsychosocial framework of each individual patient."

Stakeholders' comments and replies from NICE team on draft of March 2016

COMMENTS on TRACTION

- Spine Intervention Society*:* In terms of therapeutic non-invasive modalities, the authors have stripped therapy down to manipulation and exercise therapy. They recommend against traction, ultrasound, transcutaneous electrical nerve stimulation (TENS), and acupuncture. While these modalities do not change long-term outcome, they are palliative and one must remember that initial back pain therapy "is" palliative therapy in many cases.

  Reply NICE: The algorithm depicts the recommendations that were based on the GDG interpretation of the evidence reviewed in a graphical format.
- United Chiropractic Association*:* We are concerned that the recommendation of traction be considered as an ancillary procedure if the correct implementation of said therapy assists in improving the functional stability and integrity of the spine and its adjacent structures.

  Reply NICE: The GDG found that there was very limited evidence of benefit for traction as a single therapy, and therefore could not recommend it as an ancillary procedure.
- South West Yorkshire Partnership NHS Foundation Trust*:* In practice traction can often be helpful for reducing pain enabling to exercise and allowing a return to normal function, especially in chronic LBP

  Reply NICE: The GDG discussed the evidence, and found that there was very limited evidence of benefit for traction. Two studies showed a benefit of traction, however due to methodological concerns, the GDG did not consider this sufficient. Therefore, based on the evidence the GDG agreed that traction should not be offered for low back pain or sciatica.

COMMENTS on MANUAL THERAPY (2nd recommendation)

Methodological aspects

- Arthritis Research UK*:* The GDG acknowledge the complexity of different treatments and comment that it is easier to have sham/placebo for some treatments than others. However the GDG appear to have used different criteria for their decision-making about manual therapy than for other interventions such as self-management of exercise (i.e. they appear to have set the bar higher for manual therapy), and the evidence for it is regarded as weak. Despite this, they have recommended manual therapy as part

of a multi-model package (i.e. only to be used alongside exercise). This is an example of the inconsistency of use of the evidence for recommendations about different interventions.

Reply NICE: The GDG agreed that the evidence for manual therapy was not strong enough to recommend as a single intervention alone, however based on evidence of studies using treatment packages of 2 or 3 elements including manual therapy, they concluded that the evidence did support a recommendation for manual therapy only when part of a treatment package. This is consistent with criteria applied to all recommendations within the guideline.

- Homerton University Hospital NHS Foundation Trust: Manual therapies, exercise and acupuncture share the same difficulty in administering a valid placebo.

  Reply NICE: The GDG recognise that there is controversy over whether it is possible to effectively deliver an inert sham treatment. On discussion the GDG took the view that the included studies had included a variety of sham controls with a varied capacity to elicit physiological effects but that consistently acupuncture did not deliver clinically important effects above those shams. This was the case for both penetrating and non-penetrating shams. The GDG were of the view that the sham comparisons were essentially credible on that basis. The sham comparators included in all reviews were verified with the GDG for their appropriateness.

- Institute of Osteopathy: The decision to down-grade evidence in the manual therapy analysis due to poor blinding (page 456) is of concern. It is unfeasible to double blind trials for non-invasive therapies, which is why pragmatic trial methodology is used, yet the pragmatic trial evidence is consistently down-graded because double and single blinding is not possible. There are methods, such as where allocation concealment at the analysis and data collection stage has been thorough, by which these studies could be graded accordingly.

  Reply NICE: Quality assessment using GRADE criteria is undertaken by outcome, rather than per study, to reflect the quality of the body of evidence. A number of factors are considered in addition to blinding such as baseline comparability, dropout rates and outcome reporting, this is described in detail in the methods chapter. We also consider the likely impact of these factors before deciding whether to downgrade as per GRADE methodology. This is consistent across outcomes to reflect the overall confidence in the evidence and therefore even though blinding may not be possible in all scenarios, this is still considered a risk of bias if the outcome is subjective.

- Warwick Clinical Trials Unit*:* While it is explained in section 4.3.3.1 that in the case of marked heterogeneity (i.e. I^2>50%) predefined subgrouping would take place, in some cases the predefined subgroup analyses still yield very high I^2 values. In such cases it is stated that DerSimonian and Laird random effects models would be fitted. However, in some cases (e.g. Figure 695, where heterogeneity in the fixed effects model is 64%) it is not clear where these random effects models are? Additionally, in the cases of acupuncture and manual therapy, predefined subgroup analyses included grouping by chronicity (acute/chronic), yet chronicity is dichotomised at more/less than or equal to 4 months, rather than 3 months (as defined in Table 11). Section 4.3.1.1.1 does not sufficiently explain this decision.

  Reply NICE: the random effects model has now been applied to all forest plots with an I2 value of 50% or above. Regarding time cut-offs, the cut-off of 3 months was applied for chronicity as pre-specified in the protocols for subgroup analysis if heterogeneity was observed. The definition of acute and chronic pain has now been added to the glossary. However, the data presented in the reviews were stratified according to two time-points: equal to or less than 4 months and greater than 4 months. Reference to this cut-off in the review reflects to the time point at which the outcome was measured in the study and not to the chronicity of pain. This is detailed in section 4.3.1.1.3 of the Methods chapter.

- Warwick Clinical Trials Unit*:* We take it here that is the UK BEAM study that is being referred to. It is incorrect to state that no difference was seen in short or long term outcomes for pain and disability. Inspection of Forest Plots 637, 638, 641, and 644 show this to be incorrect. On all of these outcomes modest but statistically significant benefit was gained. This error appears to have been transmitted into the link to evidence and recommendation on page 453. We seek reassurance that the GDG were correctly appraised of these data at the time that they were formulating their recommendations on manual therapy. If not this recommendation needs to be revisited as this may be sufficient evidence to justify the use of mixed modality manual therapy as a stand-alone treatment.

  Reply NICE: The decision of whether or not a difference is meaningful is based on an MID rather than statistical significance, as described in the methods chapter. None of the values in forest plots 637, 638, 641 or 644 meet the minimal important difference (MID) for determining clinical significance, as determined by the GDG, and therefore it is correct to state that there was no clinically important benefit.

- Chartered Society of Physiotherapy: The approach taken to favour the sham-controlled evidence is not only at odds with the review question, it is also inconsistent with the approach taken for other modalities. Other modalities have been recommended despite not having evidence to show they are superior to sham interventions (e.g. psychology therapies, exercise). The approach either needs to be consistent or the inconsistencies fully explained.

Reply NICE: The GDG were careful to ensure consistency in their decision making across the evidence reviews, giving placebo/sham evidence priority across reviews. However, for some interventions, sham/placebo comparisons were either not possible to conduct or not available Where evidence reviews lack sham comparisons because they were not feasible, the GDG has had to make decisions of clinical effectiveness accordingly. Comparisons to other treatments or usual care are also taken into consideration in all reviews where available. However, where placebo or sham is available, this has been given priority in the review process to first demonstrate a treatment effect separate from the non-specific treatment effects.

- National Council for Osteopathic Research*:* The GDG down-graded evidence in the manual therapy analysis due to poor blinding (page 456), it is however impossible to fully blind a pragmatic trial. We feel the use of consensus may have led to a predominance of bias towards more invasive treatment recommendations. This is also reflected in the research recommendations: there are none for primary care. Suggestion: Manual therapy should be recommendation as a stand-alone treatment.

  Reply NICE: Finally, the GDG are aware of the difficulties of fully blinding interventions such as manual therapy, and took this into account when considering the evidence. This is detailed in section 12.6 (Recommendations and link to evidence, paragraph Quality of evidence). GRADE quality rating informs the overall confidence in the evidence due to factors including risk of bias, and therefore ratings for outcomes where blinding is more problematic are still downgraded. This is also true of other interventions included in the guideline and the approach to evidence quality appraisal and consideration is consistent as stated in the methods, section 4.3.2.

Evidence

Definition of manual therapy

- Homerton University Hospital NHS Foundation Trust: Specifically mentioning the word 'massage' within the headline recommendation is unhelpful and could give the impression that the evidence for massage is more robust than it actually is and undermine in the eyes of the public the greater value of self management approaches and active therapies such as exercise.

  Reply NICE: The manual therapy recommendation has been reworded following stakeholder feedback. This now specifically refers to exercise rather than multi-modal therapy. This recommendation emphasises that any manual therapy should only be done as part of a package including exercise. **Massage is only listed as an example of manual therapy**.

- Homerton University Hospital NHS Foundation Trust*:* Physiotherapy informed by current best practice in chronic pain takes into account psychosocial factors before considering manual techniques. Overall these guidelines on manual techniques do not consider how Physiotherapy management of low back pain or sciatica might be informed by current knowledge in chronic pain.

  Reply NICE: This guideline recommended packages of care that include spinal manipulation and psychological therapy where appropriate. The reviews consider a range of treatments that may be delivered by a physiotherapist, but look to determine the effectiveness of the specific intervention rather than focussing on the healthcare profession that may deliver it.

- National Council for Osteopathic Research*:* There is inconsistent use of the UK BEAM trial data. UK BEAM trial had 4 arms: Best practice usual care (rebranded as self-management), exercise, manipulation package of care and manipulation package of care plus exercise. These data were extracted for mixed modality vs usual care but not extracted or included in the effectiveness analysis for exercise vs usual care. We would like more information and transparency about why studies were excluded (reasons not given for UK BEAM in Appendix L rejected studies).

  Reply NICE: We note that the UK BEAM trial had the following four arms: 1) self-management; 2) self-management plus exercise; 3) self-management plus manual therapy; 4) self-management plus exercise plus manual therapy. On considering this alongside the protocols for the reviews in this guideline, comparisons of self-management plus manual therapy versus self-management (3 versus 1) and self-management plus exercise plus manual therapy versus self-management (4 vs1) had been included in the manual therapy chapter. Comparison of self-management plus manual therapy versus self-management plus exercise (3 versus 2) has now been added to the manual therapy review (chapter 12). Comparison of self-management plus exercise versus self-management (2 versus 1) has now been added to the exercise review (chapter 9). We apologise for any omissions in the consultation version of the guideline.

- Royal College of Chiropractors*:* The care offered by chiropractors for the treatment of low back pain (as described in our quality standards for Chronic Low Back Pain and Acute Low Back Pain; http://www.evidence.nhs.uk/Search?ps=20&q=Chiropractic+quality) comprises manual therapy techniques often as part of a package of care which

may include exercises, psychosocial intervention and other advice to support self-management. Thus, we are generally supportive of the recommendations regarding manual therapy.

Reply NICE: thank you for your comment

- Royal College of Chiropractors*:* To ensure consistency and to avoid any confusion among health professionals and the public, where manipulation of the spine is discussed and recommended in the documentation, the specific term 'spinal manipulation' should be used rather than simply 'manipulation' (which is sometimes used in the context of soft tissue manipulation.)

  Reply NICE: This change has been made throughout the guideline.

- Royal College of Chiropractors*:* We welcome the clear statement that, *'It is noted that mobilisation and soft tissue techniques are performed by a wide variety of practitioners; whereas manipulation is usually performed by chiropractors or osteopaths, and by doctors or physiotherapists who have undergone additional training in manipulation. Manual therapists often combine a range of techniques in their approach and may also include exercise interventions and advice about self-management.'*

  Reply NICE: Thank you for your comment

- Extended Scope Practitioners Professional Network: We feel the term "massage" should be removed from the document. This term has different meaning to therapists and the lay person. General massage is rarely used, although some therapists may use more directed soft-tissue techniques such as on trigger points or fascial release.

  Reply NICE: The recommendation has been reworded to: consider manual therapy for managing non-specific low back pain with or without sciatica, but only as part of a treatment package including exercise with or without psychological therapy, Therefore the term 'massage' has been removed from the recommendation. The term massage has been used in the review under the category of soft tissue techniques as agreed the by the GDG. The term also reflects language used in papers from which the data was extracted.

- Royal College of Chiropractors*:* The definition of manual therapies incorrectly states that these are delivered by a GP and contradicts the accurate paragraph we have highlighted above (Full, part 1; p349, lines 9-13). It should be altered for correctness and consistency.

  Reply NICE: The GDG do not agree that this statement is incorrect and are aware that manual therapies may be delivered by a range of healthcare professionals, including GPs as stated.

- National Council for Osteopathic Research*:* Please can the editors ensure the term physiotherapist is replaced with manual therapist throughout the report and the term manual therapist used consistently throughout the report. Manual therapists can be physiotherapists, osteopaths and or chiropractors all of whom are statutory registered health care professionals who provide manual therapy. Please can this also be clearly stated in the glossary. In addition this terminology would more clearly reflect the intervention based approach to the review of evidence and align with the National Back Pain Pathway that considers competencies of the practitioners delivering care rather than professions. Suggestion: consistently use the term manual therapist throughout the report in the text for the discussions, recommendations and press releases. Suggestion: Define manual therapists, in the body of the report and the glossary, as osteopaths, chiropractors and physiotherapists.

  Reply NICE: We understand your concerns regarding the terminology, however the use of 'physiotherapist' has only been used when directly reporting what the included studies have specified. Therefore it wouldn't be correct to replace the term physiotherapist with manual therapist.

- Acupuncture Association of Chartered Physiotherapists*:* Why has massage/ soft tissue techniques been recommended where it is stated that there was only low quality evidence available and there was a statement of no benefit? This potentially has a greater cost impact on the NHS than AP.

  Reply NICE: Soft tissue techniques as well as other forms of manual therapy have been recommended only as part of a treatment package including exercise with or without psychological therapy. This is based on evidence in Chapters 9, 12 and 17 of studies using a two or three element treatment package.

- Esoteric Practitioners Association: We support the inclusion of personalised one-on-one hands-on gentle manual therapy as one of the most natural and traditionally established approaches to low back pain and sciatica in combination with a holistic approach which includes the person's lifestyle choices and behaviour patterns which are influenced by psycho-social factors. This is a notable move away from the recent observed trends in therapy, which have included 'treatments by telephone' that have been advocated by some health insurance companies and NHS commissioning groups, and that we do not support. It has been our clinical experience that patients with lower back pain benefit greatly from gentle and supportive touch, as a 'role-modeling' reflection from the practitioner to the client in how they may take responsibility for the quality in which they could care for themselves. We observe that this has regularly resulted in clients taking more care of their bodies and supported overall and

ongoing body awareness. This in turn supports any personal lifestyle changes that the patient needs to make in order to aid recovery and prevention of their condition. It is important that group work such as 'Back Schools' do not replace personalised care, as each patient's symptoms and circumstances are unique and need to be addressed individually as well.

Reply NICE: We agree with you and have not included any evidence from studies of manual therapy interventions delivered over the phone within the review. We have also excluded back schools as an intervention.

Comparison to placebo/sham

- University of York*:* The trial and meta-analytic data on manual therapy compared to placebo/sham is more limited than the trial data on acupuncture compared to sham in many ways:
    - the total number of trials, total participants and mean number of participants for acupuncture vs. sham are documented as 11 trials, 1971 participants and mean sample size of 179, whereas manual therapy vs sham comprise of 7 trials, 697 patients and mean of 97;
    - of the 11 trials of acupuncture, 7 are assed as "low risk of bias" and 4 are a "high risk of bias", whereas, of the 7 trials of manual therapy vs. sham, 2 are assessed as "low risk of bias and 5 as "high risk of bias" or "very high risk of bias";
    - in a summation of quality of evidence GRADE scores, when comparing acupuncture vs. sham, 16 out of the 48 meta-analyses that are assessed as HIGH GRADE, whereas for manual therapies vs. sham, 4 of the 19 meta-analyses are assessed as HIGH GRADE.
    - in the meta-analyses, 12 show benefits that are statistically significantly better than sham over the short and longer term, whereas for manual therapy (excluding traction) vs. sham, only 5 show that manual therapy outperforms sham;
    - short term benefits (≤ 4 months) of acupuncture vs. sham are supported by a meta-analysis of 7 trials with 1359 patients showing a statistically significant reduction in pain greater than the MCID of 1 point (based on a correction to one of the errors in Figure 667, Page 153, Appendix K, as set out below) on a VAS 0-10 scale, whereas the meta-analytic evidence for manual therapy vs. sham involving five trials of 533 participants shows a borderline statistically significant reduction in pain of -0.26 (CI: -0.53 to -0.00);
    - the evidence on longer term benefits (> 4 months) of acupuncture vs. sham is supported by a HIGH GRADE meta-analysis of four trials with 1159 patients showing acupuncture is statistically significantly superior to sham (Figure 668, Appendix K), whereas for manual therapy, there is no long-term (> 4 months) data on soft tissue massage, and data from two trials involving 229 participants of manipulation/mobilisation vs. sham trials provide only a non-significant longer-term benefit (Appendix K, Figure 520).

  If manual therapies are considered sufficiently evidence-based to be recommended by the GDG, albeit as part of multi-modal treatment packages, then there is as strong a case for acupuncture to be recommended given the current state of the evidence as set out by the Draft, and that the corrections will provide an even stronger case.

  Reply NICE: The GDG discussed that there was some albeit limited evidence of benefit of soft tissue techniques and mixed modality manual therapies compared to sham treatments in terms of improving pain and quality of life. These benefits were observed in the short term follow up and somewhat inconsistent, but were not maintained in the longer term. They agreed that there was insufficient evidence to recommend the use of manual therapies in isolation. However, evidence from their use in combination with other treatments, and as part of multidisciplinary biopsychosocial rehabilitation programmes provided more evidence of benefit and therefore the GDG agreed a recommendation to consider manual therapies as part of a package of treatment was warranted. Since there was no evidence of acupuncture being used in similar treatment package, the recommendation for acupuncture was restricted to evidence included in chapter 13. The amended mean differences for figures 667 and 668 in the acupuncture review are 0.80 and 0.26 respectively, which still do not meet the MID criteria, and therefore are not clinically significant. Furthermore, a sensitivity analysis was carried out using individual patient data which impacted these forest plots (and others, please see appendix K.9) which further highlighted the lack of clinical benefit seen for acupuncture over sham. The wording of the manual therapies recommendation has been edited to the following: Consider manual therapy for managing non-specific low back pain with or without sciatica, but only as part of a treatment package including exercise with or without psychological therapy.
- Warwick Clinical Trials Unit*:* We consider there is an inconsistency in how the evidence has been interpreted here. The evidence presented supports the hypothesis that manual therapy can be superior to usual care. It does not, however, support the hypothesis that it is superior to sham therapy. If, as the GDG opine elsewhere that therapist

delivered interventions need to be shown to be superior to sham (which would require a change in the wording of the research question) to be recommended then they should not be recommending manual therapy.

Reply NICE: We recognise that the evidence does not support manual therapy alone as superior to sham. Therefore the GDG made a recommendation for manual therapy only when part of a treatment package of exercise with or without psychological therapy which was informed by evidence from manual therapies used in combination with other treatments, and also evidence within the review of multidisciplinary biopsychosocial interventions.

- United Chiropractic Association*:* We are concerned that the clinical efficacy of spinal manipulation has not been shown to be any less effective than is the case with respect to the current guideline CG88. We are concerned that this recommendation may imply that, only in addition to exercise in a multi-modal treatment package would spinal manipulation be considered valuable, clinically indicated, and cost-effective. This is simply not appropriate in all cases. Dependent upon the initial presenting criteria, and the nature of the NSLBP and Sciatica problem, clinically effective care with spinal manipulation may be indicated PRIOR to exercise being tolerated. Due consideration should be in the hands of the clinician to determine the order/ frequency of manipulation, progressing to a multi-modal treatment package when clinically appropriate.

  Reply NICE: The GDG agreed that the evidence reviewed did not provide sufficient evidence of benefit of manual therapies compared to sham to recommend their use in isolation. However, evidence from its use in combination with other treatments and from the MBR review, did show more benefit. The recommendation has been reworded following stakeholder feedback. It now reads: consider manipulation for managing non-specific low back pain with or without sciatica, but only as part of a treatment package including exercise with or without psychological therapy. This recommendation was based on evidence from two studies of treatment packages including the aforementioned components (see chapters 9, 12 and 17). The GDG agreed that based on the evidence, manual therapy could not be recommended as an independent intervention.

- Complementary and Natural Healthcare Council***:*** We are pleased to see that massage remains in the guidelines, albeit only as part of a multi-treatment package. We recommend that to ensure good practice, only massage therapists registered with an Accredited Register such as the Complementary and Natural Healthcare Council (CNHC) are used. The Accredited Register Programme is a government-backed programme to accredit voluntary registers and is a guarantee of standards. All practitioners on CNHC's Accredited Register have met UK wide standards, hold professional indemnity insurance, abide by a strict Code of Conduct, Ethics and Performance and must take part in CPD each year. For more details see www.professionalstandards.org.uk . For more details of CNHC see www.cnhc.org.uk

  Reply NICE: Your comments will be considered by NICE where relevant support activity is being planned.

- General Council of Massage Therapists*:* There is tremendous variation in the quality of education of Massage and Soft Tissue Therapists in the UK. You will also be aware that the profession is not regulated by statute and relies on the efforts of the various Professional Associations to ensure the protection of the public. We would therefore strongly suggest that the guidelines recommend that only therapists belonging to Professional Associations that are council members of the General Council of Massage Therapists (GCMT) be considered. These suggestions would ensure that therapists are educated to an appropriate standard, properly insured and are subject to the disciplinary procedures of both their professional associations and a regulatory body. Belonging to a Professional Association provides the primary level of public protection, but as a further layer of security it may also be desirable that, ideally, Massage and Soft Tissue Therapists are additionally registered with a Professional Standards Authority (PSA) accredited register. If this suggestion is adopted we would suggest that the appropriate accredited registers would be the voluntary regulator the Complementary and Natural Healthcare Council (CNHC) and the British Association of Sports Rehabilitators and Trainers (BASRaT).

  Reply NICE: It is beyond the scope of this review to specify who should deliver an intervention, the review focussed on whether or not manual therapy was clinically and cost-effective and was based on the best available evidence identified according to the review protocol.

Multimodal treatment package

- James Cook University Hospital*:* In a number of recommendations it is suggested that some treatments be offered only as part of a multimodal treatment package. The format or delivery of such a package is not defined within the guidance. It is not clear whether this is a package which might be delivered by a single individual, for example manipulative therapy delivered by a "psychologically informed therapist" with discussion and advice on other self-management techniques, or a package delivered by more than one person. Clearly the involvement of another practitioner would have significant effects on costs and cost effectiveness and might indeed alter the recommendation. It is not clear why a treatment option should become more effective simply by including it with other options. BMR programmes are examined in their own right. It is suggested that the GDG may wish to consider avoiding the recommendation to consider only as part of a multimodal treatment package with reference to single treatment

modalities, to maintain clarity of the document. If it is thought the recommendation should stand, it may be clearer if the same wording is used, i.e. multidisciplinary biopsychosocial rehabilitation (MBR) programmes.

Reply NICE: Manual therapies and psychological therapies have been recommended as part of a treatment package because there was insufficient evidence to recommend either as a standalone treatment. However there was evidence for each therapy in combination with other treatments (this evidence is in the individual reviews) as well as from the review of multidisciplinary biopsychosocial interventions (MBR). MBR programmes have also been reviewed separately as they are defined as interventions involving a physical component and at least one other element from a biopsychosocial approach, offered as an integrated programme. In this respect they are different from simple combinations of interventions. Where relevant, evidence on combinations of interventions has been collected and reported in a designated section of the chapter for each intervention. This evidence informed the recommendations on the effectiveness of interventions being offered in combination. Acknowledging the considerable variability of healthcare professionals who might deliver such combinations of interventions, and the variability in the evidence reviewed, it was not possible to make clear in the recommendation who or how many professionals should deliver such interventions.

- Society for Back Pain Research*:* It would be helpful to have a definition of multi-modal care in the recommendation table. Multi-modal is not a term currently used. An alternative may be “package of care”. We note that trials of manual therapy show an effect on its own. Clearly manual therapy will be delivered individually, but if delivered as part of a multi-modal intervention with exercise, would the exercise still be in a group. If so, this would necessitate 2 appointments! There is an error in how the Hurley et al 2004 paper is described in the table, the study took place in the United Kingdom, Furthermore, the conclusions drawn concerning the effectiveness of interferential therapy are incorrect as it was found to be as effective as manual therapy when used alone or in combination. SUGGESTION: Manual therapy integrated (with) intervention that would include ********** There are no RCTs of multi modal treatment. Only RCT's of individual treatments. INCONSISTENCY: the criteria for judging the effectiveness of manual therapy is set higher than for self-management and exercise. Despite the evidence being weak the GDG have recommended manual therapy as part of a multi-model package

  Reply NICE: Following stakeholder feedback, the recommendation has been reworded. It now reads; “Consider manual therapy for managing non-specific low back pain with or without sciatica, but only as part of a treatment package including exercise with or without psychological therapy”. Although there were some trials demonstrating clinically important effects for manual therapy alone, overall the GDG agreed that the evidence was too inconsistent to make a recommendation for manual therapy as a sole treatment, whereas there was more supportive evidence of its use in combination with other treatments. It was therefore agreed that the recommendation should be to consider manual therapy as part of treatment package only. This recommendation was based on evidence from two studies that used a treatment package, which can be found in chapters 9, 12 and 17. The GDG are aware that packages of treatment may mean more than 1 appointment for patients but agreed this was where the evidence of treatment effect was. The error in table 242 has been corrected to reflect that the study took place in the UK. The Hurley 2004 paper had two comparisons that were included in the manual therapy review, and one in the electrotherapy review. The arms included in the manual therapy review were 1) manipulation/mobilisation versus inferential therapy, and 2) manipulation + inferential therapy versus inferential therapy. The results for comparison 1) showed that there was a clinically significant benefit for manipulation/mobilisation for two of the quality of life domains at both short and long term time points, and only for one domain for inferential therapy. The results for comparison 2) showed a clinically significant benefit for 3 quality of life domains in the short term and 8 in the long term all in favour of inferential therapy with manipulation. There was no significant benefit for inferential therapy alone. None of the comparisons showed a clinically important benefit for pain or function for either intervention. Therefore inferential therapy alone was not as effective as manual therapy or manual therapy with inferential therapy in terms of quality of life.
- Warwick Clinical Trials Unit: Recommendation 12 suggests the use of manual therapy techniques only as part of a multi-modal package. So far as we can see in the guidance what constitutes a multi-modal package of care is not described; nor was the evidence for such packages appraised. For this recommendation to be helpful, the GDG needs to spell out the composition of the multi-modal intervention that is recommended. This needs to include indications of both content and dose of these interventions. The dose delivered is important as the best data showing a positive effect from manual therapy from RCTs with substantially more than the six sessions of physiotherapy care typically available from the NHS. To recommend an inadequate dose of manipulation, mobilisation or soft tissue techniques will mean that patients may fail to gain any of the potential benefits from this treatment approach. It should be noted here that the effects sizes found in trials of manual therapy are, at best, modest. The 2011 Cochrane review of spinal manipulative therapy for chronic LBP, for example, estimated the SMD for a short term effect to be 0.22 (95% CI 0.07 to 0.36). This is far below the threshold of an SMD of 0.5 specified in the methods for this guideline. The GDG do not appear to have explained why they have chosen to use a lower threshold here for recommending treatment.

Reply NICE: The term 'multi modal' has now been changed following stakeholder feedback. Therefore the revised recommendation now reads: consider manual therapy for managing non-specific low back pain with or without sciatica, but only as part of a treatment package including exercise with or without psychological therapy, where manual therapy is defined as manipulation, mobilisation or soft tissue techniques, for example massage. The GDG was unable to recommend a specific dose of the intervention from the evidence examined in the review.

- Chartered Society of Physiotherapy*:* We welcome the focus on multi-modal treatment here. Physiotherapists report that the use of manual techniques can often open a "window of opportunity" to then enable the patient to participate in more active treatment such as exercise. This recommendation reflects the practice of a number of physiotherapists who use manual techniques as just one aspect of their treatment.

  Reply NICE: Thank you for your comment.

- United Kingdom Spinal Societies Board and British Orthopaedic Association*:* In a number of recommendations it is suggested that some treatments be offered as part of a multimodal treatment package. The format or delivery of such a package is not defined within the guidance. It is not clear whether this is a package which might be delivered by a single individual, for example manipulative therapy delivered by a "psychologically informed therapist" with discussion and advice on other self-management techniques, or a package delivered by more than one person. Clearly the involvement of another practitioner would have significant effects on costs and cost effectiveness and might indeed alter the recommendation. No evidence has been brought forward concerning such a multi modal package. Further guidance on the definition of multi-modal package, by whom it should be delivered and an assessment of the evidence base would be greatly appreciated.

  Reply NICE: The term 'multimodal' has been amended. The recommendations now refer to 'a treatment package including exercise with or without psychological therapy' and 'a treatment package including exercise with or without manual therapy', to make the format and content more transparent. These recommendations are based on evidence from studies that used a treatment package consisting of these components, which can be found in chapters 9, 12 and 17. It is beyond the scope of this review to specify who should deliver an intervention, the review focussed on whether or not interventions are clinically and cost-effective and was based on the best available evidence identified according to the review protocol.

- National Council for Osteopathic Research*:* Defining a multi-modal treatment package as exercise plus manual therapy, self-management and psychological therapy (NICE guideline short version page 8) seems to imply that the effectiveness of exercise was superior to the other modalities. This is not the case according to the evidence presented by the GDG. There is no evidence to show which combinations of therapies, if any, are more effective and or active than others. This recommendation does not reflect the findings as presented. If the GDG are recommending exercise plus self-management, manual therapy and exercise they need to recommend them as treatments in their own right as there is no evidence presented to show that combining them makes them more effective. In addition on page 456 'The GDG noted that a large trial included in the combinations evidence was helpful in informing the manual therapy recommendation, because this large study showed clinical benefit of mixed modality manual therapy. If the study was mixed modal manual therapy why is exercise recommended as the only mandatory component (page 8 NICE guideline short version). Comment on implementation of multi-modal care package. Perhaps the definition of multi-modal care could be expanded upon. Most manual therapists would argue that the treatment package they give is multi-modal consisting of psychological and self-management support, exercise, general and public health advice plus hands on manual therapy. To redefine multi-modal care as separate packages as implied in the implementation would be resource intensive and costly if delivered by multiple people rather than multi-skilled practitioners such as manual therapists. The concept of multi-modal treatment intervention might be better phrased as integrated multi-modal care. This seems sensible but the implementation, description and rationale has got a bit lost in the body of the report. The guideline might incorporate a recommendation to multi-skill professionals to deliver an integrated multi-modal package of care that might include: manual therapy, exercise, self-management and psychology. Suggestion: consider manual therapy as a stand-alone intervention and recommend that therapists deliver a multi-modal package of care that includes manual therapy, exercise, psychological support, advice and guidance

  Reply NICE: The recommendation has been reworded following stakeholder feedback. It now reads 'consider manipulation for managing non-specific low back pain with or without sciatica, but only as part of a treatment package including exercise with or without psychological therapy'. This recommendation was based on evidence from studies of treatment packages including the 2 or 3 of the aforementioned elements (see chapters 9, 12 and 17). Exercise was a component in all comparisons whereas the other interventions where not. Therefore, exercise was the only compulsory element, based on the evidence.

- Institute of Osteopathy*:* We would suggest that the section on multi-modal package of care needs clarification and consistency in the recommendations. Most manual therapists would argue that the treatment package they give is multi-modal consisting of psychological and self-management support, exercise, general and public health

advice plus hands on manual therapy. This is reflected in the full guidelines (page 349, line 11) which clearly states that: *"Manual therapists often combine a range of techniques in their approach and may also include exercise interventions and advice about self-management".* However, in the short version it currently states (page 8, line 15) that: "*Multi-modal treatment include exercise and at least one of the following: Self-management,* Manual therapy, *Psychological therapy (for example, cognitive behavioural therapy)".* To redefine multi-modal care as separate packages as implied in the implementation would be resource intensive and costly if delivered by multiple people rather than multi-skilled practitioners such as manual therapists. We would suggest that the authors reflect the ability of manual therapists to deliver multi-modal care.

Reply NICE: The recommendation has been reworded following stakeholder feedback. It now reads: consider manipulation for managing non-specific low back pain with or without sciatica, but only as part of a treatment package including exercise with or without psychological therapy. Regarding the professional delivering interventions, for many of the interventions included in the guideline levels of training may differ according to the expertise of the practitioner, however this cannot be assessed within the systematic review and it has been assumed that unless otherwise stated, that the people delivering the interventions are trained to do so. Professionals delivering interventions should be appropriately trained to do so.

Adverse events

- Institute of Osteopathy: We have concerns about the statement made in chapter 12 summary that states: *'Due to the possible risk of adverse events and conflicting nature of the evidence, the GDG agreed that this recommendation should be to consider manual therapy as part of multi-modal package of care, rather than offer manual therapy alone as a sole intervention to all people with low back pain with or without sciatica.' (Part 1 page 452).* Particularly as it does not reflect the statement made on page 453 where the GDG reports the following: *'Adverse events were common, MINOR and transient, consisting of mainly muscle soreness for a few days following treatment. No serious events attributable to manual therapy were reported by any of the studies reviewed.'* We would refer the authors to the NCOR response which provides more detailed information of the context of adverse events data which shows that the risk of major adverse events is extremely rare (0.007%) after manual therapy or 0.01% per manual therapy patient, (Carnes et al Adverse events in manual therapy: a systematic review. Manual therapy 2010; 15: 355-363). In short, this recommendation has been based on an extremely low risk of serious adverse events. This is in contrast to the rationale used to recommend invasive, surgical intervention such as discectomy, discussed in part 2 of the guidelines.

  Reply NICE: The sentence in section 12.6 has been revised to clarify that the recommendation was not based on the risk of adverse events. Although the GDG were aware of the possibility of adverse events, we agree that they were minor and transient. The recommendation was based on the conflicting nature of the evidence. The GDG noted that there was mixed evidence for the effectiveness of manual therapy modalities and therefore they could not be recommended for low back pain or sciatica as independent interventions. However, evidence from their use in combination with other treatments, and as part of multidisciplinary biopsychosocial rehabilitation programmes provided more evidence of benefit. The GDG therefore agreed that the recommendation should be to consider manual therapy as part of treatment package.

- National Council for Osteopathic Research: Comment on inconsistent use of adverse event information and evidence. The GDG state that the incidence of serious adverse events is very small for manual therapy (page 453) 'Adverse events were common, MINOR and transient, consisting of mainly muscle soreness for a few days following treatment. No serious events attributable to manual therapy were reported by any of the studies reviewed. The GDG were aware of case reports and estimates of serious but very rare adverse events that may be related to spinal manipulation and took this into account when making a recommendation.' The evidence of case reports was not reviewed and should be dismissed, as other research has indicated over reporting of these extremely rare events by multiple practitioners and prospective cohort study meta-analyses have shown that the risk of major adverse events is extremely rare (0.007% after manual therapy or 0.01% per manual therapy patient) (Carnes et al Adverse events in manual therapy: a systematic review. Manual therapy 2010; 15: 355-363, CROAM study 2013. This is a prospective cohort study of adverse events in osteopathy http://www.osteopathy.org.uk/news-and-resources/document-library/research-and-surveys/the-croam-study-february-2013/). In the summary of chapter 12, it is stated 'Due to the possible risk of adverse events and conflicting nature of the evidence, the GDG agreed that this recommendation should be to consider manual therapy as part of multi-modal package of care, rather than offer manual therapy alone as a sole intervention to all people with low back pain with or without sciatica.' (Part 1 page 452). This recommendation based on an extremely low risk of a serious adverse events and minor transient muscle soreness is in contrast to the rationale used to recommend discectomy in part 2 of the guideline. Invasive therapies part II page 219. Discectomy vs usual care: 'In terms of function, the randomised evidence showed no difference between treatments, although the non-randomised data suggested a clinically important difference favouring discectomy in both short and long term' and

'The GDG noted that re-operation may not be considered as adverse events following surgery, but may be a natural history of the condition since about 5% of patients will suffer from a recurrence of disc prolapse' (3rd paragraph page 219). On page 221 Quality of evidence it is stated: 'The evidence for all comparisons and all outcomes was rated as low or very low quality, mainly due to risk of bias (and some imprecision)……later page 222 'The group agreed that surgical intervention following a period of conservative management for around 6 weeks would be reasonable. However it was noted that there was little evidence to support this time point and that the conservative treatment interval was largely historical and consensus based'. This is in contrast to the decision rationale used for the recommendations for manual therapy and illustrates inconsistent interpretation of adverse events and evidence. We question the recommendation for the use of discectomy after 6 weeks based on the evidence presented in this chapter (Chapter 28 Spinal decompression for sciatica). Suggestion: Review adverse event evidence more consistently and transparently and include prospective cohort study evidence.

Reply NICE: We are aware that it is difficult to get an accurate estimate of adverse event occurrence from clinical trial data, however this applies to all of the interventions studied in the guideline, and where adverse event data was limited, GDG expert opinion and knowledge of adverse event occurrence in clinical practice has further informed the recommendations in this area. To clarify that the GDG used expert opinion and knowledge on adverse events alongside the evidence included in the review, the sentence in Section 12.6 has now been edited to read as follows: 'The GDG were aware of possible serious but very rare adverse events that may be related to spinal manipulation and took this into account when making a recommendation'.

- Royal College of Chiropractors*:* It is incorrectly stated that Santilli 2006 did not report adverse events whereas the paper clearly states that there were no adverse events.

  Reply NICE: Data from the Santilli study has now been added to the manual therapy review (chapter 12). Data on adverse events has been added to the 'Data unsuitable for meta-analysis' table in section 12.3.1.4.

- Warwick Clinical trials Unit*:* We note that the GDG have not taken the opportunity to identify systematic reviews of adverse events from manual treatment and thus are simply relying on their opinion when considering the potential risk of this treatment approach. It is unacceptable for the GDG to use their awareness of case reports of serious adverse events as a basis for recommendation. We agree that risk of adverse events needs to be considered for all interventions. The appropriate source for data on this subject would be a systematic review of observational studies. See, for example, Carnes et al Adverse events in manual therapy: a systematic review. Manual therapy 2010; 15: 355-363 that gives numeric estimates for the incidence of serious adverse events from both observational studies and RCTs.

  Reply NICE: Regarding adverse events, the GDG considered those reported in the trials included in the review. Adverse events were common, minor and transient. They mainly consisted of muscle soreness for a few days after treatment. Furthermore, none of the studies included in the review reported serious events attributable to manual therapy. Although we are unable within the resources of the guideline to undertake additional reviews for adverse events for each intervention, GDG clinical expertise is also used to inform on this aspect. The GDG were aware of serious but very rare adverse events that may be related to spinal manipulation and this was taken into account in writing the recommendation. The paper by Carnes et al was not included in the review because the population was not restricted to people with low back pain and sciatica in the trials included.

- Royal College of Chiropractors*:* We are concerned that anecdotal evidence from GDG members, which was not described or evaluated in the guidance documentation, was apparently used to inform the recommendation to consider manual therapy only in conjunction with exercise, despite the fact that the systematically reviewed evidence did not indicate any serious adverse events. We question (a) whether this approach is in keeping with NICE guideline development policy, (b) whether the issue of adverse events associated with manual therapy of the lumbar spine was further investigated in the literature, and (c) whether anecdotal evidence in relation to other treatment modalities was considered when formulating the recommendations in this document.

  Reply NICE: The GDG considered the adverse events reported in the studies included in the review, which were common, minor and transient. They mainly consisted of muscle soreness for a few days after treatment. Furthermore, none of the studies included in the review reported serious events attributable to manual therapy. The GDG were in fact aware that adverse events are rarely reported in clinical trials. Although it is not possible within the resources of the guideline to undertake a systematic review of adverse events for all treatments, GDG clinical expertise is used to inform this area, where data from the clinical trial data is lacking, consistent with NICE guideline development policy. The GDG were aware of possible serious but very rare adverse events that may be related to spinal manipulation and this was taken into account in writing the recommendation, however the decision to only offer manual therapies as part of a package of treatment was not based solely on this evidence, but also the lack of consistent evidence for other outcomes as a sole intervention, but evidence of benefit when used in combination.

NICE changes in the final version of the guideline (November 2016)

- **In blue in the text**

NICE final recommendations on manual therapies (November 2016)

12. Do not offer traction for managing low back pain with or without sciatica.

13. Consider manual therapy (spinal manipulation, mobilisation or soft tissue techniques such as massage) for managing low back pain with or without sciatica, but only as part of a treatment package including exercise, with or without psychological therapy

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

- The word “therapy” should be replaced by “techniques” in order to avoid confusion about who could perform these techniques.
- Combined recommendation on manual techniques and on psychological therapies will be split again in 2 separate recommendations.
- The definition of manual therapy should be included in the pathway (and not in a guideline).

KCE 2017 final recommendations on manual therapies (February 2017)

X. Do not offer traction for managing low back pain with or without radicular pain

(strong recommendation based on high to low quality from RCTs)

8. Consider manipulation, mobilisation, or soft tissue techniques for managing low back pain with or without radicular pain, but only as part of a multimodal treatment with a supervised exercise programme.

(weak recommendation based on high to very low quality from RCTs)

7.9. Acupuncture

Acupuncture in patients with low back pain ± radicular pain

NICE search question
"What is the clinical and cost-effectiveness of acupuncture in the management of non-specific low back pain and sciatica?"

Introduction based on the draft version of NICE guideline (March 2016)

- In the UK, doctors, physiotherapists and manual therapists are increasingly using acupuncture on the basis of neurophysiological mechanisms, known as 'Western medical acupuncture'.
- Acupuncture involves treatment with needles, and is most commonly used for pain relief. However uncertainty remains as to the benefit of acupuncture in the management of non-specific low back pain and sciatica.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with sciatica • Populations with neurogenic claudication causing leg pain will be included
Intervention(s)	• Acupuncture
Comparison(s)	• Placebo/Sham/Attention control • Usual care/waiting list • To each other • Any other non-invasive interventions in the guideline • Combination of interventions: any combination of the non-invasive interventions in the guideline
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (>30% improvement in pain or function) • Adverse events: morbidity; mortality. • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

- Thirty RCTs (29 in the final version of the NICE guideline) on single interventions (reported in 32 papers) were included in the review. Three studies, looking at combinations of non-invasive interventions (with acupuncture as the adjunct), were also included in this review.

Acupuncture as single intervention

- **Acupuncture versus sham/placebo**
  - **Patients with LBP without sciatica:**
    - QoL (SF-36, SF-12): Clinically important benefit (CIB) of acupuncture in all but one (mental health) of the individual domain scores of SF-36 for short-term follow-up (moderate and high quality; 1 RCT; n=80). Data from 2 large trials (RCTs) also demonstrated a CIB for the composite physical score for short- and long-term follow-up in favour of acupuncture, but not for the composite mental health score (moderate and high quality; n = 952).
    - Pain (VAS): No clinically significant difference in both the short and long term (high quality; 7 RCTs; n = 1359; and 4 RCTs, n = 1159).
    - Function (RMDQ, FFbH-R, PDI, ODI): No clinical difference demonstrated using a range of measures at short term and at long term (very low to high quality; 4 RCTs; total n = 717).
    - Psychological distress (CES-D, BDI, HADS): CIB of acupuncture for depression as measured by HADS in the short term, but not in the long term (high quality; 1 RCT; n = 95), no clinical benefit for depression at either time point using the CES-D 25 and BDI measures (high to moderate quality; 2 RCTs; n = 210 and 116).
    - Adverse events: No difference in terms of treatment related and not treatment related adverse events was observed (low quality; 2 RCTs; n = 530 and low quality; 2 RCTs; n = 984)
    - Healthcare utilisation: A clinical decrease in analgesic use in favour of acupuncture (1 RCT, moderate quality; n=210).
  - **Patients with LBP with sciatica:** no studies found
  - **Mixed population (LBP with and without sciatica)**
    - Pain (VAS): no clinical differences at short term (moderate quality; 2 RCTs; n=90). No long-term data reported.
    - Function (RMDQ): no clinical differences at short term (moderate quality; 2 RCTs; n=90). No long-term data reported.
    - Adverse events: no clinical differences in treatment-related adverse events (moderate quality; 2 RCTs; n=256).
    - Responder criteria (>35% improvement in function): no clinical differences at short term (moderate quality; 1 RCT; n=205). No long-term data reported.
    - Outcomes not reported: QoL, psychological distress
- **Acupuncture versus usual care**
  - **Patients with LBP without sciatica:**
    - QoL (SF-36, SF-12): a clinically important benefit for the composite physical score (including bodily pain (moderate quality, 1 RCT, n=214)) for short- (<4mo) (high quality; 2 RCTs, n=945) and long-term (>4mo) (low quality, 1 RCT, n=737) follow-up in favour of acupuncture but not for the composite mental health score at both time points (moderate quality, 3 RCTs; n=1011 and high quality; 1 RCT; n=737).
    - Pain (VAS): A benefit of acupuncture over usual care was shown at short term (very low quality; 8 RCTs; n=1334) but not at long-term (low quality; 3 RCTs; n=950)
    - Function (RMDQ, FFbH-R, PDI): Varying results were found for function, due to range of measures, but overall could be stated that a benefit from acupuncture was found in the short term (RMDQ; moderate quality; 5 RCTs; n=777 and PDI; moderate quality; 2 RCTs; n=300 and FFbH-R; 3 RCTs; n= 3615) but this benefit was only confirmed at the long-term in a single RCT (moderate quality; n=701).
    - Psychological distress (CES-D, HADS): No clinical differences were found at short term (CES-D; moderate quality; 1 RCT; n=214 and HADS; low quality; 1 RCT; n=86) and at long-term (HADS; low quality; 1 RCT; n=86).
    - Adverse events: No clinical differences were found (low quality; 2 RCTs; n=988).
    - Healthcare utilisation: No clinical differences were found (number of providers' visits and number of filled pain medication prescriptions) (moderate quality; 1 RCT; n=184).
  - **Patients with LBP and sciatica**: no studies found
  - **Mixed population (LBP with or without sciatica)**:

- QoL (SF-36, EQ-5D): a clinically important improvement with acupuncture compared to usual care was demonstrated in the short term across all domains and measures (single RCTs; low to very low quality; total n= 495), at the long-term no benefit was shown on EQ-5D (moderate quality; 1 RCT, n= 213) whereas another single RCT showed some improvements in bodily pain (SF-36) (very low quality; n= 212).
- Pain (VAS): a short term improvement (very low quality; 1 RCT; n=45) but not at long-term (low quality; 1 RCT; n=192).
- Function (RMDQ, ODI): a short term improvement on RMDQ (very low quality; 2 RCTs; n=100) but not at long-term (ODI) (moderate quality; 1 RCT; n=191).
- Responder criteria (>35% improvement in function): a clinical difference at short term (moderate quality; 1 RCT; n=138). No long-term data reported.
- Outcomes not reported: psychological distress, adverse events

- **Acupuncture versus active comparisons (TENS, NSAIDs, massage)**
  - **Patients with LBP without sciatica**:

    Comparison acupuncture versus TENS
    - Pain (VAS): a clinically important improvement at short term with acupuncture compared to TENS (2 RCTs; low quality; n=32). No long term data reported.
    - Function (RMDQ): no clinically important difference at short term between acupuncture and TENS (1 RCT; very low quality; n=13). No long term data reported.
    - Adverse events: no clinically important difference at short term between acupuncture and TENS (1 RCT; very low quality; n=20). No long term data reported.
    - Outcomes not reported: QoL, psychological distress, healthcare utilisation

    Comparison acupuncture versus massage
    - Function (RMDQ): no clinically important difference at short term (1 RCT; very low quality; n=172) and at long term (1 RCT; low quality; n=172) between acupuncture and massage.
    - Healthcare utilisation: no clinically important differences at long term between acupuncture and massage in number of providers' visits (1 RCT; low quality; n=172) and in number of filled pain medication prescriptions (1 RCT; low quality; n=172). No short term data reported.
    - Outcomes not reported: QoL, pain, psychological distress, adverse events
  - **Patients with LBP and sciatica**: no studies found
  - **Mixed population (LBP with or without sciatica)**:

    Comparison acupuncture versus NSAIDs
    - Pain (VAS): at short term, no clinically important difference with acupuncture compared to oral Diclofenac (1 RCT; very low quality; n=44). However, a clinically important improvement in favour of NSAIDs was found in the comparison acupuncture versus intramuscular diclofenac (1 RCT; low quality; n=58). Only long term data was reported for the latter: no clinically important difference was found between acupuncture and intramuscular diclofenac (1 RCT; low quality; n=58).
    - Function (RMDQ/ODI): no clinically important differences were found compared to oral and intramuscular diclofenac (2 RCTs; low quality; n=102) at short term. At long term, only data was reported on the comparison with intramuscular diclofenac: no clinically important difference was found (1 RCT; low quality; n=58).
    - Healthcare utilisation: no clinically important differences were found between acupuncture and intramuscular diclofenac on inpatient care (1 RCT; low quality, n= 58) and duration of hospital stay (1 RCT; low quality; n= 58) (both at short term). No long term data were reported.
    - Outcomes not reported: QoL, psychological distress, adverse events

Combination of interventions-acupuncture adjunct

- **Acupuncture in combination with active comparisons versus usual care or active comparisons**
  - **Patients with LBP**:

- Acupuncture + TENS versus usual care: no clinical important differences in pain (VAS; 1 RCT; very low; n=13) and function (RMDQ; 1 RCT; very low; n=13) at short term. No long-term data reported. Other outcomes (QoL, psychological distress, adverse events, and healthcare utilisation) were not reported.
- Acupuncture + TENS versus TENS: no clinical important differences in pain (VAS; 1 RCT; very low; n=12) and function (RMDQ; 1 RCT; very low; n=12) at short term. No long-term data reported. Other outcomes (QoL, psychological distress, adverse events, and healthcare utilisation) were not reported.
- Acupuncture + massage versus usual care: no clinical important difference in pain (VAS; 1 RCT; low; n=51) at short term. No long-term data reported. Other outcomes (QoL, function, psychological distress, adverse events, and healthcare utilisation) were not reported.
- Acupuncture + exercise (group biomechanical + aerobic) + self-management (education Back book + unsupervised exercise) versus exercise (group biomechanical + aerobic) + self-management (education Back book + unsupervised exercise): at short term a clinically important improvement in QoL (EQ-5D; 1 RCT; low quality; n=51) and in pain scores (VAS; 1 RCT; low quality; n=51) was found in the group without acupuncture. No differences was found for function (ODI; 1 RCT; low quality; n=51). However at long term, the clinically important benefits were found in favour of the acupuncture group for QoL (EQ-5D; 1 RCT; low quality; n=51) and pain (VAS; 1 RCT; low quality; n=51). Also at long-term no differences were found for function (ODI; 1 RCT; low quality; n=51). Other outcomes (psychological distress, adverse events, and healthcare utilisation) were not reported.

- **Patient with LBP and sciatica**: no studies found
- **Patient with LBP with or without sciatica**. No studies found

Table 26 – Clinical effectiveness of acupuncture as component in combined interventions

Acupuncture in combination with active comparisons versus usual care or active comparisons				
Outcome	Acupuncture + TENS versus usual care (short term <4mo)	Acupuncture + TENS versus TENS (short term <4mo)	Acupuncture + massage versus usual care (short term <4mo)	Acupuncture + exercise + self-management versus exercise + self-management (short term <4mo + long term >4mo)
QoL				At short term: **CIB favouring exercise + self-management** (EQ-5D; 1 RCT; low quality; n=51) At long term: **CIB favouring acupuncture + exercise + self-management** (EQ-5D; 1 RCT; low quality; n=51)
Pain	No diff (VAS; 1 RCT; very low; n=13)	No diff (VAS; 1 RCT; very low; n=12)	No diff (VAS; 1 RCT; low; n=51)	At short term: **CIB favouring exercise + self-management** (VAS; 1 study; low quality; n=51) At long term: **CIB favouring acupuncture + exercise + self-management** (VAS; 1 RCT; low quality; n=51)
Function	No diff (RMDQ; 1 RCT; very low; n=13)	No diff (RMDQ; 1 RCT; very low; n=12)		At short term: No diff (ODI; 1 RCT; low quality; n=51) At long term: No diff (ODI; 1 RCT; low quality; n=51)

CIB: clinically important benefit

Economic evidence

One cost-utility analysis found that acupuncture + usual care was cost effective compared with usual care alone for LBP with or without sciatica. This analysis was assessed as partially applicable with potentially serious limitations.

NICE GDG considerations (March 2016)

- **Relative values of different outcomes**
  - Most critical outcome was health-related QoL with pain severity, function and psychological distress as individually critical outcomes as well as components of QoL measure.
  - Adverse events and healthcare utilisation were considered important for decision-making
  - Responder criteria, as defined as >30% improvement in pain or function, was not considered as a critical outcome.
- **Trade-off between clinical benefits and harms**
  - Necessity of a body of evidence to show specific intervention effects over and above any contextual or placebo effects.
  - Summary of clinical effects
    - Acupuncture versus placebo/sham: only clinical benefit for QoL at short term, no differences in pain, function, adverse events
    - Acupuncture versus usual care: clinical important benefits for QoL, pain and function at short term, but not for QoL and pain at long-term. Studies with varying populations and treatment and usual care descriptions. Effect of 'waiting list' group may over-estimate effects of treatment.
    - Acupuncture versus active comparisons: low quality evidence, small sample sizes, conflicting results, uncertainty regarding clinical importance for assessed outcomes
    - Acupuncture in combination with other treatments: no additional benefits of the addition of acupuncture
    - In conclusion: despite large number of trials reporting pain and inclusion of trials with large number of patients, no compelling and consistent evidence of a treatment-specific effect for acupuncture. Where clinically important effects were demonstrated, these were usually short-term. Although improvements in pain, function and QoL were found in comparison with usual care, no consistent clinically important effects was found in comparison with sham acupuncture, leading to the conclusion that the effects of acupuncture were probably the result of non-specific contextual effects.
- **Trade-off between net clinical effects and costs**
  - One economic evaluation, based on 1 RCT, found that the addition of acupuncture to usual care increased costs and improved health. However, the trial showed only effect on QoL, not on function, pain or distress, therefore questioning the mechanisms by which QoL would be improved.
  - The GDG concluded that there was insufficient evidence of an overall treatment-specific effect to support a recommendation for acupuncture and so consideration of cost-effectiveness was not considered relevant.
- **Quality of evidence:**
  - Ranging from very low to high, for some comparisons only single studies with small sample sizes available.
  - Substantial heterogeneity in meta-analyses, which could not be explained by subgroup analyses according to type of acupuncture and chronicity of pain.
  - Lack of blinding, which could lead to inflated effect sizes, was taken into account when quality of evidence was reviewed.
- **Other considerations**
  - Controversial issue: effects due to contextual mechanisms?
  - Lack of effect of acupuncture on pain outcomes, inconsistent effect on QoL
  - No evidence found to support treatment in specific subgroups (e.g. those not responding to other treatment options)
  - Potentially considerable cost impact without the strong evidence base of clinical and cost-effectiveness
  - Passive nature of acupuncture treatment might promote dependence on the procedure, or possibly discourage self-management or participation in activity or exercise but western medical acupuncture usually integrated in care pathway combined with other treatments

- Further research was unlikely to alter conclusions.

NICE 2016 first version of recommendation: 1 clinical recommendation (March 2016)

13. Do not offer acupuncture for managing non-specific low back pain with or without sciatica.

Belgian GDG considerations mentioned in the Lime survey at the beginning of June 2016

Agreement with the content of the NICE recommendation 13: 12 Yes, 0 No, 1 no opinion, 3 out of competence, 1 no answer, 6 not completed

- **Comments:**
- Ik ga akkoord met het niet aanbevelen van acupunctuur voor aCLBP door de huidige wetenschappelijke evidentie (NICE 2016). Toch zou ik graag enkele sterke argumenten willen beschrijven die de huidige kritische visie op het gebruik van acupunctuur voor pijnklachten, en ook a CLBP, weerleggen. Andere conventionele therapieën (manuele technieken, spinale manipulatieve technieken, tractietechnieken, spiergecontroleerde oefeningen, ultrasone, ea.) zijn uitkomstig uit wetenschappelijk onderzoek minder effectief als acupunctuur. Bijkomstig is de combinatie van acupunctuur met andere conventionele therapieën curatiever (pijn en funktionaliteit) dan conventionele technieken alleen. (Cochrane) Vandaar mijn advies, het niet aan raden van acupunctuur voor pijnklachten (cLBP) het ook niet aan te raden voor andere conventionele therapieën zoals in de hierboven vermelde paragraaf.
- Is there enough high quality evidence against to conclude: do not offer acupuncture?
- Applied technique of acupuncture and competence seems to influence significantly the therapeutic impact of acupuncture. Acupuncture as a holistic approach seems to fare much better but the techniques are extremely heterogeneous!

Strength of the recommendation 13: According to NICE formulation, it is a <u>strong</u> recommendation

GRADE Factors (NICE: black, GDG preference for strong recommendation: red, GDG preference for weak recommendation: orange)	
Balance between desirable and undesirable effects	• Not compelling and consistent evidence of treatment-specific effect for acupuncture • No consistent clinically important effect compared to sham • No adverse events reported • Very heterogeneous results
Quality of evidence	• High to very low • Weak evidence
Values and preferences	• Controversial issue about role of contextual effects and lack of beneficial effects in comparison to sham due to non-specific contextual factors • Comparison sham (non-invasive needles) and acup: no difference due to placebo, attention effects, strong suggestion in studies • Comparison sham (invasive needles) and acup: still specific treatment effects, studies not useful? • In the KCE report 2011 on acupuncture, a proven limited effect of acupuncture was showed for specific indications, However sham acupuncture also provided better results than no therapy + potential beneficial effects of placebo. • NICE 2009: Consider offering a course of acupuncture needling comprising up to a maximum of 10 sessions over a period of up to 12 weeks.
Costs (resource allocation)	Addition of acupuncture to usual care increased costs and improved health Cost-effectiveness was not considered relevant by NICE 206 due to insufficient evidence of an overall treatment-specific effect of acupuncture Agreement not to formulate a recommendation regarding subgroups of patients not responding to other treatment options Agreement not to formulate a recommendation on further research needs.

Agreement with the strength of the NICE draft recommendation 13: 5 strong, 5 weak, 0 no opinion, 3 no answer, 10 not completed

- **Comments for a strong recommendation**
  - Weak evidence
- **Comments for a weak recommendation**
  - Het niet aanbevelen van acupunctuur voor aCLBP berust vnl. op een significant afwezig verschil tussen echt en nep acupunctuur. Graag had ik daarbij 2 opmerkingen gemaakt.
    - 1. Wanneer nep acupunctuur gebruikt wordt dmv niet invasieve naaldtechnieken blijkt er vaak geen significant verschil met echte acupunctuur te zijn voor de uitkomstvariabelen. Hierbij moet rekening gehouden worden met sterke suggestie, placebo of aandachtseffecten die niet geëxcludeerd worden in het opzetting van vele studies.
    - 2. Vaak worden invasieve naaldtechnieken ook gebruikt als nep acupunctuur. Deze vormen van placebo gecontroleerd onderzoek kan niet gebruikt worden mits er ook specifieke behandeleffecten aldaar optreden.

    Deze opmerkingen werden al te vaak niet geëxcludeerd in de methodologische opzetting van studies die aldaar een belangrijke reden is tot kwalitatief laag wetenschappelijk onderzoek. Pas vanaf 2008 met invoering van de STRICTA norm voor wetenschappelijk acupunctuuronderzoek is de methodologiosche kwaliteit aanzienlijk aan het verbeteren. Met dus ook de verbetering van resultaten op bv review onderzoek (cfr. Nekpijn en acupunctuur Cochrane). http://www.cochrane.org/CD004870/BACK_acupuncture-neck-disorders
- Very heterogeneous results which complicates formulation of a scientific recommendation.

Belgian GDG comments during the GDG meeting on the 29th June 2016

- **Changes in formulation:**
  - After discussion on the evidence of acupuncture, a consensus was reached not to formulate a recommendation on the use of acupuncture in LBP patients. Main issues mentioned were:
    - Difference in NICE 2009 and 2016 version (going from a pro to an against recommendation)
    - No clear superior effect of acupuncture versus sham
    - No evidence available on harmful effects
    - Not sufficient evidence on the potential benefits and harms to formulate a clear recommendation. Not formulating a recommendation, gives the practitioners more free choice to offer acupuncture to his patient.
    - No preference for a research recommendation
  - Differentiation needed in evidence on patients with radicular pain or sciatica
- **Conclusion: no recommendation formulated**

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30th November 2016)

There was too much stakeholders' comments on acupuncture to be reported in this card. Most of them came from organisation that disagreed with the recommendation against acupuncture. For example:

- Professional Alliance of Chinese Acupuncturists**:** It is clear that the unit cost of a single treatment of acupuncture outweighs prescribing a course of Non Steroidal Anti-Inflammatory Drugs (hereinafter referred to as NSAID's) alongside recommending an exercise plan. With this said, the scope does not take into account the loss in productivity to the UK through absenteeism. The Guardian reported in an article published on the 24th March 2016, that lower back pain is thought to affect one in ten people, whilst it cost to the UK economy is estimated to exceed £12 billion a year in lost productivity. Furthermore, the scope fails to provide evidence that a course of combined NSAID's and exercise reduces the number of absent days from work compared to a course of acupuncture. PACHA would be willing to submit details of client experiences using traditional Chinese acupuncture to cure of NLBP. Our shared learning database concludes that patients suffering from NLBP are relieved from pain after receiving a single treatment. This would suggest a return to work of 1-2 days after treatment. Clinical research suggests that NSAID's could take up to two or more weeks to feel the full therapeutic effect of prescribed NSAID's. This would potentially suggest a return to work of up to 10+ working days. When the cost of loss productivity is factored into the equation, it is our opinion that there is a substantial indirect increase in costs which excludes the unqualified and unquantifiable cost and risk associated

with prescribing NSAID's. Our clinics collectively receive approximately 50% of new patients with NLBP conditions. The scope of the research does not include the cost savings and labour hour savings of an NHS patient turning to private traditional Chinese acupuncture clinics for treatment after exhausting all options available on the NHS. This is a fundamental cost saving that we believe should be factored in when looking at cost behaviour and impact in any guideline revision.
Reply NICE: As reported in the Manual for developing NICE Guidelines, "productivity costs and costs borne by people using services and carers that are not reimbursed by the NHS or social services should not usually be included in any analyses". This is for different reasons, for example time off work is implicitly incorporated in QALY. Also if we included productivity costs in our analyses we would favour those interventions aimed at the working population. We would discriminate against the elderly, children, unemployed people and people with disabilities.(p214/222)

NICE final recommendations on spinal fusion(November 2016)

14. Do not offer acupuncture for managing low back pain with or without sciatica.

Belgian GDG comments during the GDG meeting on the 24 January 2017: no comment

NO KCE 2017 recommendation on acupuncture (February 2017)

7.10. Electrotherapies

Electrotherapies in patients with low back pain ± radicular pain

NICE search question

"What is the clinical and cost effectiveness of electrotherapy (non-invasive interventions) in the management of non-specific low back pain and sciatica?"

Introduction based on the draft version of NICE guideline (March 2016)

- Electrotherapy is an umbrella term that defines a variety of interventions with the common feature that they all involve the application of forms of energy to the body. These all aim to produce various physiological effects with the goal of improving symptoms or recovery.
- **Interventions included in this review: Transcutaneous electrical nerve stimulation (TENS)** = delivery of a small current to pads on the skin to produce a tingling sensation and effect of controlling the activity of the peripheral, spinal and supra-spinal nervous systems**; Percutaneous electrical nerve stimulation (PENS)** = same principle as TENS, but with electrode needles through the skin into the subcutaneous tissue to produce a sensation in the tissue itself**; Interferential therapy** = application of medium frequency electrical currents by several electrodes on the skin over the affected area, sometimes with the use of suction cups; **Low level laser therapy (LLLT)** = non-invasive application of a single wavelength of light to 20 the skin over the injured area using a probe with the hypothesis that this results in local heating and effects on local chemical activity and cellular behaviour (anti-inflammatory effect and promote tissue repair); **Therapeutic ultrasound** = delivery of mechanical energy in the form of high frequency sound waves to the site of injury, usually through a probe applied to the skin with hypothesis that a thermal or mechanical stimulation may generate improved blood flow and may also facilitate the inflammatory process and tissue healing.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with non-specific low back pain • People aged 16 or above with sciatica
Intervention(s)	• Electrotherapy o TENS (Transcutaneous Electrical Nerve Stimulation) o PENS (Percutaneous Electric Nerve Stimulation) o interferential therapy o laser therapy o therapeutic ultrasound
Comparison(s)	• Placebo/Sham/Attention control • Usual care/waiting list • To each other: other interventions within the same class but not the same type (for example, TENS versus PENS, but not TENS versus another type of TENS) • Any other non-invasive interventions in the guideline • Combination of interventions: any combination of the non-invasive interventions in the guideline
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]).

	• Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (>30% improvement in pain or function) • Adverse events: morbidity; mortality. • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline

- Single interventions: Forty one studies were included in the review. Due to the limited number of high quality randomised trials, the search was extended to non-randomised studies but without providing additional non-randomised controlled trials relevant.
  NEW: in final version only 40 studies included (the RCT comparing TENS versus acupuncture is now only mentioned in the acupuncture chapter).
- Combined interventions: 13 studies were included in the review.
- NEW: Two Cochrane reviews were identified but were not included due to methodological reasons (also other populations included). The included studies were assessed and included if they matched the review protocol.

Transcutaneous electrical nerve stimulation (TENS)

- **Patients with low back pain without sciatica**
  - **TENS versus sham**
    - A clinically important benefit in short term **quality of life** (SF-36 0-100; 1 RCT; low quality; n=27) and **pain** change score (VAS 0-100; 1 RCT; moderate quality; n=30) in favour of TENS. However, no clinical difference was found in overall pain score (VAS 0-10; 2 RCTs; moderate quality; n=102). Conflicting evidence was found for short term **function**, with 3 studies showing no clinical benefit in terms of RMDQ score (moderate quality; n=490), while another study showed a clinical benefit of TENS on the ODI score (moderate quality; n=44). No long term data were reported.
    - Not reported outcomes: psychological distress, responder criteria, adverse events, healthcare utilisation
  - **TENS versus usual care**
    - No clinical difference in **pain** (VAS 0-10; 3 RCTs; low quality; n=70) and **function** (RMDQ 0-24; 2 RCTs; very low quality; n=26 and ODI 0-100; 1 RCT; moderate quality; n=44) were found. No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **TENS versus acupuncture**
    - A short term clinically benefit in **pain** was found in favour of acupuncture (VAS 0-10; 2 RCTs; very low quality; n=33). However, no clinical benefit in **function** was found (RMDQ 0-24; 1 RCT; very low quality; n=13 and JOA score 0-20; 1 RCT; low quality; n=20). No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **TENS versus corset**
    - A single study reported only one outcome: no clinical difference in short term **pain** (VAS 0-10; 1 RCT; very low quality; n=44). No long term data were reported.
    - Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **TENS versus (spinal) manipulation**

- A single study reported only one outcome: a clinically important benefit in short term **pain** in favour of manipulation (VAS 0-10; 1 RCT; very low quality; n=63). No long term data were reported.
- Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation

o **TENS versus massage**

- A single study reported only one outcome: no clinically difference in short term **pain** (VAS 0-10; 1 RCT; very low quality; n=40). No long term data were reported.
- Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation

Table 27 – Clinical effectiveness of TENS in patients with low back pain without sciatica

TENS						
Outcomes	TENS versus sham	TENS versus usual care	TENS versus acupuncture	TENS versus corsets	TENS versus manipulation	TENS versus massage
QoL	At short term: • **8/8 domains (SF-36 0-100): CIB favouring TENS** (1 RCT; Low; n=27) At long term: Not reported					
Pain	At short term: • **Evolution over time (VAS 0-100): CIB favouring TENS** (1 RCT; Moderate; n=30) • **VAS 0-10: No diff** (2 RCTs; Moderate; n=102) At long term: Not reported	At short term: • **VAS 0-10: No diff** (3 RCTs; Low; n=70) At long term: Not reported	At short term: • **VAS 0-10: CIB favouring acupuncture** (2 RCTs; Very low; n=33) At long term: Not reported	At short term: • **VAS 0-10: No diff** (1 RCT; Very low; n=44) At long term: Not reported	At short term: • **VAS 0-10: CIB favouring manipulation** (1 RCT; Very low; n=63) At long term: Not reported	At short term: • **VAS 0-10: No diff** (1 RCT; Very low; n=40) At long term: Not reported
Function	At short term: • **RMDQ 0-24: No diff** (3 RCTs; Moderate; n=490) • **ODI 0-100: CIB favouring TENS** (1 RCT; Moderate; n=44)	At short term: • **RMDQ 0-24: No diff** (2 RCTs; very low; n=26) • **ODI 0-100: No diff**	At short term: • **RMDQ 0-24: No diff** (1 RCT; very low; n=13) • **Functional ability (JOA score 0-20): No diff**			

	At long term: Not reported	(1 RCT; Moderate; n=44) At long term: Not reported	(1 RCT; Low; n=20) At long term: Not reported			

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

- **Patients with low back pain with sciatica**
  - **No evidence was available**
  - Not reported comparisons:
    - TENS versus sham
    - TENS versus usual care
    - TENS versus acupuncture
    - TENS versus corset
    - TENS versus manipulation
    - TENS versus massage
- **Mixed population (low back pain with or without sciatica)**
  - **TENS versus sham**
    - No clinical differences were found in **QoL** (SF-36 0-100; 1 RCT; moderate quality; n=174), **pain** (VAS 0-10; 1 RCT; very low quality; n=41), **function** (RMDQ 0-24; 1 RCT; low quality; n=41) and **responder criteria** (>4 points improvement in function) (RMDQ 0-24; 1 RCT; very low quality; n=222) at short term. No long term data were reported. A clinical benefit was seen in responder criteria for pain (>50% improvement) (VAS 0-10; 1 RCT; moderate quality; n=208) in favour of TENS but this result was not shown in the forest plots nor taken into account in the GDG discussion.
    - Not reported outcomes: psychological distress, adverse events, healthcare utilisation
  - **TENS versus usual care (UC)**
    - No clinical difference in **pain** (VAS 0-10; 1 RCT; low quality; n=102) and **function** (Quebec Back Pain Disability Scale 0-100; 1 RCT; low quality; n=102) were found. No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **TENS versus massage**
    - A single study reported a clinically important benefit in **pain** (McGill Pain Rating Index 0-100; 1 RCT; low quality; n=41) and a significant higher number of patients reporting more than 50% improvement in pain (**responder criteria**) (1 RCT; low quality; n=41) in favour of TENS.
    - Not reported outcomes: QoL, function, psychological distress, adverse events, healthcare utilisation

Table 28 – Clinical effectiveness of TENS in mixed population (low back pain with or without sciatica)

TENS			
Outcomes	**TENS versus sham**	**TENS versus usual care**	**TENS versus massage**
QoL	At short term: • **Physical composite score (SF-36 0-100): No diff** (1 RCT; moderate; n=174) • **Mental composite score (SF-36 0-100): No diff** (SF-36 0-100; 1 RCT; moderate; n=174) At long term: Not reported		
Pain	At short term: • **VAS 0-10: No diff** (1 RCT; very low; n=41) At long term: Not reported	At short term: • **VAS 0-10: No diff** (1 RCT; low; n=102) At long term: Not reported	At short term: • **McGill 0-100: CIB favouring TENS** (1 RCT; low; n=41) At long term: Not reported
Function	At short term: • **RMDQ 0-24: No diff** (1 RCT; low; n=41) At long term: Not reported	At short term: • **Quebec Back Pain Disability Scale 0-100: No diff** (1 RCT; low; n=102) At long term: Not reported	
Responder criteria	At short term: • **>50% improvement in pain: CIB favouring TENS** (1 RCT; moderate; n=208) • **>4 points improvement in function: no diff** (1 RCT; very low; n=222) At long term: Not reported		At short term: • **>50% improvement in pain: CIB favouring TENS** (1 RCT; low; n=41) At long term: Not reported

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

Conclusion:

- **Patients with low back pain without sciatica**
  - Overall could be stated that only some clinical benefit is seen in QoL and pain in favour of TENS compared to sham. Comparison with usual care or active comparators (acupuncture, corsets, manipulation, massage) revealed clinical benefit in pain in favour of the active comparator (acupuncture and manipulation). But most of the comparisons revealed no clinical differences in the reported outcomes. No long-term data were reported.
- **Patients with low back pain with sciatica**
  - No evidence retrieved
- **Mixed population (low back pain with or without sciatica)**
  - No clinical differences in QoL, pain and function were seen compared to sham or usual care. Only in the comparison with massage and sham, a clinical benefit was found in pain and in responder criteria (improvement in pain) in favour of TENS. No long-term data were reported.
- **TENS as adjunct (see results below)**
  - There was some evidence of improvement in the short-term for QoL when TENS was given in addition to exercise (single small study) in patients with low back pain without sciatica, however there was no benefit in combination with other interventions.
  - In mixed population only one study was found which compared a combination of BEMER, TENS, exercise and massage versus placebo BEMER, TENS, exercise and massage: conflicting results (no difference or in favour of sham) were found for QoL, but no difference in pain and function.

Percutaneous electrical nerve stimulation (PENS)

- **Patients with low back pain without sciatica**
  - **PENS versus sham**
    - At short term, a clinical benefit was found in **QoL** (SF-36 0-100; 1 RCT; low quality; n=25), **pain** (VAS 0-10; 2 RCTs; low quality; n=59), and **function** (ODI0-100; 1 RCT: very low quality; n=25 and RMDQ 0-24; 1 RCT; low quality; n=34) in favour of PENS. However, at long term no clinical differences for Qol (SF-36 0-100; 1 RCT; low quality; n=184), pain (VAS 0-10; 2 RCTs; moderate quality; n=184) and function (RMDQ 0-24; 2 RCTS; very low quality; n=184) were found anymore.
    - Not reported outcomes: psychological distress, responder criteria, adverse events, healthcare utilisation
  - **PENS versus TENS**
    - A clinical short term benefit in almost all domains of **QoL** (except for mental health) (SF-36 0-100; 1 RCT; low-very low quality; n=28), but no clinical difference in **pain** (VAS 0-10; 1 RCT; very low quality; n=28) and in **function** (ODI 0-50; 1 RCT; very low quality; n=28). No long term data were reported.
    - Not reported outcomes: psychological distress, responder criteria, adverse events, healthcare utilisation
  - Not reported comparisons:
    - PENS versus usual care (UC)
- **Patients with low back pain with sciatica**
  - **No evidence was available**
  - Not reported comparisons:
    - PENS versus sham
    - PENS versus usual care
    - PENS versus TENS

- **Mixed population (low back pain with or without sciatica)**
  - **PENS versus usual care (UC)**
    - No clinical benefit for improving short term **pain** (VAS 0-10; 1 RCT; low quality; n=102) and **function** (Quebec Back Pain Disability Scale 0-100; 1 RCT; low quality; n=102). No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **PENS versus TENS**
    - A single study demonstrated no clinical differene between TENS and PENS for **pain** (VAS 0-10; 1 RCT; very low quality; n=102) and **function** (Quebec Back Pain Disability scale 0-100; 1 RCT; very low quality; n=102) at short term. No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - Not reported comparisons:
    - PENS versus sham

In conclusion:

- **Patients with low back pain without sciatica**
  - Patients who received PENS, showed a clinical important improvement in QoL, pain and function compared to sham. However, no difference were anymore seen at long term. Compared to TENS, the evidence is less clear cut, with some clinical benefit in QoL but not for pain and function.
- **Patients with low back pain with sciatica**
  - No evidence was available
- **Mixed population (low back pain with or without sciatica)**
  - No clinical benefit in pain and function was found for PENS compared to usual care or TENS.
- **PENS as adjunct (see results below)**
  - In terms of QoL, there was some evidence that PENS in addition to exercise was less beneficial than exercise with sham PENS in patients without sciatica. No clinical difference was found for the other outcomes (pain and function), both at short and long term.

Interferential therapy (IFT)

- **Patients with low back pain without sciatica**
  - **IFT versus sham**
    - Two studies reported only one outcome: no clinical difference in **pain** was found at short term (NRS 0-10; 2 RCTs; high quality; n=117). No long term data were reported.
    - Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **IFT versus traction**
    - A single study reported only one outcome: no clinical difference in **function** was found at short term (ODI 0-100; 1 RCT; low quality; n=128). No long term data were reported.
    - Not reported outcomes: QoL, pain, psychological distress, responder criteria, adverse events, healthcare utilisation
- **Patients with low back pain with sciatica**
  - **No evidence was available**
  - Not reported comparisons:
    - IFT versus sham
    - IFT versus traction

- **Mixed population (low back pain with or without sciatica)**
  - **No evidence was available**
  - Not reported comparisons:
    - IFT versus sham
    - IFT versus traction

In conclusion:

- **Patients with low back pain without sciatica**
  - No clinical benefit of IFT compared to sham or traction could be demonstrated.
- **Patients with low back pain with sciatica**
  - No evidence was available
- **Mixed population (low back pain with or without sciatica)**
  - No evidence was available
- **IFT as adjunct (see results below):**
  - When IFT was combined with manipulation, there was clinical benefit in long-term QoL but less clear in the short term. There was no clinical benefit for pain and function.

Low level laser therapy (LLLT)

- **Patients with low back pain without sciatica**
  - **Laser versus sham**
    - There was conflicting evidence for the benefit of laser compared to sham: no clinical benefit was found on overall **pain** score (VAS 0-10; 2 RCTs; low quality; n=57), but a clinically important benefit was found in reduced pain intensity in the last 24 hours (VAS 0-10; 1 RCT; low quality; n=61) and for more than 60% pain improvement (**responder criteria**; 1 RCT; very low quality; n=71) in favour of laser therapy. No clinical difference in **function** was found (RMDQ 0-100; 2 RCTs; very low quality; n=57 and ODI 0-100; 1 RCT; low quality; n=61).
    - Not reported outcomes: QoL, psychological distress, adverse events, healthcare utilisation
  - Not reported comparisons:
    - Laser versus usual care
    - Laser versus exercise
    - Laser versus traction

- **Patients with low back pain with sciatica**
  - **Laser versus sham**
    - Some inconsistency in the results were found: the overall scores on **function** (RMDQ 0-24; 2 RCTs; low quality; n=80) and **pain** (VAS 0-10; 2 RCTs; low quality; n=80) showed no clinical benefit of laser therapy. However the change score (VAS 0-10; 1 RCT; moderate quality; n=364) and the **responder criteria** (improvement in function) (1 RCT; high quality; n=364) showed an important clinical benefit in favour of laser therapy.
    - Not reported outcomes: QoL, psychological distress, adverse events, healthcare utilisation
  - **Laser versus usual care**

- No clinical short term benefit was found for **pain** (VAS 0-10; 1 RCT; high quality; n=364), however a clinical important benefit in **responder criteria** for function was found in favour of laser therapy (1 RCT; high quality; n=364). No long term data were reported.
- Not reported outcomes: QoL, function, psychological distress, adverse events, healthcare utilisation

o **Laser versus traction**

- No clinical difference in **pain** (VAS 0-10; 1 RCT; very low quality; n=40) was found, whereas a clinical improvement in **function** was found (RMDQ 0-24; 1 RCT; very low quality; n=40). No long term data were reported.
- Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation

o Not reported comparisons:

- Laser versus exercise

Table 29 – Clinical effectiveness of Laser in patients with low back pain with sciatica

Laser			
Critical outcomes	Laser versus sham	Laser versus usual care	Laser versus traction
Pain	At short term: • **VAS 0-10: No diff** (2 RCTs; low; n=80) • **Evolution over time (change score, VAS 0-10): CIB favouring laser** (1 RCT; moderate; n=364) At long term: Not reported	At short term: • **VAS 0-10: No diff** (1 RCT; high; n=364) At long term: Not reported	At short term: • **Back pain (VAS 0-10): no diff** (1 RCT; very low; n=40) • **Radicular pain (VAS 0-10): no diff** (1 RCT; very low; n=40) At long term: Not reported
Function	At short term: • **RMDQ 0-24: No diff** (2 RCTs; low; n=80) At long term: Not reported		At short term: • **RMDQ 0-24: CIB favouring laser** (1 RCT; very low; n=40) At long term: Not reported
Responder criteria	At short term: • **Switch from moderate to minimal disability category at 3 wks: CIB favouring laser** (1 RCT; high; n=364) At long term: Not reported	At short term: • **Switch from moderate to minimal disability category at 3 wks: CIB favouring laser** (1 RCT; high; n=364) At long term: Not reported	

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

- **Mixed population (low back pain with or without sciatica)**
  - **Laser versus usual care (UC)**
    - A clinical short term benefit for **pain** (VAS; 2 RCTs; low quality; n=150) in favour of laser but no clinical difference was found for **function** (RMDQ 0-24; 1 RCT; very low quality; n=50).
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - **Laser versus exercise**
    - Similar results as in comparison with usual care: a clinical short term benefit for **pain** (VAS; 1 RCT; low quality; n=50) in favour of laser but no clinical difference was found for **function** (RMDQ 0-24; 1 RCT; low quality; n=50).
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
  - Not reported comparisons:
    - Laser versus sham
    - Laser versus traction

In conclusion:

- **Patients with low back pain without sciatica**
  - There was conflicting evidence for the benefit of laser therapy compared with sham, no clinical benefit for pain on the VAS, while further studies suggested a benefit for reduced pain intensity and for pain improvement.
- **Patients with low back pain with sciatica**
  - Similar conclusion as in patients without sciatica: conflicting results on the potential benefit for pain and function. A large study reported a benefit of laser therapy over sham for pain intensity and improvement in function.
- **Mixed population (low back pain with or without sciatica)**
  - Two studies showed a benefit of laser therapy for pain intensity but no benefit for function.
- **Laser as adjunct (see results below):**
  - Combined with exercise and self-management, a short term benefit in pain was found in favour of laser therapy in patients without sciatica. In the mixed population, no clinical difference was found for pain and function.

Therapeutic ultrasound (US)

- **Patients with low back pain without sciatica**
  - **US versus placebo/sham**
    - No clinical difference in **pain** (VAS 0-10; 1 RCT; low quality; n=39), in **function** (Functional Rating Index 0-100; 2 RCTs; low quality; n=49) and in **responder criteria** (>30% pain reduction) (1 RCT; moderate quality; n=455). No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, adverse events, healthcare utilisation
  - **US versus usual care (UC)**
    - A clinically important benefit was seen in 4 of the 8 domains of **QoL**, however no consistency in these domains was found in the direction of the benefit (in favour of US or UC) (SF-36 0-100; 1 RCT; very low-low quality; n=40). Also a clinical benefit in **pain** intensity was found in favour of US (VAS 0-10;

1 RCT; low quality; n=40). No clinical differences were found for **function** (ODI 0-100; 1 RCT; low quality; n=40) and for **psychological distress** (Beck Depression Inventory; 1 RCT; low quality; n=40).
        - Not reported outcomes: function, adverse events, healthcare utilisation
    - Not reported comparisons:
        - US versus traction
        - US versus laser

- **Patients with low back pain with sciatica**
    - **US versus placebo/sham**
        - No clinical difference in **pain** (VAS 0-10; 1 RCT; very low quality; n=30), in **function** (ODI 0-100; 1 RCT; low quality; n=30) and in **healthcare utilisation** (paracetamol use) (1 RCT; low quality; n=30). No long term data were reported.
        - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events

    - **US versus traction**
        - No clinical difference in **pain** (VAS 0-10; 1 RCT; very low quality; n=40) and in **function** (RMDQ 0-24; 1 RCT; low quality; n=40). No long term data were reported.
        - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation
    - Not reported comparisons:
        - US versus usual care
        - US versus laser
- **Mixed population (low back pain with or without sciatica)**
    - **US versus laser**
        - Only one outcome was reported: no clinical difference in **pain** was found (VAS 0-10; 1 RCT; very low quality; n=62).
        - Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, healthcare utilisation
    - Not reported comparisons:
        - US versus placebo/sham
        - US versus usual care
        - US versus traction

In conclusion:

- **Patients with low back pain with sciatica**
    - Evidence from 1 study demonstrated a clinical benefit in reducing pain compared with usual care.
- **Patients with low back pain without sciatica**
    - No clinical benefits on any of the outcomes.
- **Mixed population (low back pain with or without sciatica)**
    - No clinical benefits on any of the outcomes.
- **Ultrasound as adjunct (see results below)**
    - **The combination of US and exercise revealed no clinical benefit on pain, function, QoL and psychological distress in patients without sciatica.**

Electrotherapy as component of a multimodal intervention

- **Patients with low back pain without sciatica**
  - 7 comparisons were found (see Table 30)
    - The reviewed evidence, mainly consisting of single, small sample size studies of very low to moderate quality, on multimodal interventions with electrotherapy revealed no clinical difference in **pain**, **function** and **psychological distress**. Only regarding **QoL** some inconsistent evidence was found: some clinical benefit can be found in QoL if TENS is added to biomechanical exercises but another study on PENS demonstrated a better score on QoL in favour of the sham intervention. The combination of ultrasound and exercises showed no clinical difference in QoL.
    - Not reported outcomes: responder criteria, adverse events, healthcare utilisation

Table 30 – Clinical effectiveness of electrotherapy as adjunct in low back pain population without sciatica

Electrotherapy as adjunct							
Outcomes	Laser + self-management (education) + exercise (biomechanical) versus self-management (education) + exercise (biomechanical)	TENS + acupuncture versus acupuncture	TENS + exercise (biomechanical) versus sham TENS	TENS + exercise (biomechanical) versus exercise (biomechanical)	PENS + exercise (biomechanical + aerobic) versus sham PENS + exercise (biomechanical + aerobic)	Ultrasound + exercise (biomechanical-core stabilisation) versus exercise (biomechanical-core stabilisation)	Ultrasound + exercise (biomechanical) + self-management (semi-supervised exercise) versus exercise (biomechanical) + self-management (semi-supervised exercise)
QoL				At short term: • **SF-36 0-100: CIB favouring TENS** (1 RCT; very low; n=40) At long term: Not reported	At short term: • **Physical composite score (SF-36 0-100): CIB favouring sham** (1 RCT; low; n=89) • **Mental composite score (SF-36 0-100): CIB favouring sham** (1 RCT; low; n=89)	At short term: • **SF-36 0-100: No diff** (SF-36 0-100; 1 RCT; very low; n=39) At long term: Not reported	

					At long term: • **Physical composite score (SF-36 0-100): CIB favouring sham** (1 RCT; low; n=89) • **Mental composite score (SF-36 0-100): no diff** (1 RCT; low; n=89)		
Pain	At short term: • **VAS 0-10: CIB favouring laser** (1 RCT; low; n=100) At long term: Not reported	At short term: • **VAS 0-10: No diff** (1 RCT; very low; n=13) At long term: Not reported	At short term: • **Borg 0-10: No diff** (1 RCT; low; n=42) At long term: Not reported	At short term: • **Borg/PDI 0-10: No diff** (2 RCTs; very low; n=84) At long term: Not reported	At short term: • **McGill 0-78: No diff** (1 RCT; low; n=89) At long term: • **McGill 0-78: No diff** (1 RCT; moderate; n=89)	At short term: • **PDI 0-50: No diff** (1 RCT; very low; n=39) At long term: Not reported	At short term: • **VAS 0-10: No diff** (1 RCT; very low; n=39) At long term: Not reported
Function		At short term: • **RMDQ 0-24: No diff** (1 RCT; very low; n=13) At long term: Not reported	At short term: • **ODI 0-100: No diff** (1 RCT; low; n=42) At long term: Not reported	At short term: • **ODI 0-100: No diff** (2 RCTs; very low; n=84) At long term: Not reported	At short term: • **RMDQ 0-24: No diff** (1 RCT; moderate; n=89) At long term: • **RMDQ 0-24: No diff** (1 RCT; low; n=89)	At short term: • **ODI 0-100: No diff** (1 RCT; very low; n=39) At long term: Not reported	At short term: • **Functional Rating Index 0-40: No diff** (1 RCT; very low; n=39) At long term: Not reported
Psychological distress				At short term: • **BDI 0-63: No diff**		At short term: • **BDI 0-63: No diff**	

				(1 RCT; very low; n=40) At long term: Not reported		(1 RCT; very low; n=39) At long term: Not reported	

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

- **Patients with low back pain with sciatica**
  - Two comparisons were found:
    - **Ultrasound + exercise (biomechanical + aerobic) versus waiting list control**
      - A clinical short term benefit was found for **pain** (VAS 0-10; 1 RCT; low quality; n=30) and **healthcare utilisation** (medication use) (1 RCT; low quality; n=30). However, no clinical difference was found for **function** (ODI 0-100; 1 RCT; very low quality; n=30). No long term data were reported.
      - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events
    - **Ultrasound + exercise (biomechanical + aerobic) versus exercise (biomechanical + aerobic)**
      - No clinical difference was found for **pain** (VAS 0-10; 1 RCT; very low quality; n=30), **function** (ODI 0-100; 1 RCT; low quality; n=30) and **healthcare utilisation** (medication use) (1 RCT; low quality; n=30). No long term data were reported.
- **Mixed population (low back pain with or without sciatica)**
  - 5 comparisons were found (see Table 31)
    - Overall, across the 5 different comparisons of moderate to very low quality, could be stated that a multimodal intervention with electrotherapy induced no clinical benefit in terms of **function** and **healthcare utilisation**. Regarding **pain** and **QoL**, the evidence is less consistent: the addition of IFT showed some clinical benefit at short term (in 2 of the 8 domains of SF-36) but mainly at long term (in 7 of the 8 domains of SF-36 and EQ-5D) in favour of IFT. In the contrary, in the comparison with TENS, a clinical benefit in QoL was found in favour of the placebo TENS. For pain improvement, a short term clinical benefit was found in the comparisons with electro-acupuncture and laser, both in favour of the electrotherapy modalities.
    - Not reported outcomes: psychological distress, responder criteria, adverse events

Table 31 – Clinical effectiveness of electrotherapy as adjunct in mixed population (low back pain with or without sciatica)

Electrotherapy as adjunct					
Outcomes	**Electro-acupuncture + self-management (education + home exercises) + exercise (mixed) versus self-management (education + home exercises) + exercise (mixed)**	**IFT + manipulation versus manipulation**	**Laser + self-management (home exercise) versus self-management (home exercise)**	**HILT laser + self-management (unsupervised exercise) versus placebo HILT laser + self-management (unsupervised exercise)**	**BEMER + TENS + exercise (mixed) + massage versus placebo BEMER + TENS + exercise (mixed) + massage**
QoL		At short term: • **EQ-5D 0-1: No diff** (1 RCT; moderate; n=129) • **2/8 domains SF-36 0-100: CIB favouring IFT** (1 RCT; moderate-very low; n=129) At long term: • **EQ-5D 0-1: CIB favouring IFT** (1 RCT; low; n=103) • **7/8 domains SF-36 0-100: CIB favouring IFT** (1 RCT; moderate-very low; n=103)			At short term: • **3/8 domains SF-36 0-100: CIB favouring placebo** (1 RCT; very low; n=26-33) • **Physical composite score (SF-36 0-100): no diff** (1 RCT; very low; n=16) • **Mental composite score (SF-36 0-100): CIB favouring placebo** (1 RCT; very low; n=16) At long term: Not reported
Pain	At short term: • **NRS 0-10: CIB favouring electro-acup** (1 RCT; low; n=49) At long term:	At short term: • **VAS 0-10: No diff** (1 RCT; low; n=129) At long term:	At short term: • **VAS 0-10: No diff** (2 RCTs; very low; n=87) At long term:	At short term: • **VAS 0-10: CIB favouring laser** (1 RCT; very low; n=52) At long term:	At short term: • **VAS 0-10: No diff** (1 RCT; very low; n=37) At long term:

	Not reported	• **VAS 0-10: No diff** (1 RCT; low; n=103)	Not reported	Not reported	Not reported
Function	At short term: • **ALBPS 0-10: No diff** (1 RCT; very low; n=49) At long term: Not reported	At short term: • **RMDQ 0-24: No diff** (1 RCT; moderate; n=129) At long term: • **RMDQ 0-24: No diff** (1 RCT; low; n=103)	At short term: • **ODI 0-100: No diff** (2 RCTs; very low; n=87) At long term: Not reported	At short term: • **RMDQ 0-24: No diff** (1 RCT; very low; n=52) • **MODQ 0-100: No diff** (1 RCT; low; n=52) At long term: Not reported	At short term: • **ODI 0-100: No diff** (1 RCT; very low; n=37) At long term: Not reported
Healthcare utilisation	At short term: • **Analgesic use: no diff** (1 RCT; very low; n=52) At long term: Not reported				

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y; BEMER: Bio-Electro-Magnetic-Energy-regulation therapy

Economic evidence

- **No relevant economic evaluations were identified.**

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:**
  - Most critical outcome was health-related QoL with pain severity, function and psychological distress as individually critical outcomes.
  - Adverse events and healthcare utilisation were considered important for decision-making
  - Responder criteria, as defined as >30% improvement in pain or function, was not considered as a critical outcome
- **Trade-off between clinical benefits and harms**
  - **TENS:** The GDG concluded that the evidence was conflicting and overall there was insufficient evidence of clinical benefit to support a recommendation for the use of TENS for low back pain or sciatica.
  - **PENS:** The GDG discussed whether there should be concern regarding possible adverse events given that PENS involved penetrating the skin. However, it was felt that the risks would be similar to acupuncture which has an acceptable safety profile. Overall, the GDG noted that, while the evidence was in places positive, it was of low quality with low patient numbers. It was highlighted that PENS is currently not widely used and so a recommendation for its use would be a significant change in practice. It was thus concluded that there was insufficient evidence of clinical benefit to support a recommendation for the use of PENS for low back pain or sciatica.
  - **Interferential therapy:** The GDG concluded that there was a lack of evidence of clinical benefit to support a recommendation for the use of IFT as a treatment for low back pain or sciatica.
  - **Laser:** The GDG noted the key evidence of benefit was from the sham comparison in a group of people with acute LBP with sciatica. They highlighted that overall while the sham evidence was conflicting; this evidence of clinical benefit was of moderate quality in a reasonable large patient group whereas the evidence of no benefit was of lower quality and in smaller patient groups. However, this was conducted in an inpatient setting in Serbia, there were concerns of the applicability

of this evidence to a UK healthcare context. The GDG felt that the evidence of clinical benefit was insufficient to base a recommendation on. However, it was considered an area where future research may be of benefit.

NICE 2009: do not offer laser therapy

- **Ultrasound:** The GDG concluded that there was a lack of sufficient evidence of clinical benefit to support a recommendation for the use of ultrasound (US) as a treatment for low back pain or sciatica. The only evidence of benefit was of low quality and based on low patient numbers; for the majority outcomes no benefit was seen.

- **Trade-off between net clinical effects and costs**
  - No economic evaluations were identified from the published literature.
  - The GDG noted that **TENS** machines are currently often purchased by the patient, however they may also be provided on loan to the patient at a cost to the NHS in terms of the machine itself and also related personnel time explain how to use it. However, given the conflicting evidence on its clinical benefit, the cost of providing this intervention were not considered justified.
  - Although some indications of possible benefit were seen for **PENS**, overall the GDG concluded that it was insufficient to support a conclusion of clinical benefit and thus also insufficient to justify intervention costs. In addition, PENS is not widely used and might require higher implementation costs.
  - Although some indications of possible benefit were seen for laser therapy, overall the GDG concluded that it was insufficient to support a conclusion of clinical benefit and thus also insufficient to justify intervention costs. In addition they highlighted that even if laser therapy was clinically effective, the regimen in the key trial was very intensive (5 daily sessions for 3 weeks) and cost effectiveness may depend on whether or not clinical benefit is maintained when treatment stops which was unclear from the current evidence**.**
  - However, given the lack of evidence of clinical benefit for ultrasound therapy, intervention costs were not considered justified.
- **Quality of evidence**
  - Ranged from very low to high, mainly downgraded for imprecision of the effect estimate and the risk of bias

- **Other considerations**
  - **TENS:** The GDG highlighted that in trials of TENS, a problem affecting all studies is that the intervention only works while in progress providing temporary relief rather than intending to have long term benefits, however the trials are not designed to look at this when they record outcomes at later follow-up times.
  - **Laser:** The positive results for laser interventions are largely driven by one study that the GDG has concerns regarding the applicability of, and there is conflicting evidence from other sources (albeit of lower quality). The GDG therefore concluded that while they did not want to dismiss the evidence of clinical benefit entirely, it should be treated with caution and hence a research recommendation was produced. The GDG were aware of existing NICE interventional procedure guidance for Peripheral nerve-field stimulation for chronic low back pain which recommends special arrangement for clinical governance, consent, audit and research. This specific therapy has therefore been excluded from this review. If its use is being considered for people with non-specific low back pain and/or sciatica, the existing guidance should be followed. Interventional procedures guidance for Percutaneous intradiscal electrothermal therapy for low back pain (IPG319) was being updated during development of this guideline, details of the updated is available at the following link: https://www.nice.org.uk/guidance/indevelopment/gid-ip2803. No evidence on this procedure was identified within this review and therefore the updated guidance for this procedure should be followed for people with non-specific low back pain.

- **Research recommendation:**
  - Laser therapy involves the non-invasive application of a single wavelength of light to the skin over the painful area using a probe. There are various laser devices and probe configurations in clinical use. The light is absorbed in the tissues and it is hypothesised that this results in local heating and effects on local chemical activity and cellular behaviour. It is through those effects that laser therapy is purported to have an anti-inflammatory effect and promote tissue repair. Conflicting evidence was found comparing laser with sham and usual care for pain and function outcomes. While evidence of clinical benefit was observed in some comparisons for pain and function there were concerns with the quality and applicability of the evidence. There remains uncertainty regarding the efficacy and

effectiveness of laser therapy, though there is some promising evidence. There is therefore a need for high quality trials into the effectiveness and cost effectiveness of laser therapy for low back pain with and without sciatica.

NICE 2016 recommendations: 4 clinical recommendations and 1 research recommendation

14. Do not offer ultrasound for managing non-specific low back pain with or without sciatica.
15. Do not offer PENS for managing non-specific low back pain with or without sciatica.
16. Do not offer TENS for managing non-specific low back pain with or without sciatica.
17. Do not offer interferential therapy (IFT) for managing non-specific low back pain with or without sciatica.

Research recommendation

1. What is the clinical and cost-effectiveness of laser therapy in the management of low back pain and sciatica?

Belgian GDG considerations mentioned in the Lime survey at the end of June 2016

Agreement with the content of the NICE recommendation 14 on TENS: 12 Yes, 2 No, 0 no opinion, 0 out of competence, 0 no answer, 2 not completed

- **Comments from those who do not agree:**
  - Not all forms of electrotherapy have been included in the review, what about micro-ampère electrotherapy (MET/CES)?
    TENS can provide short term analgesic efficacy at no side effects and fully controlable by the patient self. No recommendation for back pain without sciatica, but certainly in the case of sciatica.
  - In some patients short term relieve can be meaningfull in case of failure of medical treatment
- **Other comments:**
  - I agree; however in patients with very very severe pain (very small subgroup of patients), it might be the only physical treatment which can be proposed for the patient and providing a temporary pain relief.

Strength of the recommendation 14 on TENS: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	Conflicting results and Insufficient evidence on TENS benefit.
Quality of evidence	Moderate to very low
Values and preferences	No info provided by NICE 2016 NICE 2009: Do not offer TENS
Costs (resource allocation)	Currently, TENS machines are purchased by the patient in U.K. Given the conflicting evidence on its clinical benefit, the cost of providing this intervention (provided on loan to the patient at a cost to the NHS in terms of the machine itself and also related personnel time explain how to use it) were not considered justified by the NICE GDG.

Agreement with the strength of the NICE draft recommendation 14: 7 strong, 2 weak, 1 no opinion, 2 no answer, 4 not completed

- **Comments for a weak recommendation**
  - Because of the conflicting evidence and the fact that TENS is a no-harm therapy that can be applied by the patient itself, my recommendation should be weak.

Agreement with the content of the NICE recommendation 15 on PENS: 14 Yes, 0 No, 0 no opinion, 0 out of competence, 0 no answer, 2 not completed

- **No comments**

Strength of the recommendation 15 on PENS: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	Insufficient evidence on benefit for PENS. Moreover, PENS is currently not widely used in UK and so a recommendation for its use would be a significant change in practice.
Quality of evidence	Moderate to very low
Values and preferences	No info provided by NICE 2016 NICE 2009: no recommendation
Costs (resource allocation)	No economic evaluations. Given that PENS is not widely used, higher implementation costs are expected and there is insufficient evidence according to NICE 2016 to justify intervention costs.

Agreement with the strength of the NICE draft recommendation 15: 8 strong, 3 weak, 1 no opinion, 2 no answer, 2 not completed

- **Comments for a strong recommendation**
  - Because of the conflicting evidence, the more invasive therapy with possible adverse events and the fact it's not common used, I recommend strong.

Agreement with the content of the NICE recommendation 16 on IFT: 14 Yes, 0 No, 0 no opinion, 0 out of competence, 0 no answer, 2 not completed

- **No comments**

Strength of the recommendation 16 on IFT: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	Lack of evidence of clinical benefit for IFT (few studies)
Quality of evidence	High and low
Values and preferences	No info provided by NICE 2016 NICE 2009: do no offer interferential therapy
Costs (resource allocation)	No economic evaluations.

Agreement with the strength of the NICE draft recommendation 16: 10 strong, 1 weak, 1 no opinion, 2 no answer, 2 not completed

- **Comments for a strong recommendation**
  - Strong recommendation against considering the absence of effectiveness reported in literature and the controversial rationale of this kind of current.
  - Because of the lack of evidence and more specifically the fact there is no difference compared to sham in 2 high quality RCT's, I would advise a strong recommendation.

Agreement with the content of the NICE recommendation 17 on US: 14 Yes, 0 No, 0 no opinion, 0 out of competence, 0 no answer, 2 not completed

- **Comments**
  - Why didn't they consider shock waves (they are mechanic waves as ultrasound)? e.g.: http://www.aapainmanage.org/resources/research-abstract/the-effects-of-extracorporealshock-wave-therapy-on-pain-disability-and-depression-of-chronic-low-back-pain-patients/

Strength of the recommendation 17 on US: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	The only evidence of benefit was of low quality and based on low patient numbers; for the majority outcomes no benefit was seen.
Quality of evidence	Moderate to very low
Values and preferences	No info provided by NICE 2016 NICE 2009: Do not offer therapeutic ultrasound
Costs (resource allocation)	No economic evaluation Cost not considered justified by the GDG given the lack of evidence of clinical benefit.

Agreement with the strength of the NICE draft recommendation 17: 8 strong, 3 weak, 1 no opinion, 2 no answer, 2 not completed

- **Comments for a weak recommendation**

Because of the limited evidence with rather low quality, I would advise a weak recommendation

Agreement with the NICE research recommendation 1 on Laser therapy: 5 Yes, 2 No, 6 no opinion, 1 out of competence, 0 no answer, 2 not completed

- **Comments from those who do not agree:**
  - Why a question as recommandation!
  - Why to further spend time, energy and money in research on another technique of "electrotherapy" (NB: this is in fact no electrotherapy)

- **Other comments:**
  - Dit is geen richtlijn - maar een klinische vraag???
  - Dit is niet echt een aanbeveling. Is er ergens iets fout gegaan?
  - There are more relevant and important studies to do first...
  - The question formulated is probably placed at the wrong place, normally we would expect a recommendation at this place. There is no evidence for laser therapy hence it is not to be recommended.
  - This is not a recommendation but a question ?

Belgian GDG comments during the GDG meeting on the 29 September 2016:

No comments

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30th November 2016)

TENS

- Homerton University Hospital NHS Foundation Trust: The guidelines found no studies evaluating TENS for sciatica and only one for a mixed population, yet the guidelines make a recommendation to cover the use of TENS in populations where research does not exist. In clinical physiotherapy practice TENS would never be used in isolation, but only as an adjunct to other therapies as part of a range of self management strategies explored with the patient. TENS has an advantage over the

passive modalities (massage, corset, manual therapy used as comparators in the research cited) as being delivered independently by the patient, it is unfortunate that self-efficacy was not included as an outcome measure, which might demonstrate the advantage of TENS. TENS can be useful, provided it is issued on a 2 week trial basis. If patients find it helps their self management, then purchase may be considered.
Reply NICE: The recommendation is based on evidence from the 'without sciatica' and the 'with or without sciatica' populations. Although there was no evidence available for the 'with sciatica' population, the GDG were aware that 139 of the 236 people included in the 'with or without sciatica' population had sciatica. Therefore people with sciatica could not be excluded from the recommendation. The GDG considered evidence of TENS compared to sham TENS, usual care, and active comparisons. Although there were some clinically significant benefits for TENS, this was overall inconsistent and conflicting, therefore the GDG concluded that there was insufficient evidence of a clinical benefit to support a positive recommendation. Self-efficacy was not considered as a critical or important outcome in the scope or the protocols, and therefore was not reviewed. No evidence was found that considered TENS with self-management and therefore the GDG are unable to make any recommendations on this. (p54/111**)**

- Extended Scope Practitioners Professional Network*:* Acupuncture is a useful part of the multi-modal package provided by physiotherapists. It often gives short-term pain relief which allows patients to then more actively participate in exercise or manual therapy. Staff should be encouraged to use treatment modalities with the most supporting evidence initially but treatments such as acupuncture and TENS have a role to play. Making such dogmatic statements that they should not be used may result in CCGs refusing to fund such treatments. Patients who had previously found acupuncture to be helpful may find they can no longer get the treatment that they find helpful. Perhaps the wording should be "do not offer acupuncture/TENS alone but as part of a multimodal treatment."
Reply NICE: The GDG did not find any evidence in favour of acupuncture or TENS as part of treatment packages, and therefore the GDG could not consider these in a combined treatment context. (p37/222)
- Chartered Society of Physiotherapy***:*** We recognise that much of the literature around the use of TENS is conflicting. However, this is not uncommon for other modalities covered in this guideline. The evidence review suggests that TENS is effective at improving quality of life and decreasing pain in the short term in patients with low back pain only, when compared to sham (page 560, lines 25-27). Whilst the evidence is conflicting around the effect of TENS on function when compared to sham, this is unsurprising given research cross-matching patient-reported functional benefits of TENS against the RMDQ, which found RMDG has limited capacity to capture patient-reported benefits (Gladwell, 2013).
Reply NICE: Although a clinical benefit was seen for quality of life and pain in the low back pain population when compared with sham, this was from very limited evidence in a small sample, and overall the body of evidence did not demonstrate benefit. The GDG agreed that outcomes should be measured consistently throughout reviews and across interventions and agreed that RMDQ should be included as an appropriate measure of function. On the basis of the evidence reviewed, the GDG concluded that there was insufficient evidence of clinical benefit to support a recommendation for the use of TENS for low back pain or sciatica. (p50/222)
- Homerton University Hospital NHS Foundation Trust*:* The **cost of a TENS** unit is inaccurate and misleading. Only a simple dual channel variable unit in most cases is required, this costs no more than £30 e.g Body clock http://bodyclock.co.uk/1st-choice-plus-tens/. Each machine can be used on a trial basis by multiple patients (thereby reducing this cost considerably), with those who find the machine helpful purchasing their own.
Reply NICE: When calculating unit costs they report the cost incurred to the NHS and therefore sourced this cost from the NHS Supply Chain Catalogue, 2014. As there are multiple types of machine, a cost range has been reported. It is also noted in the report that "TENS devices may either be provided on loan to people with low back pain and sciatica or purchased by the individuals themselves" and was therefore taken into consideration by the GDG. This discussion is noted in the 'Trade-off between net clinical effects and costs' section of the LETR. (p139/222)
- Homerton University Hospital NHS Foundation Trust*:* The GDG highlighted that "in trials of TENS, a problem affecting all studies is that the intervention only works while in progress providing temporary relief rather than intending to have long term benefits," This statement irrelevant as TENS works via the pain gate mechanism so is only intended to provide temporary relief during the time it is operated by the patient. The value of TENS lies particularly in helping particularly to manage pain flare ups, which may help patients avoid attending A&E or GP appointments with flare ups they feel unable to manage.
Reply NICE: From the evidence reviewed, they were unable to demonstrate that TENS was helpful for a subgroup of patients who might otherwise attend A&E or GP appointments. NICE believe this statement is important to retain as it highlights the limitations of the evidence. (p139/222)
- South West Yorkshire Partnership NHS Foundation Trust*:* In practice TENS can often be helpful for reducing pain enabling to exercise and allowing a return to normal function. It can also reduce the need for pharmacological intervention.

Reply NICE: The GDG considered evidence of TENS compared to sham TENS, usual care, and active comparisons. Although there were some benefits for TENS, this was overall inconsistent and conflicting, therefore the GDG concluded that there was insufficient evidence of clinical benefit to support a positive recommendation. (p211/222)

INFERENTIAL THERAPY

- Society for Back Pain Research*:* there is an error in how the Hurley et al 2004 paper is described in the table, the study took place in the United Kingdom, Furthermore, the conclusions drawn concerning the effectiveness of interferential therapy are incorrect as it was found to be as effective as manual therapy when used alone or in combination. SUGGESTION: Manual therapy integrated (with) intervention that would include **********.
  Reply NICE: The error in table 242 has been corrected to reflect that the study took place in the UK. The Hurley 2004 paper had two comparisons that were included in the manual therapy review, and one in the electrotherapy review. The arms included in the manual therapy review were 1) manipulation/mobilisation versus inferential therapy, and 2) manipulation + inferential therapy versus inferential therapy. The results for comparison 1) showed that there was a clinically significant benefit for manipulation/mobilisation for two of the quality of life domains at both short and long term time points, and only for one domain for inferential therapy. The results for comparison 2) showed a clinically significant benefit for 3 quality of life domains in the short term and 8 in the long term all in favour of inferential therapy with manipulation. **There was no significant benefit for inferential therapy alone**. None of the comparisons showed a clinically important benefit for pain or function for either intervention. Therefore inferential therapy alone was not as effective as manual therapy or manual therapy with inferential therapy in terms of quality of life. (p66/111)
- Homerton University Hospital NHS Foundation Trust*:* Ultrasound and interferential therapy are already considered inappropriate modalities in modern NHS physiotherapy due to lack of evidence (p195/222)

ULTRASOUND

- Homerton University Hospital NHS Foundation Trust: Ultrasound and interferential therapy are already considered inappropriate modalities in modern NHS physiotherapy due to lack of evidence (p195/222)
- Spine Intervention Society*:* In terms of therapeutic non-invasive modalities, the authors have stripped therapy down to manipulation and exercise therapy. They recommend against traction, ultrasound, transcutaneous electrical nerve stimulation (TENS), and acupuncture. While these modalities do not change long-term outcome, they are palliative and one must remember that initial back pain therapy “is” palliative therapy in many cases.
  Reply NICE: The algorithm depicts the recommendations that were based on the GDG interpretation of the evidence reviewed in a graphical format. (p81/111)

NICE changes in the final version of the guideline (November 2016)

NICE final recommendations on spinal fusion(November 2016)

15. Do not offer ultrasound for managing low back pain with or without sciatica.
16. Do not offer percutaneous electrical nerve simulation (PENS) for managing low back pain with or without sciatica.
17. Do not offer transcutaneous electrical nerve simulation (TENS) for managing low back pain with or without sciatica.
18. Do not offer interferential therapy for managing low back pain with or without sciatica.

Research recommendations 1. What is the clinical and cost-effectiveness of laser therapy in the management of low back pain and sciatica?

Belgian Stakeholders comments

What about the results of the SR of Huang 2015 that showed based on five studies, the WMD in visual analog scale (VAS) pain outcome score after treatment was significantly lower in the LLLT group compared with placebo (WMD = -13.57 [95 % CI = -17.42, -9.72], I2= 0 %). No significant treatment effect was identified for disability scores or spinal range of motion outcomes. During the meeting it was agreed to maintain the research question, as formulated by NICE with the addition that new trials on this topic should be monitored.

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017
KCE 2017 final recommendations on electrotherapy (February 2017)
15. Do not offer ultrasound for managing low back pain with or without radicular pain
16. Do not offer percutaneous electrical nerve simulation (PENS) for managing low back pain with or without radicular pain
17. Do not offer transcutaneous electrical nerve simulation (TENS) for managing low back pain with or without radicular pain
18. Do not offer interferential therapy for managing low back pain with or without radicular pain
Research recommendations 1. What is the clinical and cost-effectiveness of laser therapy in the management of low back pain and sciatica?

7.11. Psychological interventions

Psychological interventions in patients with low back pain ± radicular pain

NICE search question

"What is the clinical and cost effectiveness of psychological therapies in the management of non-specific low back pain and sciatica?"

Introduction based on the draft version of NICE guideline (March 2016)

- Cognitive behavioural approaches have played an increasingly central role in the management of chronic pain. Cognitive approaches are aimed at altering unhelpful or inappropriate beliefs as a basis for changing behaviour, such as pain- associated disability.
- In the 1990s, Mindfulness, Acceptance and Commitment Therapy (ACT) and Compassion Focused Therapy (CFT) emerged, emphasising the importance of experiencing undesirable thoughts and feelings, in the absence of influence of 'judgemental, evaluative and analytic thought content'. The approaches aim to enhance what has been termed 'psychological flexibility'.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with non-specific low back pain • People aged 16 or above with sciatica
Intervention(s)	• Psychological interventions: • Behavioural therapies • Cognitive therapies • Cognitive behavioural approaches • Mindfulness • Acceptance and commitment therapy (ACT)
Comparison(s)	• Placebo/Sham/Attention control • Usual care/waiting list • To each other • Any other non-invasive interventions in the guideline • Combination of interventions: any combination of the non-invasive interventions in the guideline
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (> 30% improvement in pain or function) • Adverse events: morbidity • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

Single intervention: Twenty-one RCTs (reported in twenty-five papers) were included; the search was also extended to cohort studies for mindfulness and acceptance and commitment therapy, but no relevant cohort studies were identified. Comparators were usual care, waiting list, sham or other psychological therapy. No RCT was found for acceptance and commitment therapy. No evidence was identified for responder criteria or adverse events from the included studies. Results are presented separately for 4 kind of psychological interventions: Cognitive behavioural approaches, Behavioural therapy, Mindfulness and Cognitive therapy.

Cognitive behavioural approaches: Mixed of cognitive therapy, education, engaging in fear-provoking activities, stress reduction, wellbeing therapy…

- **Cognitive behavioural approaches versus sham, usual care or waiting list controls**
  - **Mixed population (LBP with or without sciatica)**
    - No clinical benefit for the majority of reported outcomes, with measures of pain and function being the most commonly reported (moderate to very low quality; total of 7 studies; range of n = 47–458).
    - The one exception was function as measured by RMDQ at less or equal to 4 months, which showed **a clinical benefit of cognitive behavioural** approaches compared with waiting list control (low quality; 2 studies; n = 240).
  - No data available for the **individual sciatica or low back pain populations**
- **Cognitive behavioural approaches versus behavioural therapy**
  - **Mixed population (LBP with or without sciatica)**
    - No difference between the treatments in terms of pain at either time point (1 study; low quality; n=73).
    - **Potential** clinical benefit in favour of cognitive behavioural approaches at greater than 4 months when measured by RMDQ (1 study; low quality; n=73), but not the Quebec back pain disability scale (1 study; very low quality; n=73).
  - No data available for the **individual sciatica or low back pain populations**

Table 32 – Clinical effectiveness of cognitive behavioural approaches compared to other sham, usual care/waiting list or behavioural therapy in mixed population (LBP with or without sciatica)

Cognitive behavioural approaches (CBA)			
Outcomes	**CBA = Video with education component & elements targeting beliefs and self-management. skills (20 min to be watched at home at least 1/3 mo during 1 year)** **versus sham = Video using traditional education approach emphasizing information and technical skills (20 min to be watched at home at least 1/3 mo)**	**CBA* = Stress reduction and problem solving, adaptive coping skills, self-monitoring, pain management, change in dysfunctional cognitions, reduction of avoidance behaviour, and wellbeing therapy (varied number of sessions, e.g. 3, 6, 12)** **versus Usual care or waiting list (3 or 10 weeks)**	**CBA = Exposure in vivo (cognitive therapy, education, engaging in fear-provoking activities) for approximately 16 sessions** **versus Behavioural therapy = operant graded activity (positive reinforcement of healthy behaviours, education, activity quotas)**
Pain	At short term: Not reported At long term: • **Pain and impairment relationship scale: no diff** (1 RCT; Low; n=118)	At short term: • **VAS 0-10: No diff** (6 RCTs; Very low; n=458) At long term: • **VAS 0-10: No diff** (1 RCT; Very low; n=47)	At short term: • **VAS 0-10: No diff** (1 RCT; Low; n=77) At long term: • **VAS 0-10: No diff** (1 RCT; Low; n=73)
Function	At short term: Not reported At long term: • **ODI 0-100: No diff** (1 RCT; Low; n=118)	At short term: • **RMDQ 0-24: CIB favouring CBA** (Mean diff: -2.95 [95%CI -4.26, -1.65]; 2 RCTs; Low; n=240) • **PDI 0-70: No diff** (1 RCT; Very low; n=103) At long term: Not reported	At long term: • **RMDQ 0-24: Potential CIB** (Mean diff:-2.11 [95%CI -4.71, 0.49]RCT; Low; n=73) • **Quebec pain disability scale 0-100: no diff** (1 RCT; Very low; n=73) At long term: Not reported
Psychological distress		At short term: • **BDI 0-63: No diff** (1 RCT; Low; n=109) At long term: Not reported	
Quality of Life		At short term: • **SF-36 0-100 (perceived general health): No diff** (1 RCT; Moderate; n=314) At long term: • **SF-36 0-100 (perceived general health): No diff** (1 RCT; Moderate; n=314)	

CBA: Cognitive behavioural approaches; CIB: clinically important benefit; RCT: randomized clinical trial

*In one study, detailed sessions are provided: Exploration phase (the GP explored the presence of psychological prognostic factors by asking standardised questions); Information phase (the GP provided general information on the cause, course, and possibilities of treatments of low back pain and included the patient's cognitions, emotions and behaviour); Self-care phase (the GP and patient set specific goals on resuming activities or work and discussed time contingent use of analgesic drugs, and the doctor gave the patient a booklet based on the back book).

In another study, CBA = wellness workbook = an on-line self-help intervention consisting of a mind/body treatment rationale, pain education and cognitive behavioural approach techniques including cognitive restructuring, stress management, relaxation training, mindfulness and vales-based behavioural activation) versus waiting list (information they would receive access to the wellness workbook in 3 weeks or no treatment.

In a third study, CBA = operant behavioural graded activity training (3 group sessions followed by a max of 17 individual sessions of 30 minutes) and problem solving training (3 explanatory sessions, next 6 teaching sessions with max of 4 people, course book and homework assignments).

Sometimes CBA was combined with usual care (mainly medication)

Behavioural therapy: EMG biofeedback or relaxation or operant conditioning (activity prescribed of specified intervals, with determined and fixed exercise content), with participation of spouses, group discussion, role playing, feedback versus sham, usual care or waiting list controls

- **Mixed population (LBP with or without sciatica)**
  - Compared with sham biofeedback: **Potential clinical benefit of behavioural therapy** (EMG biofeedback or Relaxation) for improving **pain** at short term (low quality; 1 study; n = 24). No evidence available for pain in long term nor for quality of life, function, psychological distress or healthcare utilization at any point of time.
  - Compared with waiting list controls: No clinical benefit of behavioural therapy approach for pain intensity measured on the McGill scale (very low quality; 2 studies; n = 122) but **potential CIB of behavioural therapy in improving pain** measured by Back pain log at short term when compared to **usual care** (very low quality; 1 study; n = 20). No clinically important difference for function or healthcare utilisation (very low quality; n = 103). No evidence available in terms of quality of life, or psychological distress.
- No data available for the **low back pain populations with sciatica.**
- Only 1 study **(Turner 1990; exercise vs Waiting list; n=96)** concerned **low back pain population without sciatica** and is included in the exercise chapter.

Table 33 – Clinical effectiveness of behavioural therapy compared to other sham or usual care/waiting list in mixed population (LBP with or without sciatica)

Behavioural therapy		
Outcomes	**Behavioural therapy = EMG biofeedback or Relaxation** **versus Placebo/sham = same physical set up but no feedback from the EMG electrodes and no instructions in specific relaxation techniques for the first 8 sessions**	**Behavioural therapy* = EMG biofeedback (15 sessions over 3 weeks) or Operant conditioning (activity prescribed of specified intervals, with determined and fixed exercise content), participation of spouses, group discussion, role playing, feedback (2 hour/week until 8 weeks)** **versus Usual care or Waiting list (until 9 weeks)**
Pain	At short term: • **VAS 0-10: CIB favouring behavioural therapy** (Mean diff: -1.44 [95%CI -2.88, 0.00]; 2 RCTs; Low; n=24) At long term: Not reported	At short term: • **Back pain log: Potential CIB favouring behavioural therapy** (Mean diff: -4.80 [95%CI -15.84, 6.24]; 1 RCT; Very low; n=20) • **Mc Gill 0-78: Potential CIB favouring behavioural therapy** (Mean diff: -3.42 [95% CI -8.08, 1.24]; 2 RCT; Very low; n=122) At long term: Not reported
Function		At short term: Not reported At long term: • **Modified Activity Form score: CIB favouring behavioural therapy** (1 RCT; Very low; n=103)
Healthcare utilisation		At short term: Not reported At long term: • **Estimated costs in last month: Potential CIB favouring behavioural therapy** (at 9-12 months; 1 RCT; Very low; n=103) • **Number of hospitalisations: Potential CIB favouring behavioural therapy** (at 9-12 months; 1 RCT; Very low; n=103) • **Number of medications taken: Potential CIB favouring behavioural therapy** (at 9-12 months; 1 RCT; Very low; n=103) • **Number of treatment visits: Potential CIB favouring behavioural therapy** (at 9-12 months; 1 RCT; Very low; n=103)

CIB: clinically important benefit; Not reported outcomes: Quality of life, psychological distress and adverse events

*In one study, behavioural therapy was combined with analgesia prescription (time contingent basis- analgesia prescribed at fixed times and prescription not renewable) and compared with usual care (analgesia prescribed as required and repeat prescriptions allowed; activities limits decided by patient on when pain subsided sufficiently, and the exercises prescribed wither to be undertaken according to how much pain was being experienced)

Mindfulness: meditation sessions and meditation homework assignments versus usual care or waiting list controls

- **Mixed population (with or without sciatica)**
  - No clinically important benefit of a mindfulness intervention compared to waiting list control on pain (very low quality; 2 studies; n=124), function (low quality; 1 study; n=37) or the majority of quality of life outcomes reported (very low to low quality; 1 study; n=37) **except for the quality of life composite measures of mental health and physical health, which showed a clinical benefit of mindfulness** (2 studies, very low quality, n=124) at short term. No data on long term outcomes.
  - No evidence available to assess the clinical benefit of mindfulness in terms of psychological distress or healthcare utilization.
- No data available for the **individual sciatica or low back pain populations**, nor for the comparison of mindfulness with placebo or sham.[c]

Cognitive therapies: explanation of pain mechanisms, illness perception, functional examination with individual feedback and advice

- **Low back pain population without sciatica**
  - Compared to usual care/waiting list: **Potential clinical benefit** of cognitive therapy in terms of **quality of life (SF-36) and pain** (Mean diff VAS 0-10: -1.09 [95%CI -2.20, 0.02] at long term but no difference for function (very low quality; 1 study; n = 63). No data at short term for these outcomes and no data for psychological distress at any point of time.
  - Compared with biomechanical plus aerobic exercise: Conflicting evidence on the clinical benefit of cognitive therapy for the quality of life components at long term (Clinical benefit favouring cognitive therapy on physical function, bodily pain, vitality, social function, role emotional and mental health but clinical benefit in favour of exercise on role function, and no clinically important difference was seen for general health or health transition). There was also no clinical benefit observed for function or pain (very low quality; n = 64). No evidence was available for these outcomes at short term and for psychological distress at any point of time.
- **Mixed population (with or without sciatica)**
  - **Potential clinical benefit of cognitive therapy** compared with waiting list control in terms of **pain intensity** at short term, but no clinical difference on psychological distress or function assessed with the sickness impact profile (Mean diff VAS 0-10: -1.12 [95% CI -2.51, 0.28], very low quality; 1 study; n = 34). No evidence was available in long term for these outcomes and in terms of quality of life at any point of time. [d]
  - **No data were available for the sciatica population, nor for the comparison of cognitive therapies with placebo or sham.**

Combined intervention: Three studies (reported in six papers) looking at combinations of non-invasive interventions (with psychological therapy as the adjunct) were included.

Combination of psychological therapy (behavioural therapy) and aerobic exercise versus waiting list controls or aerobic exercise alone

- **Low back pain population without sciatica**
  - No clinical benefit of psychological therapy (behavioural therapy) in combination with aerobic exercise in terms of pain (McGill 0-78) at long term when compared to waiting list controls or aerobic exercise alone (very low quality; 1 study; n=37 or 39). No data available for other outcomes.

Combination of psychological therapy (cognitive behavioural approaches) plus aerobic exercise versus aerobic exercise alone

- **Mixed population (with or without sciatica)**
  - No clinical benefit in the short-term but **benefit in the longer term** for the psychological therapy on both pain and function (low quality; 1 study; n=84).

Combination of psychological therapy (cognitive behavioural approaches) plus self-management versus self-management alone

- **Mixed population (with or without sciatica)**

---

[c] Morone 2009 compared Mindfulness and Active control (Keep your brain alive). It is quoted in the list of articles found and in the ET but no results, no forest plot because in older people (65 y and +)…

[d] Siemonsma 2013 compared cognitive therapy vs waiting list in 156 LBP patients with and without sciatica. Not mentioned in the forest plots and results on function.

- **Clinically important benefit of cognitive behavioural approaches in terms of quality of life** when assessed by EQ-5D and SF-12 physical component in both the short and longer term, but not for the mental component of the SF12.
- No difference between treatments in terms of pain and function with the exception of function assessed by the von Korff scale at longer term follow up when **self-management alone was more beneficial in terms of improvements in function** (moderate and low quality evidence, 1 study, n=545 to 598).

Economic evaluation

Three economic evaluations concerned cognitive behavioural approach were included. No studies were identified relating to behavioural therapies, cognitive therapies, mindfulness or acceptance and commitment therapy. One additional economic evaluation (Critchley et al 2007) of a MBR programme which included a psychological component was identified. This is included in the MBR chapter.

- One cost-utility analysis found that **usual care** was dominant (less costly and more effective) compared to cognitive behavioural approach for the management of low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations.
- One cost-utility analysis found that **cognitive behavioural approach** was dominant (less costly and more effective) compared to mixed modality exercise for the management of low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations.
- One cost-utility analysis found that **cognitive behavioural approach** was dominant (less costly and more effective) when compared to a 2-element MBR (physical, psychological) programme and mixed manual therapy plus self-management for treating low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations.

The main cost of delivering psychological interventions will be the personnel costs. Psychological interventions may be delivered by a psychologist or another health care professional trained to give the therapy such as a nurse or physiotherapist. In addition, the Personal Social Services Research Unit (PSSRU) reports a cost per individual cognitive behavioural approaches session of £91. This is based on a session lasting 55 minutes and conducted by a clinical psychologist, mental health nurse or specialist doctor. Note this is based on costs estimated for a RCT of interventions for adolescents with depression

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:** Health related quality of life, pain severity, function and psychological distress were the outcomes that were critical for decision making.
- **Trade-off between clinical benefits and harms:**
  - Majority of evidence concerned mixed populations with low back pain with or without sciatica. Some data were available for people without sciatica for cognitive therapies and combinations of interventions, noted below.
  - Wide variation in length of interventions in the studies included (from 3 weeks to 1 year)**.**
  - Different results:
    - **Cognitive behavioural approaches:** no clinical benefit for cognitive behavioural approaches compared to sham, usual care or waiting list for any reported outcome (except function at the longer term follow-up when compared to waiting list control). Six studies were meta-analysed for short term pain outcome in people receiving cognitive behavioural approaches compared to usual care or waiting list which, demonstrated no difference in outcomes, with little uncertainty, albeit of very low quality overall. One study was included which compared cognitive behavioural approaches to sham cognitive behavioural approaches, but this did not demonstrate a meaningful difference between treatments for pain or function. The GDG were aware that in some of the included studies, the interventions were not provided by a qualified clinical psychologist. For example, one study assessed cognitive behavioural approaches delivered by video which the patient followed themselves. This was considered by the GDG to be a valid method of delivering a cognitive behavioural approach. It was also considered that cognitive behavioural approaches are rarely provided in isolation to other treatments and is intended to be part of a package of care (see MBR, chapter 17). The primary aim of a cognitive behavioural approach is not to directly improve pain and function, but reduce the fear of pain, thus increasing people's confidence in undertaking physical rehabilitation and therefore the GDG considered it unsurprising that meaningful effects were not seen in these outcomes.
    - **Behavioural therapies:** Although there was some evidence of benefit for behavioural therapy (EMG biofeedback) versus sham biofeedback in improving pain, it was noted that this was only from one small study of 24 participants. The evidence comparing behavioural therapies to usual care or waiting list

controls was conflicting when looking at the benefit of behavioural therapy on improving pain at ≤4 months, with no clinically important difference observed for function or healthcare utilisation when compared to usual care. Three of the included studies compared the intervention to a group acting as waiting list controls. As discussed elsewhere in this guideline, waiting list controls may inflate intervention effect sizes due to a negative effect on people randomised to wait, but knowing that they will receive treatment later. Additionally, the lack of difference seen in these outcomes when compared to waiting list control groups does not provide evidence that this intervention is effective for improving function or reducing healthcare utilisation. A further study was included in this review comparing cognitive behavioural approaches and behavioural therapy which demonstrated no difference between treatments in terms of pain and function when measured with Quebec pain disability scale at longer term follow-up.

- **Mindfulness:** Two small studies comparing mindfulness with waiting list control were included, however there was no clinically important benefit observed on pain, function or quality of life, except for the two SF-36 composite measures of physical and mental health, which showed clinical benefit of mindfulness at ≤ 4 months. The GDG considered that there was insufficient evidence for this therapy from this evidence review.
- **Cognitive therapies**: There was some evidence from two small studies (one in people with low back pain without sciatica, and one in people with or without sciatica) to suggest a clinical benefit of cognitive therapy when compared to usual care or waiting list controls on pain outcomes at ≤4 months and in one study for quality of life outcomes at ≤4 months, but not difference on psychological distress or function in either study. The GDG considered that this evidence was too limited to inform a recommendation. The GDG noted that only one of the included studies reported evidence on psychological distress relevant to this review protocol, and therefore were unable to determine whether this aspect may have improved. However, the lack of consistent observed benefit in quality of life was suggestive that other aspects of wellbeing may not have improved significantly. The GDG therefore agreed that there is no consistent good quality evidence from this review to recommend that any of the psychological therapies reviewed were effective for people with low back pain or sciatica when delivered in isolation,
- **Combinations of non-invasive interventions**: Evidence came mainly from a single large study, which looked at group cognitive behavioural approaches in combination with self-management and did not show clinical benefit to a change in pain and function. There was however, improvement in terms of quality of life (SF-12 physical and EQ-5D in the short and longer term). It was also noted that no difference was observed when cognitive behavioural approaches was provided in combination with aerobic exercise, compared to exercise alone, in people without sciatica but this evidence was from a small study (n-34) which was at high risk of bias. The GDG noted that although it was disappointing that there was not a bigger change in function, the positive evidence in favour of cognitive behavioural approaches in combination with self-management was from a large trial, and indicated there was some benefit of cognitive behavioural approaches when provided alongside other interventions such as self-management.

- **Trade-off between net clinical effects and costs**
  - Usual care was dominant compared to cognitive behavioural approach in one study of low back pain with or without sciatica (>12 weeks or exacerbation of mild symptoms).
  - However cognitive behavioural approach was dominant compared to mixed modality exercise in the same population in another study (> 3 months resulting in disability (RMDQ >3) and ability to walk at least 100m). Both studies are within-trial analyses, each based on one of nine clinical studies included for this comparator and so do not reflect full body of available evidence for this comparison. Both studies were assessed as partially applicable with potentially serious limitations.
  - Cognitive behavioural approach in combination with self-management (active management) was cost-effective compared to self-management alone (ICER £1,786 per QALY gained) in a third study which included a psychological intervention. This analysis was assessed as partially applicable with potential serious limitations.
  - The GDG considered the conflicting economic evidence and felt that there was too much uncertainty regarding the clinical and cost-effectiveness of cognitive behavioural approach as a standalone intervention to make a strong recommendation. They acknowledged that the economic evidence showing cognitive behavioural approach being more cost effective than mixed modality exercise was based only on one RCT which showed cognitive behavioural approach to be more effective than usual care in terms of pain severity, however this was in conflict with the remaining body of evidence showing no difference between cognitive behavioural approach and usual care. In addition, the comparison between cognitive behavioural approach and mixed modality exercise in Smeets 2009 was based on clinically insignificant effectiveness data, therefore the GDG did not believe cognitive behavioural approach to be more clinically and cost effective than mixed modality exercise. However cognitive behavioural approach was considered cost effective if provided as part of a MBR programme or as part of a package of combined physical and psychological treatments, based on the evidence in the MBR review. No economic evidence was identified relating to behavioural

therapies, cognitive therapies, mindfulness or acceptance and commitment therapy. The main cost of delivering these psychological interventions would be the personnel costs. The unit costs for a clinical psychologist or another health care professional trained to give psychological therapy such as a nurse or physiotherapist was presented to the GDG for consideration. In addition, the NHS cost per session of individual cognitive behavioural approach was also presented to the GDG. Overall the GDG considered that the clinical evidence was not strong enough to base a recommendation for any of these interventions as stand alone treatments.

- **Quality of evidence**
  - Ranged from moderate to very low; serious or very serious risk of bias (due mostly to the difficulty of adequate blinding with such interventions) in most of the studies included.
  - Waiting list controls as comparator groups in a number of the studies although this is not reflective of usual practice and often lead to inflated estimates of effect sizes in the intervention groups due to the negative effect on people randomised to delayed treatment.
  - Lack of detail about the background care that the participants received apart from the intervention, and therefore impossibility to assess in some cases whether the care in the two groups was comparable, with a risk of overestimating effects in subjective outcomes such as pain and function.
  - For behavioural therapies, all included studies published prior to 1990. The GDG agreed this was not unexpected as this treatment is now less commonly used to treat people with low back pain.
  - For mindfulness, evidence very limited (1 small study compared to waiting list control, and 1 compared to sham which only reported data in graphical format and therefore could not be analysed within this review). No observational studies identified.
- **Other considerations**
  - Much of the evidence in this review is based on individual studies for each comparison. It was consequently agreed that there was not enough evidence to make any recommendations for the use of psychological therapies in isolation. The GDG discussed that the evidence suggests psychological therapies are of limited effectiveness in isolation for low back pain or sciatica; however, there is an indication from this review that in combination with other therapies such as self-management, they may be of benefit. This is also reviewed in the chapter on multimodal therapy where there were evidence suggesting benefits from a package of treatment including a psychological element. The GDG noted that this evidence relates to psychological therapies for low back pain and sciatica and not for co-morbid conditions such as anxiety or depression that may be present in people with low back pain or sciatica. In these individuals other relevant NICE guidance should apply.

NICE 2016 recommendation 18 (According to the NICE formulation, this is a weak recommendation)

18. Consider psychological therapies for managing non-specific low back pain with or without sciatica but only as part of multi-modal treatment packages.

Belgian GDG considerations mentioned in the Lime survey at the beginning of June 2016

Agreement with the content of the NICE recommendation 18: 11 Yes, 1 No, 1 no opinion, 1 out of competence, 0 no answer, 2 not completed

- **Comments from the one respondent who does not agree:**
  - Als STart Back Tool wordt gebruikt, dan wel OK. Anders is het natte vinger werk.
- **Other comments:**
  - In principle I agree, but would suggest splitting the different sorts of psychological therapies. From our psychological group I received following comments: We do not agree, based on shortcomings in methods and outcome measurements for the included studies. However, we do support the value and role of psychological interventions and therapies in managing non-specific low back pain and its consequences. Attention to these methodological issues in further research and analyses is warranted
  - I would prefer reading that a "psychological screening test" is necessary in patients with LBP to be able to refer patients who need a psychological intervention (to prevent passage or persistence of chronicity). It is also strange that, in the section related to psychological intervention, is included cognitive therapies dedicated to explain pain mechanisms. I would not consider such education as a psychological intervention...

Strength of the recommendation 18: According to NICE formulation, it is a weak recommendation

GRADE Factors	
Balance between desirable and undesirable effects	No consistent good quality evidence to recommend that any of the psychological therapies reviewed were effective for pe with low back pain or sciatica when delivered in isolation.
Quality of evidence	From moderate to very low; serious or very serious risk of bias (due mostly to the difficulty of adequate blinding with s interventions) in most of the studies included.
Values and preferences	No info provided by NICE 2016
Costs (resource allocation)	Conflicting economic evidence and uncertainty regarding the clinical and cost-effectiveness of cognitive behavioural appro as a standalone intervention. Importance of the personnel costs.

Agreement with the strength of the NICE draft recommendation: 4 strong, 6 weak, 1 no opinion, 0 no answer, 5 not completed

- **Comments for a weak recommendation**
  - Quality of evidence
- **Comments for a strong recommendation**
  - Although the evidence is not very consistent and the quality rather moderate I would strongly recommend to consider it as part of a broader package. It will not be necessary for everyone or at any time, but for some (in case of yellow flags) at some time (subacute and chronic stadium) it could be important as part of a multimodal approach. Looking at chronic pain management ACT is much more promising then CBT, especially at long term. This could also be the case for at least chronic back pain (but actually no RCT for ACT in back pain).
  - Early patient selection or systematic screening for early detection of yellow flags

Belgian GDG comments during the GDG meeting on the 29th June 2016

No comments

- **Conclusion: recommendation NICE 2016 unchanged**

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30th November 2016)

- **Problem with the critically important outcomes**: Acupuncture Now Foundation: The primary aim of a cognitive behavioural approach is not to directly improve pain and function, but reduce the fear of pain, thus increasing people's confidence in undertaking physical rehabilitation. However it is unclear whether the GDG found any specific evidence that cognitive behavioural approaches actually do reduce fear of pain or increase confidence in physical rehabilitation, or any evidence of a specific effect for cognitive approaches in the MBR literature that was clearly separate from non-specific effects. **NICE reply:** When setting the protocols the GDG agreed that the outcomes to be considered should be the same across reviews for consistency of decision making. Although fear of pain was not considered as a separate outcome, **psychological distress** was an outcome for all reviews, which a priori, the GDG believed would cover the important outcomes for decision making. Regarding the evaluation of non-specific effects in the MBR review, it was not possible to determine how much of the effect of the treatment was specific. Where possible, it was taken into account. (p11/111)
- **Errors and missing reference:** SH Arthritis Research UK:The GDG state that 'a further study was included in this review comparing cognitive behavioural approaches and behavioural therapy which demonstrated no difference between treatments in terms of pain and function when measured with the Quebec pain disability scale at longer term follow-up'. However studies did show (Page 601) clinical benefit in favour of cognitive behavioural approaches at greater than 4 months when measured by RMDQ. Why has this finding not been included in the summary on page 604? **NICE reply**: Section 15.7 has been edited to include reference to the missing function outcome (RMDQ scale, > 4 months) showing clinical benefit in favour of cognitive behavioural approaches over behavioural therapy.(p54/**222)**

- **Lack of sham/placebo comparison:**
  - University of York: The GDG placed more weight on the comparison between an intervention and placebo/sham whenever a placebo/sham was available and it was feasible to do so. The same consideration should be implied for acupuncture. Therefore for consistency when interpreting the evidence, if the recommendation of combined physical and psychological programmes is sustained, then acupuncture should also be considered as a recommendation, as there is clear proof of principle, as documented elsewhere, that acupuncture outperforms sham/placebo, as well as delivering a minimum clinical difference that is cost-effective when compared to usual care. **NICE reply**: In the case of psychological therapies, there was evidence of benefit for behavioural therapies over placebo/sham for pain, with low quality evidence coming from a single small study, and no evidence of benefit for cognitive behavioural approaches compared to placebo/sham. However the GDG discussed that cognitive behavioural approaches were unlikely to be provided in isolation and that the improvement of pain and function are not primary aims of this type of interventions. These factors would explain why meaningful effects were not seen in these outcomes. The evidence supporting the psychological therapies recommendation came from the combination section of the review, alongside the single intervention section and the MBR chapter. This is detailed in section 15.7 Recommendations and link to evidence.(p90/111)
  - British Acupuncture Council. Psychological therapies aren't even effective, let alone efficacious, and the case for recommending them is particularly baffling. Thus CBT failed to reach clinical significance for any of the pre-defined critical outcomes: it didn't even manage to out-perform a waiting list for psychological distress! The GDG appear to have moved the goal posts to accommodate this: a) re-specifying the outcome to 'reducing the fear of pain', b) recommending packages of care even where the individual interventions are ineffective. Even in combination the evidence is not encouraging: a two-element MBR programme (physical and psychological) did not differ from waiting list for pain or psychological distress. There's a similar story with paracetamol and opioids: neither is better than sham and even combined they aren't very convincing. The likelihood that any of these are operating through specific effects rather than placebo seems pretty low. **NICE reply**: Regarding psychological therapies, the GDG acknowledged that the evidence from single intervention CBT trials was not convincing and therefore were unable to recommend its use in isolation. The GDG considered however, that psychological therapies would often be offered in combination with other interventions in clinical practice, and that the improvement of pain and function is not the primary aim of this type of intervention, possibly explaining the lack of meaningful effects observed in these outcomes. Evidence from the combination and the MBR supported the recommendation of psychological therapies to be offered as part of a treatment package including exercise, with or without manual therapy. This is detailed in section 15.7 (Recommendations and link to evidence). (p24/111)
- **Only in multi-modal packages.**
  - Warwick Clinical Trials Unit**:** Recommendation 18 suggests the use of psychological therapies only as part of a multi-modal package. So far as we can see in the guidance what constitutes a multi-modal package of care is not described; nor the evidence for such packages appraised. For this recommendation to be helpful the GDG needs to spell out what a multi-modal intervention would consist of. This needs to include indications of style, content and dose. Delivering an ineffective psychological intervention, or a watered down version of a proven intervention may well not achieve the beneficial effects the GDG are hoping for. We note here our conflict in that one of the key papers referred to be GDG was a study done at this unit of a particular group intervention package that would not lend itself to being subsumed into an unspecified 'multi-modal intervention'. We are most disappointed that GDG did not find the data from this trial (Lamb 2010), conducted in the UK sufficiently persuasive to suggest that this intervention should be considered as an option. It has shown clear benefits on pain, function and quality of life at four and 12 months and the within trial cost-utility analysis shows that represents good value for money. Furthermore, although not included in the data extractions here it has effects sustained for up to three years. It is an intervention that would be easily deliverable in the NHS. We request that the GDG re-visit their discussion on this paper and consider if this a treatment option, delivered as designed, they would people living with back pain. We note again here that there is some evidence for effectiveness of psychological interventions but little for their efficacy. It is not possible from the data presented to separate the contextual effects related to the intervention, including group effects from the actual effect of the modality being tested. **NICE reply**: Recommendation 1.2.13 has now been reworded to clarify and the term 'multi-modal' is no longer used. The recommendation now reads as follows: Consider psychological therapies using a cognitive behavioural approach for managing non-specific low back pain with or without sciatica but only part of a treatment package including exercise with or without manual therapy. Regarding the Lamb trial (Lamb 2010b), it was not possible to include outcomes at 3 years as it was agreed at protocol stage that outcomes would be reported at up to 4 months and at 1 year. These were agreed as appropriate time points to assess effectiveness of interventions. Evidence from this study has been considered and it did not show clinical benefit to a change in pain and function. The improvement in terms of quality of life (SF-12 physical and EQ-5D in the short and longer term) was noted by the GDG. Effectiveness is used here as a broad term to include efficacy and we will clarify this in the glossary. All of the reviews do look to determine both (using 'effectiveness' as a broad term to cover both situations). We agree that without evidence against

sham it is not possible to separate intervention effect from the non-specific effects that arise out of the process of treatment (such as the effects the therapeutic context might have) rather than directly from the active treatment components. However, as discussed the recommendations are based on the best evidence available for each intervention, and on this basis it was agreed there is not sufficient. (p54/222**)**

- South Devon Healthcare NHS Foundation Trust: Our chief concern is the way it states that psychology should "only" be part of multi modal packages. The point needs to be made about the importance of psychology in dealing with avoidance**/**therapy readiness and motivation to change**/**using values as a motivation to re-engage with activities**/**extreme distress**/**managing attachment styles (which may be a barrier to engagement)**/**helping the high proportion of people with a trauma background for whom their past experience has served to sensitise their pain systems.Many of these patients can benefit initially from input from psychology to enable them to engage further in more multimodal packages, and need this as their entry point into self management. We also have patients seen in our team for only pain psychology who have good outcomes. **NICE reply:** The GDG agreed that the reviewed evidence suggests psychological therapies are of limited effectiveness in isolation for low back pain or sciatica. However, the evidence from the combination section of the review and the MBR chapter suggested benefit of psychological therapies in combination with other interventions. The GDG felt it was appropriate to recommend psychological therapies as part of a treatment package including other therapies exercise with or without manual therapy. The MBR chapter also includes evidence suggesting benefits from a package of treatment including a psychological element. Please see section 15.7 (Recommendations and link to evidence) for more details. (p77/111)
- United Kingdom Spinal Societies Board and British Orthopaedic association: In a number of recommendations it is suggested that some treatments be offered as part of a multimodal treatment package. The format or delivery of such a package is not defined within the guidance. It is not clear whether this is a package which might be delivered by a single individual, for example manipulative therapy delivered by a “psychologically informed therapist” with discussion and advice on other self-management techniques, or a package delivered by more than one person. Clearly the involvement of another practitioner would have significant effects on costs and cost effectiveness and might indeed alter the recommendation. No evidence has been brought forward concerning such a multi modal package. Further guidance on the definition of multi-modal package, by whom it should be delivered and an assessment of the evidence base would be greatly appreciated. **NICE reply**: The term ‘multimodal’ has been amended. The recommendations now refer to ‘a treatment package including exercise with or without psychological therapy’ and ‘a treatment package including exercise with or without manual therapy‘, to make the format and content more transparent. These recommendations are based on evidence from studies that used a treatment package consisting of these components, which can be found in chapters 9, 12 and 17. It is beyond the scope of this review to specify who should deliver an intervention, the review focussed on whether or not interventions are clinically and cost-effective and was based on the best available evidence identified according to the review protocol (p175/222)

- **Varied training of clinician:**
  - Arthritis Research UK: A frequent criticism of cognitive behavioural or psychological studies is that the intervention was not actually delivered, either because it wasn’t defined, wasn’t actually what it claimed to be (e.g. cognitive behavioural therapy), wasn’t delivered by clinicians with appropriate or sufficient training, was delivered by clinicians with insufficient expertise and/or the treatment dose was suboptimal (e.g. van der Windt D, Spine 2008; 33(1)). A greater distinction between treatment provided by accredited cognitive and/or behavioural psychotherapists (usually CBT therapists or psychologists http://www.babcp.com/files/Public/what-is-cbt-web.pdf.), and cognitive/behavioural approaches, delivered by other clinicians (usually physiotherapists) should be interested. **NICE reply**: Behavioural therapies, cognitive therapies, cognitive behavioural approaches, mindfulness and acceptance and commitment therapy (ACT) were separately reviewed in the Psychological therapies chapter. Details regarding interventions featured in the included studies can be found in the Summary of evidence tables (Table 285, section 15.3) and Appendix H, section H.4. The GDG agreed there was no evidence to recommend who should deliver the intervention, but agreed it should be an appropriately trained healthcare professional. (p18/111)
  - Society for Back Pain Research**:** With appropriate training and measured competencies, a range of profession can deliver this intervention and these are likely to be experienced clinicians of a band similar to a psychologist**. NICE reply:** The GDG agreed there was no evidence to recommend who should deliver the intervention. The GDG agreed important to note that for all interventions the person delivering the therapy would have a large effect on the outcome of treatment and that it should be delivered by an appropriately trained individual. This is acknowledged in section 17.6 (Recommendations and link to evidence).(p65/111)
  - Extended Scope Practitioners Professional Network: Psychological support is often used in secondary care and Pain Services programmes. It would seem appropriate to be able to provide more psychological support in Primary care to prevent unnecessary referrals into secondary and tertiary services. This would involve up-skilling current staff and/or moving secondary care services into the community. **NICE reply**. Your comment will be considered by NICE where relevant support activity is being planned.(p63/222)

- University Hospitals Birmingham NHS Foundation Trust: Could the GDG confirm that “psychological therapies” as part of multimodal treatment packages can be undertaken within a therapy led service (e.g. Cognitive behavioural informed physiotherapy) as opposed to conducted by a psychologist/ cognitive behavioural therapist. **NICE reply**: Psychological therapies should be offered by an appropriately trained specialist.(p185/222)

- **Chronic pain or not.** Arthritis Research UK**:** While the GDG defined behavioural therapy as a treatment to help change potentially self-destructing behaviours in people with chronic low back pain**,** they did not mention the terms chronic pain in the definition of cognitive-behavioural approaches. **NICE answered** that the population considered can be found in table 284, section 15.2. However, only age was quoted in the PICO**.** (p18/111)
- **Misclassification of the Back Skills Intervention and Trial.**
  - Centre for Rehabilitation Research, University of Oxford: As authors of the Back Skills Intervention and Trial, currently included in the section on Psychological Interventions, we disagree with the way that the intervention has been classified. The study should be re-classifed as MDR. The Back Skills Intervention uses cognitive behavioural approaches to target physical activity and exercise as the key behaviours. The intervention included assessment and prescription of exercise tailored to each individual, and identification of a physical activity goal which also formed an important part of the intervention. The importance of exercise was reinforced during the sessions, and in each one and a half hour session, dedicated time was given to performing and reviewing exercises. This is much more similar to the “exercise and cognitive intervention” described by Smeets and included in the Multidisicplinary Biopsychosocial Rehabilitation (MBR) section (p673). The Back Skills Training intervention fulfils the criteria stated on p 674 Table 348 as “A uni-disciplinary programmes including combined concepts: where it is one profession (usually Physio) who may be using cognitive - behavioural principles or a cognitive - behavioural approach, alongside exercise / education”. The description of the intervention is brief in the Lancet paper (Lamb et al Lancet. 2010; 375(9718):916-923), but expanded in Hansen, Z., Daykin, A. and Lamb, S., A cognitive-behavioural programme for the management of low back pain in primary care: a description and justification of the intervention used in the Back Skills Training Trial (BeST; ISRCTN 54717854), Physiotherapy, 2010, 96(2):87-94. See Table 1/Page 92. And also in Lamb, S. E., Lall, R., Hansen, Z., Castelnuovo, E., Withers, E. J., Nichols, V., Griffiths, F., et al., A multicentred randomised controlled trial of a primary care-based cognitive behavioural programme for low back pain. The Back Skills Training (BeST) trial, Health Technol Assess, 2010, 14(41):1-253, iii-iv. See page 7.We know that exercise component was implemented. In quality assurance checks, 97% of the groups observed (34/35) exercise was part of the session. The psychological elements which predominate were focused towards increasing physical activity, exercise and normal function despite pain. **NICE reply**: The intervention has been classified as a combination of psychological therapy (cognitive behavioural approach) and self-management (advice to stay active, the Back Book). This meets the criteria for inclusion in the Psychological therapies review and has therefore not been re-classified.(p38/111)
- **Cost impact**
  - Acupuncture Association of Chartered Physiotherapists: “Talking therapies” have been recommended. The cost impact on the NHS for this therapy, particularly given the national shortage of clinical psychologists and long waiting lists already (1 year in some areas) then the potential burden of disease would magnify. How do the GDG propose to deal with this? Particularly in light of perceived non-compliance of previous guidelines due to funding issues. **NICE reply**: Given the national shortage of clinical psychologists and long waiting lists (1 year in some areas), the talking therapy will have a cost. The guideline recommends psychological therapies only if offered as part of a package of treatment with exercise with or without manual therapy. The cost issue will be discussed afterwards. (p2/111)
  - Arthritis Research UK: Personnel costs: Delivery of psychological approaches requires training and expertise. These interventions have historically been provided by psychologists, however, increasingly, physiotherapists and other professionals are receiving training to deliver psychologically informed approaches. We can understand NICE desire to create 'low cost solutions' because of the challenges of implementation. However, we can see no evidence from the guidelines that a band 5 practice nurse can effectively deliver psychological interventions to people with low back pain, with or without sciatica. We suggest the GDG highlight the importance of adjusting the intensity / quality / expertise required to deliver the treatment according to the complexity of the patient, i.e. psychological approaches for straightforward people with relatively acute back pain may be deliverable by less specialist staff with appropriate training but patients with chronic LBP and significant distress / disability require clinicians with a higher level of expertise, working together with other professional disciplines, as part of an interdisciplinary team. The assumption that physiotherapists and psychologists see the same number of LBP patients in the same amount of time is incorrect. Our experience is that physiotherapists see more. However in the absence of data regarding this, we suggest that the GDG remove the statement pertaining to this. **NICE reply**: We agree and we have amended the costing for nursing staff to reflect a band 7 is required to deliver this intervention.Footnote c in the table is not about how

many patients are seen by physiotherapists and psychologists in the same amount of time; it is simply the ratio between the total number of hours spent with actual patients and the total number of hours worked.(p53/222)

  - Guy's and St. Thomas NHS Foundation Trust**:** There is lack of availability of Psychological Therapies needed to provide CBT for the high risk group identified by StartBack**;** Review of funding for psychological therapies would enable more complete multidisciplinary pain management pathways to be developed. **NICE reply**: Your comment will be considered by NICE where relevant support activity is being planned. (p203/222)

- **Obstacle to recovery.** Centre for Rehabilitation Research, University of Oxford: There is no description or definition of psychosocial obstacles to recovery. This should be much more transparent. What evidence is there to suggest that this treatment does not help unless previous treatment has failed? Many trials have demonstrated that using MDR or psychological interventions as a first off is helpful. The evidence that STARTback provides on a variety of treatments as well as stratification seem to be missing. **NICE reply**: The GDG acknowledged the difficulty of defining who should be offered a CPP programme, as discussed in the 'other considerations section of the 'evidence and link to recommendations' section of this chapter. They agreed that a CPP programme might be helpful and appropriate in the early stages in some group of people, i.e. those with significant psychosocial obstacles to recovery. Otherwise, the GDG felt that such intervention would be most effective when previous treatments have failed as part of a stepped care approach. This is reflected in the wording of the recommendation. (p61/222)
- **Access of care:** Guy's and St. Thomas NHS Foundation Trust: Psychological support is difficult to access. Group classes do discriminate against non English speaking patients. The implementation challenge in a multicultural locality is to ensure access and equity of provision of these services for all. **NICE reply**: Your comment will be considered by NICE where relevant support activity is being planned. (p203/222)

NICE changes in the final version of the guideline (November 2016)

In the "Trade-off between clinical benefits and harms" chapter, there were several change

- **In the introduction, a paragraph was added:**

  The GDG discussed the necessity of a body of evidence to show specific intervention effects, that is, over and above any contextual or placebo effects. It was therefore agreed that if placebo or sham-controlled evidence is available, this should inform decision making in preference to contextual effects. However, if there was a lack of placebo or sham-controlled evidence, evidence against usual care will be given priority when decision making.

- **A sentence was changed in the paragraph "In the behavioural therapies":**

  A further study was included in this review comparing cognitive behavioural approaches and behavioural therapy which demonstrated no difference between treatments in terms of pain and mixed evidence in terms of function (clinical benefit for cognitive behavioural approaches when measured with RMDQ, no difference between treatments when measured with Quebec pain disability scale) at longer term follow-up.

- **Another sentence was changed in the paragraph "Combinations of non-invasive interventions"**

  Evidence came mainly from a single large study, which looked at group cognitive behavioural approaches in combination with self-management and did not show clinical benefit to a change in pain and function. There was however, improvement in terms of quality of life (SF-12 mental in the long term and EQ-5D in the short and longer term).

- **A summary was added:**

  Summary The GDG highlighted that much of the evidence in this review is based on individual studies for each comparison. It was consequently agreed that there was not enough evidence to make any recommendations for the use of psychological therapies in isolation. The GDG discussed that the evidence suggests psychological therapies are of limited effectiveness in isolation for low back pain or sciatica; however, there is an indication from this review that in combination with other therapies such as self-management, they may be of benefit. This is also reviewed in Chapter 17 where there was evidence suggesting benefits from a package of treatment including a psychological element. The evidence from Chapter 17, together with the evidence from this review, supported the recommendation of a cognitive behavioural approach as psychological element in the treatment package. The GDG did not feel that psychological therapy should be a mandatory component of a treatment package, but that it is one optional modality that might be considered alongside exercise.

In the "Trade-off between net clinical effects and costs",

- **A piece of sentence was added:**

Two economic evaluations of cognitive behavioural approach for low back pain were included, whereas no studies were identified relating to behavioural therapies, cognitive therapies, mindfulness or acceptance and commitment therapy.

- **One sentences was added and another changed**

  In addition, the NHS cost per session of individual cognitive behavioural approach was also presented to the GDG.

  In the absence of evidence on these specific interventions, the GDG decided to only make a recommendation on interventions which have a cognitive behavioural approach. Instead of 'Overall the GDG considered that the clinical evidence was not strong enough to base a recommendation for any of these interventions as stand-alone treatments'

In the "Other considerations" chapter, two sentences was removed

The GDG highlighted that much of the evidence in this review is based on individual studies for each comparison. It was consequently agreed that there was not enough evidence to make any recommendations for the use of psychological therapies in isolation. The GDG discussed that the evidence suggests psychological therapies are of limited effectiveness in isolation for low back pain or sciatica; however, there is an indication from this review that in combination with other therapies such as self-management, they may be of benefit. This is also reviewed in Chapter 17 where there were evidence suggesting benefits from a package of treatment including a psychological element.

NICE final recommendations on psychological interventions (November 2016)

19. Consider psychological therapies using a cognitive behavioural approach for managing low back pain with or without sciatica but only as part of a treatment package including exercise, with or without manual therapy (spinal manipulation, mobilisation or soft tissue techniques such as massage).

GDG comments on the last formulation during the meeting on the 24th January 2017: none

KCE 2017 final recommendations on psychological interventions (February 2017)

9. Consider a psychological intervention using a cognitive behavioural approach for managing low back pain with or without radicular pain, but only as part of a multimodal treatment* with a supervised exercise programme. *Psychological interventions are optional and are only applied to certain patients at certain time period and depending on their risk stratification. (weak recommendation based on moderate to very low quality from RCTs)

7.12. Multidisciplinary biopsychosocial rehabilitation (MBR) programs

Multidisciplinary biopsychosocial rehabilitation (MBR) programmes in patients with low back pain ± radicular pain

NICE search question

"What is the clinical and cost effectiveness of MBR programmes (non-invasive interventions) in the management of non-specific low back pain and sciatica?"

Introduction based on the draft version of NICE guideline (March 2016)

- The MBR approach combines education and physiotherapy, with different forms of cognitive-behavioural psychology to address participants' unhelpful beliefs about their pain, reduce 'fear-avoidance' behaviours and catastrophic thinking and improve mood, thus decreasing disability and improving function.
- The definition of MBR programmes that has been used for the purposes of this review has been adapted from the 2014 Cochrane review which defines these as follows: MBR was defined as an intervention that involves a **physical component** (such as specific exercise modalities, mobilisation, massage) and at least one other **element from a biopsychosocial approach**, that is **psychological or social and occupational or educational** (defined educational intervention e.g. education on anatomy, psychology, imaging, coping, medication, family, work and social life). The intervention program had to have been delivered by **clinicians from different disciplines**,that is a minimum of two healthcare professionals from different professional backgrounds had to be involved in the intervention delivery. The different components of the intervention had to be offered as **an integrated programme** involving communication between the providers responsible for the different components. Further discussion with the GDG agreed that these programmes may in fact include various components delivered by one individual, and that the multi-disciplinary aspect can apply to the interventions included in the package (across disciplines), not to the number of people/disciplines delivering this.
  For this reason, the included interventions in this review were agreed as:

PICO used by NICE (March 2016)

Population	• People aged 16 or above with non-specific low back pain • People aged 16 or above with sciatica
Intervention(s)	• Multidisciplinary biopsychosocial rehabilitation programmes 1. Uni-disciplinary programmes including combined concepts: where it is one profession (usually physio) who may be using cognitive-behavioural principles or a cognitive-behavioural approach, alongside exercise/education 2. Multidisciplinary biopsychosocial programmes: Multidisciplinary defines as: targeting factors from the different domains (physical, psychological and social) o Irrespective of the number of people who deliver the programme o Must have a physical component plus at least 1 other core elements (psychological/educational): ▪ 3 core elements: physical + psychological + educational ▪ 2 core elements: physical + psychological ▪ 2 core elements: physical + educational o Tailored components are acceptable as long as these components are described and must be given in addition to a defined component
Comparison(s)	• Placebo/Sham/Attention control • Usual care/waiting list • To each other • Any other non-invasive interventions in the guideline

	• Combination of interventions: any combination of the non-invasive interventions in the guideline
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (> 30% improvement in pain or function) • Adverse events: morbidity • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit) • Return to work

Literature quoted by NICE 2016 guideline(March 2016)

- Twenty-two RCTs were included in the review. Results are presented in three categories: MBR programme 3 elements (physical + psychological + education); MBR programme 2 elements (physical + psychological); and MBR programme 2 elements (physical + education).

MBR programme 3 elements: physical + psychological + education

- **Low back pain population without sciatica**
  - **3-element MBR versus usual care (may have been referred to physiotherapy, including manipulation)**
    - MBR programme with 3 elements (delivered by a unidisciplinary team): physical (stretching, aerobic exercises and strength) + psychological (cognitive-behavioural principles) + education (educational message encouraging self-reliance)
    - No clinical differences were found for **pain** (Aberdeen pain scale 0-100; 1 RCT; low quality; n=179-171) and **function** (RMDQ 0-24; 1 RCT, low quality; n=179-171), both at short and long term.
    - Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation, return to work
  - **No studies found for following comparisons:**
    - 3-element MBR versus placebo/sham
    - 3-element MBR versus single intervention
    - 3-element MBR versus combined intervention
    - 3-element MBR versus 2-element MBR (physical + psychological)
    - 3-element MBR versus 2-element MBR (physical + education)
- **Low back pain population with sciatica**
  - No evidence was available
- **Mixed population (low back pain with or without sciatica)**
  - **3-element MBR versus usual care (waiting list control)**
    - MBR programme, delivered by a multidisciplinary team: physical (postural therapy, strength, stretching) + psychological (relaxation) + education (information in group discussions)

- A single study reported a clinical important benefit at long term favouring the MBR programme for **pain** (Vas 0-10; low quality; n=52) but an improvement in **function** (ODI 0-100; very low quality; n=53) in the waiting list control. No short term data were reported.
- Not reported outcomes: QoL, psychological distress, responder criteria, adverse events, healthcare utilisation, return to work

o **3-element MBR versus single intervention (individual aerobic exercise (walking))**
- MBR programme delivered by a unidisciplinary team: physical (mobility training, interferential therapy) + psychological (cognitive therapy) + education (Back Care booklet)
- Both at short term and at long term, no clinical differences were found in **QoL** (at both time points: SF-12 0-100 physical and mental composite score; 1 RCT; low quality; n=99), in **pain** (NRS 0-10; 1 RCT; moderate-very low quality; n=99) and in **function** (RMDQ 0-24; 1 RCT; low-moderate quality; n=99 and back performance scale 0-15; 1 RCT; moderate quality; n=100).
- Not reported outcomes: psychological distress, responder criteria, adverse events, healthcare utilisation, return to work

o **3-element MBR versus combined intervention**
- Two studies were found with different combined interventions:
  - Monticone 2015: 3-element MBR (delivered by a multidisciplinary team; physical (group exercises on mobility and muscle awareness, task oriented exercises, exercises to recover coordination, balance and walking stability) + psychological (group-based cognitive-behavioural approaches) + education (information, ergonomic advice)) versus combination of biomechanical exercise (strength) + manual therapy (mobilisation) + postural therapy (postural control exercises) + self-management (educational booklet)
  - Critchley 2007: 3-element MBR (delivered by a unidisciplinary team; physical (group strength, stretching and light aerobic exercises) + psychological (cognitive-behavioural approach) + education (structured back pain education)) versus combination of manual therapy (mobilisation, manipulation, massage) + biomechanical home exercises (stretching) + self-management (advice)
- Compared to a combined intervention of exercise, manual therapy, postural therapy and self-management (Monticone 2015), a (short term and long term) clinical important benefit was found in **QoL** (SF-36 0-100; low quality; n=150) and **pain** (NRS 0-10; low quality; n=150), however not in **function** (both at short and long term; ODI 0-100; low quality; n=150). The study of Critchley 2007 revealed no clinical difference (at long-term) between MBR and the combined intervention (exercise, manual therapy and self-management) in **QoL** (EQ-5D 0-1; moderate quality; n=101), **pain** (VAS 0-10; low quality; n=101) and **function** (RMDQ 0-24; low quality; n=101). No short term data were reported in this study.
- Not reported outcomes: responder criteria, psychological distress, adverse events, healthcare utilisation, return to work

o **3-element MBR (physical + psychological + education) versus 2-element MBR (physical + education)**
- Two comparisons were found
  - 3-element MBR programme: physical (strength, aquatherapy) + psychological (cognitive therapy) + education (written handouts), delivered by a multidisciplinary team (in 2 RCTs)
  - 3-element MBR programme: physical (strength, aquatherapy) + psychological (behavioural therapy) + education (written handouts), delivered by a multidisciplinary team (in 1 RCT)
- Evidence from 2 studies comparing a 3-element MBR programme with a cognitive component to a 2-element MBR programme (physical + education) showed no clinical benefit for any of the outcomes reported (see Table 34) (very low quality; n=35). One study compared a 3-element MBR programme with a behavioural component to a 2-element MBR programme (similar to 3-element; physical + education) and found only a long term clinical benefit in **psychological distress** in favour of the 2-element MBR programme (BDI 0-63; very low quality; n=15).
- Not reported outcomes: QoL, adverse events, return to work, responder criteria

o **No studies were found for following comparisons:**
- 3-element MBR versus placebo/sham
- 3-element MBR versus 2-element MBR (physical + psychological)

Table 34 – Clinical effectiveness of 3-element MBR in mixed population (low back pain with or without sciatica)

3-element MBR (physical + psychological + education)				
Outcomes	**3-element MBR versus usual care**	**3-element MBR versus single intervention (walking)**	**3-element MBR versus combined interventions (exercise + manual therapy + self-management)**	**3-element MBR versus 2-element MBR**
QoL		At short term: • **SF-12 0-100 physical composite score: No diff** (1 RCT; low; n=99) • **SF-12 0-100 mental composite score: No diff** (1 RCT; low; n=99) At long term: • **SF-12 0-100 physical composite score: No diff** (1 RCT; low; n=99) • **SF-12 0-100 mental composite score: No diff** (1 RCT; low; n=99)	At short term: • **SF-36 0-100 (Monticone 2015): CIB favouring MBR (in all 8 subdomains)** (1 RCT; low; n=150) At long term: • **SF-36 0-100 (Monticone 2015): CIB favouring MBR (in all 8 subdomains)** (1 RCT; low; n=150) • **EQ-5D 0-1 (Critchley 2007): no diff** (1 RCT; moderate; n=101)	
Pain	At short term: Not reported At long term: • **VAS 0-10: CIB favouring MBR** (1 RCT; low; n=53)	At short term: • **NRS 0-10: No diff** (1 RCT; moderate; n=99) At long term: • **NRS 0-10: No diff** (1 RCT; very low; n=99)	At short term: • **NRS 0-10 (Monticone 2015): CIB favouring MBR** (1 RCT; low; n=150) At long term: • **NRS 0-10 (Monticone 2015): CIB favouring MBR** (1 RCT; low; n=150) • **VAS 0-10 (Critchley 2007): no diff** (1 RCT; low; n=101)	At short term: • **Pain rating chart 0-5 (cogn ther): no diff** (2 RCTs; very low; n=35) • **Pain rating chart 0-5 (behav ther): no diff** (1 RCT; very low; n=17) At long term: • **Pain rating chart 0-5 (cogn ther): no diff** (2 RCTs; very low; n=29) • **Pain rating chart 0-5 (behav ther): no diff** (1 RCT; very low; n=13)

Function	At short term: Not reported At long term: • **ODI 0-100: CIB favouring waiting list control** (1 RCT; very low; n=53)	At short term: • **RMDQ 0-24: No diff** (1 RCT; low; n=99) • **Back performance scale 0-15: No diff** (1 RCT; moderate; n=100) At long term: • **RMDQ 0-24: No diff** (1 RCT; moderate; n=99)	At short term: • **ODI 0-100 (Monticone 2015): no diff** (1 RCT; low; n=150) At long term: • **ODI 0-100 (Monticone 2015): no diff** (1 RCT; low; n=150) • **RMDQ 0-24 (Critchley 2007): no diff** (1 RCT; low; n=101)	At short term: • **Sickness impact profile 0-100 (cogn ther): no diff** (2 RCTs; very low; n=35) • **Sickness impact profile 0-100 (behav ther): no diff** (1 RCT; very low; n=17) At long term: • **Sickness impact profile 0-100 (cogn ther): no diff** (2 RCTs; very low; n=32) • **Sickness impact profile 0-100 (behav ther): no diff** (1 RCT; very low; n=15)
Psychological distress				At short term: • **BDI 0-63 (cogn ther): no diff** (2 RCTs; very low; n=35) • **STAI-state (cogn ther): no diff** (1 RCT; very low; n=17) • **BDI 0-63 (behav ther): no diff** (1 RCT; very low; n=17) • **STAI-state (behav ther): no diff** (1 RCT; very low; n=17) At long term: • **BDI 0-63 (cogn ther): no diff** (2 RCTs; very low; n=32) • **STAI-state (cogn ther): no diff** (1 RCT; very low; n=15) • **BDI 0-63 (behav ther): CIB favouring 2-element MBR** (1 RCT; very low; n=15) • **STAI-state (behav ther): no diff**

				(1 RCT; very low; n=15)
Healthcare utilisation				At short term: • **Medication use (cogn ther): no diff** (1 RCT; very low; n=17) • **Medication use (behav ther): no diff** (1 RCT; very low; n=17) At long term: • **Medication use (cogn ther): no diff** (1 RCT; very low; n=15) • **Medication use (behav ther): no diff** (1 RCT; very low; n=15)

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y
Outcomes not reported: responder criteria, adverse events, return to work

MBR programme 2 elements: physical + psychological

- **Low back pain population without sciatica**
  - **2-element MBR (physical + psychological) versus usual care (waiting list control: paracetamol 500mg every 6h if necessary)**
    - 2-element MBR programme with physical (muscle relaxation, strength) and psychological (cognitive restructuring techniques) component, delivery of the MBR programme was unclear
    - A clinical benefit was found on short term **pain** (VAS 0-10; 1 RCT; very low quality; n=52) and **function** (RMDQ 0-24; 1 RCT; very low quality; n=52). For **psychological distress** conflicting results were found (BDI 0-63; STAI state; STAI trait; 1 RCT; very low quality; n=52). No long term data were reported.
    - Not reported outcomes: QoL, healthcare utilisation, responder criteria, return to work, adverse events
  - No studies were found for following comparisons:
    - 2-element MBR programme (physical + psychological) versus placebo/sham
    - 2-element MBR programme (physical + psychological) versus single intervention
    - 2-element MBR programme (physical + psychological) versus combined intervention
    - 2-element MBR programme (physical + psychological) versus 2-element MBR (physical + education)
- **Low back pain population with sciatica**

- No evidence was available

- **Mixed population (low back pain with or without sciatica)**
  - **2-element MBR (physical + psychological) versus usual care (waiting list control/'non-intervention group')**
    - Two studies was found:
      - Smeets 2008: 2-element MBR consisting of a physical (active physical training with graded activity) and psychological (problem solving training) component, delivered by multidisciplinary team.
      - Gatchel 2003: 2-element MBR consisting of a physical (physical reconditioning: stretching, strength, relaxation, aerobic exercises, recreational activities)) and psychological (psychosocial and return to work issues) component, delivered by multidisciplinary team.
    - Compared to a waiting list control (Smeets 2008), no clinical difference in **pain** (VAS 0-10; low quality; n=106) and in **psychological distress** (BDI 0-63; very low quality; n=106) was shown, only a short-term clinical benefit was found in **function** (RMDQ 0-24; moderate quality; n=106). No long term data were reported in this study.
    - The study of Gatchel 2003 on the comparison to usual care ('non-intervention group') reported only results on the number of patients who **returned to work** and a clinical benefit was shown in the MBR group (Risk Ratio; very low quality; n=70).
    - Not reported outcomes: QoL, responder criteria, adverse events, healthcare utilisation
  - **2-element MBR (physical + psychological) versus single interventions**
    - Three studies (4 comparisons) were found with different single interventions
      - Khan 2014: 2-element MBR (physical (aerobic and biomechanical exercises) + psychological (cognitive-behavioural therapy/problem solving training), delivered by a unidisciplinary team) versus mixed exercises (biomechanical + aerobic, 12 weeks)
      - Smeets 2008/2009: 2-element MBR (physical (active physical training with graded activity) + psychological (problem solving training), delivered by a multidisciplinary team) versus mixed exercises (biomechanical + aerobic, 10 weeks)
      - Smeets 2008: 2-element MBR (physical (active physical training with graded activity) + psychological (problem solving training), delivered by a multidisciplinary team) versus psychological therapy (cognitive behavioural approach-CBA)
      - Jousset 2004: 2-element MBR (physical (stretching, strength, aerobic exercises, balneotherapy) + (psychological (individual cognitive therapy), delivered by a multidisciplinary team) versus individual biomechanical exercises (core stability)
    - In all comparisons, only a clinical benefit was found in short term **pain** relief (VAS 0-10; 1 RCT; low quality; n= 54) and **function** (RMDQ 0-24; 1 RCT; low quality; n=54) in favour of the 2-element MBR programme compared to a mixed modality exercise intervention (Khan 2014). No long term data were reported in this study. The other studies found no differences for pain, function, **psychological distress, return to work and healthcare utilisation** at short and long term.
    - Not reported outcomes: QoL, adverse events, responder criteria
  - **2-element MBR (physical + psychological) versus combined interventions**
    - Three studies were found with different combined interventions
      - Monticone 2013: 2-element MBR (physical (biomechanical exercises, postural control, mobilisation) + psychological (cognitive-behavioural approach), delivered by a multidisciplinary team) versus combined intervention of (biomechanical) exercises + manual therapy (mobilisation)
      - Vibe 2013: 2-element MBR (physical (specific movement exercises and physical activity programme tailored to movement classification) + psychological (behavioural management approach), delivered by a unidisciplinary team) versus combined intervention of (biomechanical) exercises + manual therapy (mobilisation + manipulation)
      - Monticone 2014: 2-element MBR (physical (motor training, stability) + psychological (cognitive-behavioural approach delivered by a multidisciplinary team) versus combined intervention of (biomechanical) exercises + manual therapy (mobilisation) + postural therapy (postural control)

- Compared to a combined intervention of biomechanical exercise + manual therapy (Monticone 2013), a clinical benefit favouring MBR programme was found in **QoL** (SF-36 0-100; moderate-low quality; n=90), **pain** (NRS 0-10; moderate quality; n=90) and **function** (RMDQ 0-24; moderate quality; n=90) for both time points.
- The combined intervention with the postural therapy added (Monticone 2014), showed a short term clinical benefit in **QoL** (SF-36 0-100; low-very low quality; n=20) and **pain** (NRS 0-10; very low quality; n=20) in favour of the MBR programme but no difference in **function** (ODI 0-100; low quality; n=20) and **healthcare utilisation** (medication use; very low quality; n=20). No long term data were reported in this study.
- The study of Vibe 2013 in which 2-element MBR programme was compared to a combined intervention of biomechanical exercises and mobilisations, showed at both time points a clinical benefit in **pain** (NRS 0-10; moderate-low quality; n=94) and in **healthcare utilisation** (care-seeking after intervention; low quality; n=94) in favour of the MBR programme but no difference was found in **function** (ODI 0-100; moderate-low quality; n=94).
- Not reported outcomes: psychological distress, return to work, adverse events, responder criteria

o **No studies were found for following comparisons:**
- 2-element MBR (physical + psychological) versus placebo/sham
- 2-element MBR (physical + psychological) versus 2-element MBR (physical + education)

Table 35 – Clinical effectiveness of 2-element MBR (physical + psychological) in mixed population (low back pain with or without sciatica)

2-element MBR (physical + psychological)			
Outcomes	**2-element MBR versus usual care/waiting list control**	**2-element MBR versus single interventions**	**2-element MBR versus combined interventions**
QoL			At short term: • **SF-36 0-100 (Monticone 2013): CIB favouring MBR** (1 RCT; moderate-low; n=90) • **SF-36 0-100 (Monticone 2014): CIB favouring MBR** (1 RCT; low-very low; n=20) At long term: • **SF-36 0-100 (Monticone 2013): CIB favouring MBR** (1 RCT; moderate-low; n=90)
Pain	At short term: • **VAS 0-10: No diff** (1 RCT; low; n=106)	At short term: • **VAS 0-10 (Khan 2014): CIB favouring MBR** (1 RCT; low; n=54) • **VAS 0-10 (Smeets 2008): no diff** (1 RCT; low; n=107) • **VAS 0-10 (Smeets 2008-CBA): no diff** (1 RCT; low; n=110)	At short term: • **NRS 0-10 (Monticone 2013): CIB favouring MBR** (1 RCT; moderate; n=90) • **NRS 0-10 (Vibe 2013): CIB favouring MBR** (1 RCT; moderate; n=94)

	At long term: Not reported	At long term: • **VAS 0-10 (Jousset 2004): no diff** (1 RCT; very low; n=112) • **VAS 0-10 (Smeets 2008): no diff** (1 RCT; low; n=104) • **VAS 0-10 (Smeets 2008-CBA): no diff** (1 RCT; low; n=105)	• **NRS 0-10 (Monticone 2014): CIB favouring MBR** (1 RCT; very low; n=20) At long term: • **NRS 0-10 (Monticone 2013): CIB favouring MBR** (1 RCT; moderate; n=90) • **NRS 0-10 (Vibe 2013): CIB favouring MBR** (1 RCT; low; n=94)
Function	At short term: • **RMDQ 0-24: CIB favouring MBR** (1 RCT; moderate; n=106) At long term: Not reported	At short term: • **RMDQ 0-24 (Khan 2014): CIB favouring MBR** (1 RCT; low; n=54) • **RMDQ 0-24 (Smeets 2008): no diff** (1 RCT; moderate; n=107) • **RMDQ 0-24 (Smeets 2008 CBA): no diff** (1 RCT; low; n=110) At long term: • **RMDQ 0-24 (Smeets 2008): no diff** (2 RCTs; low; n=212) • **RMDQ 0-24 (Smeets 2008 CBA): no diff** (2 RCTs; low; n=213)	At short term: • **RMDQ 0-24 (Monticone 2013): CIB favouring MBR** (1 RCT; moderate; n=90) • **ODI 0-100 (Vibe 2013): no diff** (1 RCT; moderate; n=94) • **ODI 0-100 (Monticone 2014): no diff** (1 RCT; low; n=20) At long term: • **RMDQ 0-24 (Monticone 2013): CIB favouring MBR** (1 RCT; moderate; n=90) • **ODI 0-100 (Vibe 2013): no diff** (1 RCT; low; n=94)
Psychological distress	At short term: • **BDI 0-63: no diff** (1 RCT; very low; n=106) At long term: Not reported	At short term: • **BDI 0-68 (Smeets 2008): no diff** (1 RCT; low; n=105) • **BDI 0-68 (Smeets 2008 CBA): no diff** (1 RCT; low; n=110) At long term: • **BDI 0-68 (Smeets 2008): no diff** (1 RCT; low; n=104)	

		• **BDI 0-68 (Smeets 2008 CBA): no diff** (1 RCT; moderate; n=105) • **HADS 0-21 (Jousset 2004): no diff** (1 RCT; very low; n=83)	
Return to work	<u>At short term:</u> Not reported <u>At long term:</u> • **Risk ratio (Gatchel 2003): CIB favouring MBR** (1 RCT; very low; n=70)	<u>At short term:</u> • **Risk ratio (Jousset 2004): no diff** (1 RCT; very low; n=75) <u>At long term:</u> • **Risk ratio (Jousset 2004): no diff** (1 RCT; very low; n=112)	
Healthcare utilisation		<u>At short term:</u> Not reported <u>At long term:</u> • **Number of GP visits (Smeets 2008): no diff** (1 RCT; low; n=108) • **Number of GP visits (Smeets 2008 CBA): no diff** (1 RCT; low; n=108) • **Number of medical specialist visits (Smeets 2008): no diff** (1 RCT; moderate; n=108) • **Number of medical specialist visits (Smeets 2008 CBA): no diff** (1 RCT; low; n=108) • **Number of radiology visits (Smeets 2008): no diff** (1 RCT; low; n=108) • **Number of radiology visits (Smeets 2008 CBA): no diff** (1 RCT; moderate; n=108)	<u>At short term:</u> • **Medication use (Monticone 2014): no diff** (1 RCT; very low; n=20) <u>At long term:</u> • **Care-seeking after intervention (Vibe 2013): CIB favouring MBR** (1 RCT; low; n=94)

		• **Number of occupational physician visits (Smeets 2008): no diff** (1 RCT; moderate; n=108) • **Number of occupational physician visits (Smeets 2008 CBA): no diff** (1 RCT; low; n=108) • **Number of psychologist visits (Smeets 2008): no diff** (1 RCT; moderate; n=108) • **Number of psychologist visits (Smeets 2008 CBA): no diff** (1 RCT; moderate; n=108) • **Number of therapist sessions (Smeets 2008): CIB favouring single intervention** (1 RCT; low; n=108) • **Number of therapist sessions (Smeets 2008 CBA): no diff** (1 RCT; moderate; n=108) • **Number of alternative therapist visits (Smeets 2008): no diff** (1 RCT; low; n=108) • **Number of alternative therapist visits (Smeets 2008 CBA): no diff** (1 RCT; low; n=108)	

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

MBR programme 2 elements: physical + education

- **Low back population without sciatica**
  - No studies were found for the following comparisons:
    - 2-element MBR (physical + education) versus sham/placebo
    - 2-element MBR (physical + education) versus usual care/waiting list control
    - 2-element MBR (physical + education) versus single interventions
    - 2-element MBR (physical + education) versus combined interventions
- **Low back pain population with sciatica**
  - No evidence was available
- **Mixed population (low back pain with or without sciatica) (see Table 36)**

- **2-element MBR (physical + education) versus single interventions**
  - **Three studies were found with different single interventions**
    - **Dufour 2010:** 2-element MBR (physical (aerobic, strength exercise, ball games, training in hot water, fitness centre) + education (postural techniques and pain management) (delivered by a multidisciplinary team) versus exercise (biomechanical-core stability)
    - **Preyde 2000a:** 2-element MBR (physical (stretching, strength, mobility exercise) + education (posture and body mechanics), delivered by a unidisciplinary team) versus manual therapy (manipulation)
    - **Preyde 2000b:** 2-element MBR (physical (stretching, strength, mobility exercise + soft-tissue manipulation) + education (posture and body mechanics), delivered by a unidisciplinary team) versus manual therapy (soft-tissue manipulation)
  - Compared to exercise alone (Dufour 2010), conflicting results were found for **QoL** (SF-36 0-100; low-very low quality; n=272), no clinical difference in **pain** (at both time points; VAS 0-10; very low quality; n=272) and short term **function** (RMDQ 0-24; very low quality; n=272), whereas only at long term a clinical benefit in **function** was found (RMDQ 0-24; very low quality; n=272).
  - In the studies of Preyde 2000 the physical component of the 2-element MBR programme comprised exercise and manipulation (Preyde 2000b) or exercise alone (Preyde 2000a). The addition of manipulation (Preyde 2000b) revealed conflicting results for **pain** (McGill Present Pain score 0-5 and McGill Pain Rating Index 0-79; very low quality; n=46) but no clinical difference for **function** (RMDQ 0-24; very low quality; n=46) and **psychological distress** (STAI 20-80; very low quality; n=46). The MBR programme with only exercise (Preyde 2000a) in the physical component showed only a clinical benefit in **function** in favour of the single intervention (manipulation) (RMDQ 0-24; very low quality; n=43). No long term data were reported in the studies of Preyde 2000.
  - Not reported outcomes: healthcare utilisation, return to work, adverse events, responder criteria
- **No studies were found for following comparisons:**
  - 2-element MBR versus placebo/sham
  - 2-element MBR versus usual care/waiting list control
  - 2-element MBR versus combined interventions

Table 36 – Clinical effectiveness of 2-element MBR (physical + education) in mixed population (low back pain with or without sciatica)

Outcomes	2-element MBR versus single interventions
QoL	<u>At short term:</u> • **SF-36 0-100 (Dufour 2010): CIB favouring MBR in 4 subdomains** (1 RCT; low-very low; n=272) • **SF-36 0-100 composite mental score (Dufour 2010): no diff** (1 RCT; low; n=272) • **SF-36 0-100 composite physical score (Dufour 2010): CIB favouring MBR** (1 RCT; low; n=272) <u>At long term:</u> • **SF-36 0-100 (Dufour 2010): CIB favouring MBR in 6 subdomains** (1 RCT; low; n=272) • **SF-36 0-100 composite mental score (Dufour 2010): no diff** (1 RCT; low; n=272)

	• **SF-36 0-100 composite physical score (Dufour 2010): CIB favouring MBR** (1 RCT; low; n=272)
Pain	<u>At short term:</u> • **VAS 0-10 (Dufour 2010): No diff** (1 RCT; very low; n=272) • **McGill Present Pain score 0-5 (Preyde 2000b): CIB favouring MBR programme** (1 RCT; very low; n=46) • **McGill Pain Rating Index 0-79 (Preyde 2000b): no diff** (1 RCT; very low; n=46) • **McGill Present Pain score 0-5 (Preyde 2000a): no diff** (1 RCT; very low; n=43) • **McGill Pain Rating Index 0-79 (Preyde 2000a): no diff** (1 RCT; very low; n=43) <u>At long term:</u> • **VAS 0-10 (Dufour 2010): No diff** (1 RCT; very low; n=272)
Function	<u>At short term:</u> • **RMDQ 0-24 (Dufour 2010): no diff** (1 RCT; very low; n=272) • **RMDQ 0-24 (Preyde 2000b): no diff** (1 RCT; very low; n=46) • **RMDQ 0-24 (Preyde 2000a): CIB favouring single intervention (manipulation)** (1 RCT; very low; n=43) <u>At long term:</u> • **RMDQ 0-24 (Dufour 2010): CIB favouring single intervention (exercise)** (1 RCT; very low; n=272)
Psychological distress	<u>At short term:</u> • **STAI 20-80 (Preyde 2000b): no diff** (1 RCT; very low; n=46) • **STAI 20-80 (Preyde 2000a): no diff** (1 RCT; very low; n=43)

	At long term: Not reported

CIB: clinically important benefit; short term <4mo and/or long term 4mo-1y

Economic evidence

- **Two economic evaluations were found:**
  - One cost-utility analysis found that a 3-element MBR (physical, psychological, education) programme was dominant (less costly and more effective) compared to biomechanical exercises and a combination of mixed manual therapy + self-management for treating low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations.
  - One cost-utility analysis found that a 2-element MBR (physical, psychological) programme was dominated (more costly and less effective) compared to cognitive behavioural approaches and mixed manual therapy plus self-management for treating low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations.

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:**
  - Most critical outcome was health-related QoL with pain severity, function and psychological distress as individually critical outcomes.
  - Responder criteria (>30% for pain and function), adverse events, healthcare utilisation and return to work were considered important for decision-making
- **Trade-off between clinical benefits and harms**
  - The GDG noted that there was very little evidence for usual care comparisons and no studies were identified that could be classified as a placebo/sham comparison.
  - **3-element MBR programme (physical, psychological and educational element):** Compared to waiting list control in people with or without sciatica, there was evidence of long-term clinical benefit for pain and function (> 4 months), but this was not confirmed in people without sciatica. The GDG considered these improvements in the critical outcomes (for the waiting list control comparison) to be of some value, but noted that the evidence was low and very low quality and from a small single study (n=65). The GDG also noted that a **waiting list control comparison would be likely to overestimate the benefit of the MBR programmes** because of the negative effect on people randomised to wait. There was no evidence of benefit when 3-element MBR was compared to single intervention (biomechanical exercise). When compared to combined intervention, two studies showed mixed results. There was some evidence of clinical benefit of 3-element MBR for pain outcomes in the short and long term, and function outcomes in the long term. The GDG observed that 3-element MBR was clinically beneficial in terms of quality of life in the short and long term, compared to combined intervention (manual therapy in combination with exercise, postural therapy and self-management) (n=150), but no effect was seen in another study that compared 3-element MBR to a combined intervention without postural advice (n=101).
  - **2-element MBR programme (physical and psychological elements):** The GDG noted that mixed evidence for 2 element programmes (physical and psychological) was from a single study compared to waiting list control. Another study comparing 2-element MBR (physical and psychological) versus usual care showed a clinical benefit for functional outcome and return to work in the longer term (> 4 months) (n=106), but not for pain outcomes. **Mixed evidence** was also available for pain and function outcomes when the 2-element MBR was compared to single intervention (psychological; exercise). There was evidence of both clinical harm and clinical benefit for the healthcare utilisation (number of therapist sessions) outcome when MBR was compared to exercise and psychological intervention, respectively. When compared to combinations of interventions (biomechanical exercise and manual therapy; biomechanical exercise with manual therapy and postural therapy), there was clinical benefit in favour of MBR in terms of most of the outcomes (pain, function, quality of life, and healthcare utilisation) reported in both the short-term and longer term follow-up. Pain levels were noted to be higher at 12 months than at 3 months, but the GDG discussed that this

may reflect that the intervention time for one of the studies was shorter (12 weeks) than the final follow-up period (12 months) and could be related to a failure to build on the initial improvements because of the difficulties in generalisation outside an intensive treatment setting. Data came from 3 studies of very different treatment intensity. All studies were of people with chronic low back pain (>3 months duration), however one consisted of a 12 week intervention, with weekly sessions for the first 2-3 weeks then 1 session every 2-3 weeks; another featured 6-8 weeks intervention followed by 3 months follow up, whereas the third one was in a specialised rehabilitation centre with 1 individual cognitive behavioural approaches session per week for 5 weeks followed by once a month for 11 months, accompanied by 10 exercise sessions over 5 weeks and encouragement to continue for the rest of the year by telephone. All studies demonstrated improvements in outcomes in favour of MBR programmes. For the more intensive programme results have been reported at 1 year in this review, and the study reported that benefits remained at 3 years. The GDG noted that one of the shorter studies created subgroups within the participants and tailored both the exercise and cognitive-behavioural components to movements that were painful. It was consequently not possible to determine exactly **which element in this study was responsible for the effects**, however, it was considered that that tailoring the approach would be reflective of how the treatment would be delivered in clinical practice. The GDG discussed that the **year-long programme would not be feasible to implement in a UK NHS setting**, but the shorter programmes, which also demonstrated benefits, would be feasible in an NHS setting. **The GDG considered that the benefits seen in multiple outcome measures when using a 2-element MBR programme, involving physical and psychological elements (compared to usual care and to combinations of interventions), outweighed the small harms seen in healthcare use when compared to a single intervention.**

  - **2-elements MBR programme (physical and education elements):** The GDG noted that there was no evidence for 2 element (physical and education) MBR programmes with a usual care or waiting list control comparison. All evidence came from a single large study and only looked at single intervention comparisons (biomechanical exercise). The evidence was mixed, showing some benefit of this type of MBR programme for several outcomes (most of the SF-36 domains). However there was evidence of clinical harm of MBR for function and one quality of life domain at >4 months. The GDG noted the **mixed evidence in terms of benefits, harms or lack of effect for each of the outcome measures**, and were therefore unable to recommend that an educational component should be part of an MBR programme.
  - **3-elements MBR programmes versus 2-elements MBR programme (physical and education**): When the 3 element MBR programme (using a cognitive approach) was compared to the 2 element MBR programmes (physical and education), the evidence showed no clinical benefit for any of the outcomes reported. Another study with a 3 element MBR programme (using a behavioural approach) was compared to a 2 element MBR programme (physical and education). However, the evidence for these comparisons was very low quality and from single small studies so the GDG were **unable to draw any conclusions from this.**
  - **In summary,** the GDG found the evidence for MBR programmes to be **mixed** with clinical benefits seen for some comparisons, but also many instances where no benefit was observed and a few where the comparator was favoured over MBR. In addition interpretation was complicated by the **variety of comparators** used in the studies. However, the quantity, quality and applicability of the evidence where a benefit for MBR was observed, was considered higher by the GDG. This was mostly from three studies consisting of 3-element MBR containing physical, psychological and educational elements, 2-element MBR with physical and psychological elements and 2-element MBR with physical and psychological elements. The GDG considered this evidence alongside the evidence from the individual non-invasive intervention reviews discussed earlier in this guideline involving cognitive behavioural approaches, and agreed that **MBR programmes should be recommended**. It was not clear from the evidence reviewed if 3-element MBR offered benefits over the 2-element MBR. However the GDG noted that the **consistent components of the programmes with benefit were physical and psychological components**. The recommendation was therefore made for MBR with a physical and psychological element. The majority of the evidence for the psychological element in this review and in the combination and single reviews was for a cognitive behavioural approach and so the GDG felt the **psychological element of a combined programme should incorporate a cognitive behavioural approach.** The GDG noted that evidence was mixed for the 2 element programmes which included education, but also noted that the 3 element programme compared to a 2 element programme which included education showed no difference. The GDG were **unable to determine which aspect of the educational intervention was important and chose not to make a recommendation in this regard**.

- **Trade-off between net clinical effects and costs**
  - The single cost-utility analysis of **a 3-element MBR** (physical, psychological, education) programme compared to a combination of mixed manual therapy and self-management, and biomechanical exercise, demonstrated the **lowest costs and highest QALYs in the MBR programme**. The GDG noted that this evidence related to one course of treatment and it was unknown if treatment effectiveness and thus cost effectiveness would be the same if repeated. In addition, the MBR was cost effective only in 67% if the simulations, which shows a high uncertainty.

- The second economic analysis compared a **2-element MBR** (physical + psychological), mixed modality exercises and cognitive behavioural approaches. In contrast to the first analysis MBR was **not the most cost effective option** (cognitive behavioural approaches had the lowest costs and highest QALYs).
- Taking into account the overall body of clinical effectiveness evidence for 2-element MBR (physical and psychological) the GDG concluded that the evidence for a clinical benefit (which largely came from 2 RCTS) was more compelling than the evidence of no benefit from other studies which included the RCT used to inform the economic analysis in this review. It was noted that while the **cost of GP support and cost of supervising physician** were not incorporated into the cost estimate, due to insufficient information, this is unlikely to form part of clinical practice if implemented and this would probably not apply to the UK setting where physiotherapists operate with more autonomy. In addition the GDG noted that for both interventions there may also be additional costs in practice such as **patient transport and specialist training** for staff delivering the interventions.
- It was noted that the intervention costs above do not take account of the possibility that MBR might be offered as an alternative to another active treatment option – if this were the case then the incremental cost would be the difference between MBR and the cost of the other active treatment, which would be less than the cost of MBR.
- Taking into account the overall body of clinical effectiveness evidence for MBR programmes the GDG concluded there was **mixed evidence of its effectiveness and cost-effectiveness**. However, based on the considerations already discussed in the 'Trade-off between clinical benefits and harms' section, the GDG considered MBR to be likely to be cost effective. If MBR is effective, upfront intervention costs may be offset by downstream cost savings due to reduced healthcare utilisation or may be justified due to the benefits to the patient.

- **Quality of evidence**
  - Ranged from very low to moderate, mainly downgraded for high risk of bias due to inadequate blinding and high drop-out rates.
  - The GDG noted that one of the studies informing the recommendation reported a high drop-out rate and used per protocol analysis. It is therefore possible that these factors might have **underestimated the effect of the MBR programme** and had more people continued in the trial, or an intention to treat analysis been used, that the results may have differed. The **population recruited was also very specific** (non-specific low back pain where the pain could be provoked and relieved with specific postures, movements or activities, and where the movement behaviours had a clear association with their pain disorder), for which the classification based-cognitive functional therapy intervention was designed. The GDG therefore considered this narrow population **might limit the applicability of this evidence to clinical practice**. However as benefits were observed in trials that included less specific populations, it was considered that the benefit of this type of MBR programme could be transferable.
  - One of the other key studies informing the recommendation was a 3-year long study with a 1 year treatment period. It was noted that there were no reported drop-outs from this study. The population recruited in the study was considered by the GDG to be applicable to clinical practice as patients were low back pain lasting >3 months, and all causes of specific low back pain were excluded. However, this potential bias was accounted for in the quality rating of the in the outcomes reported and the evidence remained as moderate quality.
- **Other considerations**
  - The GDG noted that interpreting the evidence in terms of **when and which people should be offered MBR was complicated**. The group discussed tailoring treatments for individual patients or selecting populations of patients to receive specific treatments, including a psychosocial approach. The GDG noted that the papers included in this review did not stratify people on the basis of severity but noted that evidence from the risk stratification review (see chapter 6) informed recommendations for identifying people who might benefit from a combined physical and psychological approach. However, the GDG acknowledged that an MBR programme is usually undertaken by people with chronic low back pain. Furthermore, the GDG debated whether people who had undertaken a course of MBR should have repeated treatment if their back pain didn't resolve or recurred. They highlighted that trials often excluded people who had the intervention before and so did not address this key clinical issue.
  - For all interventions it was agreed important to note that the **person delivering the therapy would have a large effect on the outcome of treatment**. The GDG discussed that in practice the psychological element of this type of intervention may be delivered by a psychologist or by another healthcare professional trained in these techniques. It was considered important that the individual was appropriately trained with the competency to deliver the intervention. It was considered that this may have been a factor in the studies included in the review. The GDG felt strongly that where a psychologist was not delivering the intervention directly, services should to set up such that the team included a psychologist to train and support those delivering the intervention, as was generally the case in the trials

where this occurred. The GDG commented that the delivery of the cognitive behavioural approaches programmes reviewed required clinical expertise in health-related psychology rather than in treating psycho-pathology.

- The GDG debated whether a psychological intervention in the context of an MBR programme would have an impact on people who do not show fear-avoidance behaviours or psychosocial distress. It was noted that the studies included in the review did not consider **stratification of participants on a psychological basis**. The GDG also pointed out the low scores on the Tampa scale for Kinesiophobia reported in by the relevant study. The GDG noted that the psychological aspects of low back pain should be considered and a **group psychological intervention should be favoured where possible**. Furthermore, the GDG felt that a psychologically informed physiotherapy or rehabilitation programme would be particularly useful for people with chronic pain and psychosocial distress. However, the GDG advised that main focus for their recommendation for combined physical and psychological treatments was for people with psychosocial distress resulting from chronic low back pain and sciatica, rather than people presenting with pain and additional psychological problems. The GDG therefore felt that people who have not responded to previous treatments would also benefit from a psychologically informed rehabilitation programme, as part of a risk assessment-based, stepped care approach.
- The GDG noted that the Cochrane review reached similar conclusions that patients with chronic low back pain receiving MBR will experience less pain related disability than those receiving usual care or exercise treatment.
- The GDG noted that the intensity of the interventions where clinical benefits were seen varied and it was not clear whether the more intensive interventions produced better results – although this was not studied directly.

- **Research recommendation:**
  - Chronic non-specific low back pain is a very common, potentially disabling, long-term health condition and by definition not amenable to curative medical treatment. In the absence of effective self-management strategies people with long-term conditions are likely to disengage from their normal roles, becoming increasingly disabled and dependent on health and social care. The Kings Fund 2013 long term conditions report cites evidence that multidisciplinary rehabilitation programmes (MBR), in the form of self-management support, have been shown to reduce unplanned hospital admissions for other long term conditions such as chronic obstructive pulmonary disease and asthma and to improve adherence to treatment and medication, but evidence that this translates into cost savings, particularly in reduced healthcare utilization is unclear. Further the cost effectiveness of providing long term support beyond MBR programmes for people with non-specific low back pain is unknown.

NICE draft recommendations MBR (March 2016): One clinical recommendation and one research recommendation is proposed

28. Consider a combined physical and psychological programme (preferably in a group context, that takes into account a person's specific needs and capabilities) for people with persistent non-specific low back pain or sciatica:

- When they have significant psychological obstacles to recovery,
  Or
- When previous treatments have not been effective.

Research recommendation

R4. What is the cost-effectiveness of providing long term support (>12 months) for people with chronic, non-specific low back pain (NSLBP) with or without sciatica, in reducing health care utilization?

Belgian GDG considerations mentioned in the Lime survey at the beginning of September 2016

Agreement with the content of the NICE recommendation 28 on MBR: 10 Yes, 2 No, 1 no opinion, 2 out of competence, 0 no answer, 2 not completed

- **Comments from those who do not agree:**
  - "...ou d'une sciatique" persistante également je suppose?/ "faisant obstacle": je dirais plutôt "susceptible de faire obstacle"/"...traitements antérieurs n'ont pas été efficaces": faut-il préciser "bien conduit": car si traitement antérieur = massage et électro, je ne pense pas que cela justifie ce type de prise en charge

- persisterende sciatica hoort hier niet thuis; Franse vertaling (antérieurs als vertaling voor vroegere) is niet correct.

- **Other comments:**
  - Given the mixed results concerning the effects of MBR, we advise further research into tailoring multidisciplinary programs to specific patient subgroups/profiles. Individual programs are probably more suited for some patient profiles
  - The concept of 'tailored approach' (e.g. based on the STarT Back questionnaire) would merit to be more considered, as subgroups will probably benefit more than others.
  - I feel doubtful with 'preferably in a group context'.
    - Why?
    - Is this possible within the M nomenclature? (physiotherapists?)
    - It seems a bit contradictory to me that a combined program is advised - preferably in a group (!) session - for those patients with persistent pain/most pronounced individual needs
    - With respect to the Dutch translation of 'persistent': gevoelsmatig zou ik eerder 'aanhoudend' of 'blijvend' gebruiken (nadruk eerder op tijdspaspect) dan wel 'hardnekkig'.

    Anderzijds ligt de kunst (en de moeilijkheid er uiteraard in significante psychosociale belemmeringen voor herstel net vroegtijdig te identificeren (en er desgevallend op in te spelen middels educatie/psychologisch programma), net om trachten te vermijden dat iemand in een 'persistent' condition terecht komt.
  - The "significant psychological obstacles to recovery" need to be specified and operationalized, preferably with reference to Yellow flags (in analogy with Red flags).
  - Did we agree to use the term aspecific LBP? Rather LBP.

Strength of the recommendation 28 on MBR programme: According to NICE formulation, it is a weak recommendation

GRADE Factors	
Balance between desirable and undesirable effects	Mixed evidence with no clear benefits of MBR programme compared to usual care of other interventions No potential harms identified The GDG considered this evidence alongside the evidence from the individual non-invasive intervention reviews discussed earlier in this guideline involving cognitive behavioural approaches, and agreed that MBR programmes should be recommended.
Quality of evidence	Very low to moderate
Values and preferences	Psychologist part of multidisciplinary rehabilitation teams? Involvement of primary care? Back schools?
Costs (resource allocation)	NIHDI nomenclature specific for intensive rehabilitation but restricted access and conditions

Agreement with the strength of the NICE recommendation 28 on MBR: 2 strong, 6 weak, 1 no opinion, 1 no answer, 7 not completed

- **Comments for a weak recommendation**
  - The concept of 'tailored approach' (e.g. based on the STarT Back questionnaire) would merit to be more considered, as subgroups will probably benefit more than others.
  - As a result of the mixed evidence, the rather low quality of evidence and the questionable cost/effectiveness I would rather make it a weak recommendation.
  - Individual variation in attitude and intelligence of patients; Psychological treatment only in case of yellow flags? Screening tool.

- **Comments for a strong recommendation**
  - This is probably the best of care we can offer, although improvements are possible and need to be further developed
- **Other comments**
  - It's difficult to answer because balance benefits and harms is good but cost effectiveness is unclear - neccesity to definite a groud in the low back chronic pain population?

Agreement with the content of the NICE research recommendation 4 on MBR: 8 Yes, 3 No, 2 no opinion, 2 out of competence, 0 no answer, 2 not completed

- **Comments from those who do not agree:**
  - Following comments:
    - 'by definition not amenable to curative medical treatment': does this mean that every single patient stays in a chronic pain state, till death? And this message should be given to the patients (e.g., in the education part?). I do not agree with that statement. Having a flare up may not be that unusual (the 'normal' population (i.e., without chronic LBP in history) may also experience episodes of LBP. If this happens in a patient with a history of chronic LBP, it does not mean that treatment has failed.
    - A long-term support (> 12 months) may feed helplessness in patients / confirm that there is a serious medical problem that requires medical follow-up for a long time when the correct information (education) is not given in an early phase.
    - How should a long-term support be seen in a clinical context, in the Belgian setting?
    - Long-term follow-up research is relatively scarce, and long-term follow-up of long-term support will be even more challenging.
    - personally, I do not think that providing long term support (> 12 months) will be the key to success. On the other hand, I do believe in the importance of (1) the content of the education that is given to the patients, and (2) taking advantage of psychosocial factors that play, on an individual basis (e.g. fear of doing specific activities) in an early phase.
  - this is not a recommendation but a question !
  - Dit is een vraag en geen aanbeveling.
- **Other comments:**
  - This seems to be rather a critical question than a recommendation
  - This is a question, not a recommendation !?
  - Answer will be: It depends of the patients. But overall, long term support should be proposed only to a minority of the patients.
  - see above
  - see previous comment
  - It is unclear what you actually mean here....
  - Term NSLBP?

Belgian GDG comments during the GDG meeting on the 15th September 2016

- **No comment**
- **Conclusion: recommendation NICE 2016 unchanged**

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30th November 2016)

- British Acupuncture Council: Even in combination the evidence is not encouraging: a two-element MBR programme (physical and psychological) did not differ from waiting list for pain or psychological distress. **NICE reply**: Regarding MBR, CPP programmes showed some benefit over usual care/waiting list comparator. Although there was no clinical difference between groups for pain and psychological distress outcomes, there was evidence of benefit of a 2-element MBR programme for the function and return to work outcomes compared to usual care/waiting list in people with or without sciatica. There was also clinical benefit there of a 2-element MBR for pain and function in people with low back pain without sciatica. The GDG acknowledged that the evidence for 3-element MBR versus usual care/waiting list was mixed. Overall the

GDG felt that CPP should nonetheless be recommended on the basis of the evidence showing benefit over waiting list, single and combined interventions, alongside evidence from single intervention chapters. This is detailed in section 17.6 (Recommendations and link to evidence). (p24/111)

- Acupuncture Now Foundation: The GDG wrote that the primary aim of a cognitive behavioural approach is not to directly improve pain and function, but reduce the fear of pain, thus increasing people's confidence in undertaking physical rehabilitation. However it is unclear whether the GDG found any specific evidence that cognitive behavioural approaches actually do reduce fear of pain or increase confidence in physical rehabilitation, or any evidence of a specific effect for cognitive approaches in the MBR literature that was clearly separate from non-specific effects. **NICE answered** that when setting the protocols the GDG agreed that the outcomes to be considered should be the same across reviews for consistency of decision making. Although fear of pain was not considered as a separate outcome, psychological distress was an outcome for all reviews, which a priori, the GDG believed would cover the important outcomes for decision making. Regarding the evaluation of non-specific effects in the MBR review, it was not possible to determine how much of the effect of the treatment was specific. Where possible, it was taken into account. (p11/111)
- University Hospitals Birmingham NHS Foundation Trust: This guideline will be challenging to implement where the terminology differs to that used in the NHSE spinal Pathfinder document. This is because our local CCGs are commissioning services specified in Pathfinder and our Trust requires us to strictly implement NICE guidelines. It is recognised that the GDG used the term "Multidisciplinary Biopsychosocial Rehabilitation (MBR) programmes" which has also been used by the Cochrane Collaboration. However, the NHSE Pathfinder document recommends inclusion of low intensity combined psychological and physical programmes (CPPP), high intensity combined psychological and physical treatment programmes (CPPTP) and pain management programmes (PMP). Is the GDG able to describe how "psychological therapies" and "MBR" recommendations equate to Pathfinder terminology? **NICE reply**: The concept of MBR was used as a basis to review the evidence, consistent with the Cochrane review. However, the recommendation that results from that review is for combined physical and psychological programmes (CPP) as this is where there was most evidence of benefit, therefore the term CPP is used in the recommendation.(p83/111)
- University of York: The GDG has noted, "that there was very little evidence for usual care comparisons (with combined physical and psychological programmes) and no studies were identified that could be classified as a placebo/sham comparison."(Full version – Part 1, Page 736, Line 1) Furthermore, "no clinical benefit was observed for people with low back pain with / without sciatica when cognitive behavioural approaches was compared to sham or usual care or waiting list controls for the majority of reported outcomes"(Page 601, Lines20-22) This recommendation is therefore in marked contrast to the expectation of the GDG that an intervention should demonstrate evidence beyond context effects, as stated, "The GDG first discussed the necessity of a body of evidence to show specific intervention effects, that is, over and above any contextual or placebo effects."(Page 493, Line 7) Therefore for consistency when interpreting the evidence, if the recommendation of combined physical and psychological programmes is sustained, then acupuncture should also be considered as a recommendation, as there is clear proof of principle, as documented elsewhere, that acupuncture outperforms sham/placebo, as well as delivering a minimum clinical difference that is cost-effective when compared to usual care. **NICE reply**: The GDG placed more weight on the comparison between an intervention and placebo/sham whenever a placebo/sham was available and it was feasible to do so. In the case of MBR the GDG agreed a sham was not feasible. The GDG had therefore to base the recommendation on the best evidence available. Although the GDG acknowledged that the evidence was mixed, the GDG felt that MBR; specifically CPP programmes should be recommended on the basis of MBR showing benefit over waiting list, single and combined interventions, alongside evidence from single intervention chapters.(p90/111)
- University of York: The GDG states that, "no clinical benefit was observed for people with low back pain with / without sciatica when cognitive behavioural approaches was compared to sham or usual care or waiting list controls for the majority of reported outcomes" The recommendation of combined physical and psychological programmes is therefore in marked contrast to the expectation of the GDG that an intervention should demonstrate evidence beyond context effects, given the GDG's point regarding "the necessity of a body of evidence to show specific intervention effects, that is, over and above any contextual or placebo effects."(Page 493, Line 7). **NICE reply:** The review of multidisciplinary biopsychosocial rehabilitation programmes informed the recommendation for combined physical and psychological programmes (CPP). The GDG agreed a sham was not feasible for such a complex intervention. The GDG had therefore to base the recommendation on the best evidence available. Although the GDG acknowledged that the evidence was mixed, the GDG felt that CPP should be recommended on the basis of CPP showing benefit over waiting list, single and combined interventions, alongside evidence from single intervention chapters.(p52/222)
- Arthritis Research UK: The GDG state that the MBR approach combines education and physiotherapy, with different forms of cognitive-behavioural psychology to address participants' unhelpful beliefs about their pain, reduce 'fear-avoidance' behaviours and catastrophic thinking, and improve mood, thus decreasing disability and improving function. Many however would argue that the primary aim of a MBR approach for people with chronic pain is to increase quality of life with pain, we therefore suggest the

GDG reword this statement to reflect this. **NICE reply**: The GDG acknowledges there is no consensus on the definition of MBR programmes. The definition used in the guideline is adapted from the Cochrane review by Kamper et al. cited in the introduction, Section 17.1. (p60/222)

- Chartered Society of Physiotherapy: Multidisciplinary biopsychosocial rehabilitation (MBR) Would it be more accurate to focus on the improvement in quality of life as the primary aim of MBR, rather than decreasing disability and improving function? **NICE reply**: The GDG agreed that the outcomes should be consistent across reviews, and that quality of life was a critical outcome to decision making, as well as function, pain and psychological distress. This is defined in the protocols and the 'relative value of different outcomes' section of each 'evidence and link to evidence' table in the chapters. (p60/222)

NICE changes in the final version of the guideline (November 2016)

- No changes were found between the draft and the final version of this chapter.

NICE final recommendations on MBR (November 2016)

30. Consider a combined physical and psychological programme, incorporating a cognitive behavioural approach (preferably in a group context that takes into account a person's specific needs and capabilities), for people with persistent low back pain or sciatica:

• when they have significant psychosocial obstacles to recovery (for example, avoiding normal activities based on inappropriate beliefs about their condition) or

• when previous treatments have not been effective.

Research recommendation 4.

What is the cost-effectiveness of providing long term support (>12 months) for people with chronic, low back pain with or without sciatica, in reducing health care utilization?

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

No comment

KCE 2017 final recommendations on MBR (February 2017)

10. Consider a multidisciplinary rehabilitation programme, which combines a physical and a psychological component, incorporating a cognitive behavioural approach, and which takes into account a person's specific needs and capabilities, for people with persistent low back pain or radicular pain:

• when they have psychological obstacles to recovery,

or

• when previous evidence-based management has not been effective

(weak recommendation based on moderate to very low evidence from RCTs)

Research recommendation

What is the ideal duration of a MBR programme?

7.13. Return to work programmes

Return to work programmes in patients with low back pain ± radicular pain

NICE search question

"What is the clinical and cost-effectiveness of return to work programmes in the management of non-specific low back pain and sciatica?"

Introduction based on the draft version of NICE guideline (March 2016)

- Back problems and employment are often closely linked in the minds of patients, employers, other stakeholders and the general public. Low back pain or sciatica commonly begins in people of working age, and a high proportion of people are in employment at the time that they develop back problems**. Employment-related factors** might contribute to the onset of back symptoms, and onset of symptoms might occur during or shortly after engagement in activities undertaken in the course of employment.
- Low back pain and sciatica are common causes of work disability, leading not only to absenteeism, but also impaired productivity in those who continue to work (**presenteeism**). Back problems pose challenges to both patient and employer due to disability and the unpredictability of recurrent episodes. Inability to work contributes to poverty through loss of income, and work and socioeconomic status are the main drivers of social gradients in health. Loss of employment can contribute to altered self-image, psychological distress and social exclusion.
- Presentation to health care providers with back problems might sometimes be an indication of other difficulties at work such as conflicts with management or low job satisfaction. Therefore, an inappropriate return to employment might adversely affect both physical and psychological health. However, for many people, an early return to work might be an effective means of encouraging physical activity and increasing fitness, reducing the risk of chronic disability from low back problems. Return to work is an important outcome for many people with low back problems, and might mediate improvements in pain and other aspects of health, quality of life and well-being. The shifts from work to sickness absence to unemployment can occur over short time frames and return to work might be more difficult for those who have already lost their employment.
- Return to work programmes are structured interventions with the specific aim of facilitating return to gainful employment. They share much with programmes designed to improve clinical outcomes, often being multidisciplinary and including components of exercise and education, as well as commonly addressing psychological factors. However, their primary focus is on vocational rehabilitation and engaging corresponding specialised skills.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with non-specific low back pain • People aged 16 or above with sciatica
Intervention(s)	Interventions/multidisciplinary programmes with a specified return to work focus (or including ergonomic interventions) • Uni-disciplinary programmes including combined concepts • Multidisciplinary biopsychosocial programmes **Inclusion criteria**: RTW must be the main focus of the intervention Including any combinations of interventions or 'programmes' Irrespective of the number of people who deliver the intervention

	Tailored components are acceptable as long as these components are described, and must be given in addition to a defined component (eg. Acupuncture + tailored versus tailored=acceptable; tailored versus tailored=exclude). Tailored studies will be analysed separately (different strata). Irrespective of whether patients are sick listed **Exclusion criteria:** If the study does not clearly describe the interventions used (it must specify the modality as well as the class) If the intervention or comparison group contains an invasive interventions (eg. surgery, epidurals, facet-joint blocks/injections) Studies where all the interventions are tailored
Comparison(s)	• Placebo/Sham/Attention control • Usual care/waiting list • To each other • Any other non-invasive interventions in the guideline • Combination of interventions: any combination of the non-invasive interventions in the guideline
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) • Return to work **Important** • Responder criteria (> 30% improvement in pain or function) • Adverse events: morbidity • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

- Eight randomised controlled trials studies were included in the review. Following comparisons were found:
  - Individual programme (in 6 RCTs)
  - Group and individual (mixed) RTW programme (in 2 RCTs)
- *NEW in the final version of NICE 2016*: One Cochrane review (Schaafsma 2013) on return to work programmes was identified but it was not included as it included studies in people with back pain but not specifically low back pain, and therefore did not meet the review protocol. The studies included in this Cochrane review were individually assessed and included if they matched the review protocol.

Individual RTW programme

- **Patients with low back pain without sciatica**
  - Individually delivered RTW programme (multidisciplinary) versus usual care
    - **RTW programme =** Multidisciplinary programmes with a specific return to work focus, consisting on graded activity, a physical exercise programme based on operant-conditioning behavioural principles: Two 1-hour sessions per week (up to 3 months), performed by physiotherapist: education, exercises (aerobic, abdominal, back and leg) and individually tailored exercises to simulate and practice problematic tasks at work or ADL (gradually increased), return to work plan.
    - A single study reported no clinical difference in **pain** (NRS 0-10; 1 RCT; moderate quality; n=124-119) and **function** (RMDQ 0-24; 1 RCT; low-moderate quality; n=126-120) compared to usual care, both at short term and long term. Regarding the different measures of **healthcare utilisation**, only a clinical benefit in favour of usual care was found for physio/paramedical therapy sessions (i.e. an increased number of sessions in group who received the RTW programme) (1 RCT; moderate quality; n=134).
    - Not reported outcomes: QoL, psychological distress, return to work, responder criteria, adverse events.
  - Individually delivered RTW programme (uni-disciplinary) versus usual care
    - **RTW programme=** Single interventions with a specific return to work focus. Initial counselling session by occupational physician (OP), workplace visit if required, 6-week status interview with focus on compliance and adherence to the plan made together with the OP; 3-month follow up concluding counselling session with OP. Duration 3 months.
    - A single study reported a clinical benefit of the RTW programme in short term **QoL** (SF-36 0-100 bodily pain and physical functioning; 1 RCT; low quality; n=224) and **sick leave** (1 RCT; low quality; n=300) compared to usual care, however no clinical differences were found for **pain** (NRS 0-10; 1 RCT: low quality; n=224) and **function** (RMDQ 0-24; 1 RCT; low quality; n=224). No long term data were reported.
    - Not reported outcomes: psychological distress, responder criteria, adverse events, healthcare utilisation.
  - Individually delivered RTW programme (multidisciplinary) versus combined intervention
    - **RTW programme=** Single interventions with a specific return to work focus. Physiotherapists: individual treatment. A cognitive behavioural approach was adopted for the patients receiving treatment in the integrated work rehabilitation programme. The main focus of the programme was functional improvement. Individualised graded activity programme, pacing techniques, work conditioning, return-to-work goal setting, self-management strategies, job analysis, and ergonomic advice were taught to the patients with the aim of improving their physical and functional capabilities with proper attention to return to work. Duration: up to 3 months.
    - A single, small study reported no clinical difference in short term **pain** (NRS 0-10; 1 RCT; low quality; n=47) and **function** (RMDQ 0-24; 1 RCT; low quality; n=47) compared to a combined intervention of physiotherapy (interferential therapy, transcutaneous electrical nerve stimulation, lumbar traction, manual therapy and exercise therapy). No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, adverse events, responder criteria, return to work, healthcare utilisation.

Table 37 – Clinical effectiveness of individual RTW programmes in patients with low back pain without sciatica

RTW programmes in patients with LBP without sciatica			
Outcomes	**Individually delivered RTW programme (multidisciplinary) versus usual care**	**Individually delivered RTW programme (uni-disciplinary) versus usual care**	**Individually delivered RTW programme (multidisciplinary) versus combined intervention of physiotherap**
QoL		At short term (<4mo): • **SF-36 0-100 bodily pain: CIB favouring RTW programme** (1 RCT; low; n=224) • **SF-36 0-100 physical functioning: CIB favouring RTW programme** (1 RCT; low; n=224) At long term (4mo-1y): Not reported	
Pain	At short term (<4mo): • **NRS 0-10 (change score): no diff** (1 RCT; moderate; n=124) At long term (>4mo): • **NRS 0-10 (change score): no diff** (1 RCT; moderate; n=119)	At short term (<4mo): • **NRS 0-10 (change score): no diff** (1 RCT; low; n=224) At long term (>4mo): Not reported	At short term (<4mo): • **NRS 0-10 (final score): no diff** (1 RCT; low; n=47) At long term (>4mo): Not reported
Function	At short term (<4mo): • **RMDQ 0-24 (change score): no diff** (1 RCT; low; n=126) At long term (>4mo): • **RMDQ 0-24 (change score): no diff** (1 RCT; moderate; n=120)	At short term (<4mo): • **RMDQ 0-24 (change score): no diff** (1 RCT; low; n=224) At long term (>4mo): Not reported	At short term (<4mo): • **RMDQ 0-24: no diff** (1 RCT; low; n=47) At long term: Not reported
Healthcare utilisation	At short term (<4mo): Not reported At long term (>4mo): • **Number of consultations with GP: no diff**		

	(1 RCT; low; n=134) • **Number of consultations with occupational physician: no diff** (1 RCT; moderate; n=134) • **Number of CT scans/MRI scans: no diff** (1 RCT; moderate; n=134) • **Number of X-ray lumbar back: no diff** (1 RCT; high; n=134) • **Number of physio/paramedical therapy sessions: CIB favouring usual care** (1 RCT; moderate; n=134) • **Number of consultations to specialist: no diff** (1 RCT; high; n=134) • **Number of consultations to alternative therapist: no diff** (1 RCT; high; n=134) • **Medication use: no diff** (1 RCT; moderate; n=134)		
Return to work		At short term (<4mo): • **Sick leave: CIB favouring RTW programme** (1 RCT; low; n=300) At long term (>4mo): Not reported	

CIB: clinically important benefit

- **Low back pain population with sciatica**
  - No evidence found for this patient group
- **Mixed population (low back pain with or without sciatica)**
  - **Individually delivered RTW programme (multidisciplinary) versus usual care**
    - Three RCTs were found on the comparison of an individual RTW programme versus usual care, however due to the different interventions within the RTW programmes, the results could not be pooled.
    - **RTW programme:**

- **Anema 2007:** The workplace intervention involved the occupational physician (OP) and GP working together to reach consensus on counselling the worker in return to work according to a protocol, communication between the GP, OP and employer regarding the OPs management policy, optional work place visit by occupational therapist, implementation of the participative work adjustment protocol by the OHS's ergonomist or Occupational Health nurse for workplace assessments and modifications to aid return to work. Duration Up to 8 weeks.
- **Lambeek 2010:** Integrated care management by clinical occupational physician. The overall aim of the integrated care was to restore occupational functioning and achieve lasting return to work for patients in their own job or similar work, and not to reduce pain. The integrated care was coordinated by a clinical occupational physician and consisted of a workplace intervention based on participatory ergonomics and a graded activity programme, which is a time contingent programme based on cognitive behavioural principles (duration 12 weeks).
- **Whitfill 2010:** Early intervention: medical examination; 6-9 physical therapy sessions (stretching and exercises to maintain/improve strength, endurance and range of motion); 6-9 behavioural medicine sessions (tailored) of 45 minutes each following a protocol focusing on stress management/biofeedback and CBT skills (coping, distraction etc); half of patients also received work transition component of up to 6 sessions of 45 minutes each + case management by occupational therapist; printed workbook and didactic sessions tailored to specific situations. Duration 4-10 weeks. Comments: Originally randomised into EI (n=46) or EI + WT (n=43) but groups combined for comparison vs. standard care

- In the study of Annema 2007 a clinical harm of a RTW programme was found for short term **QoL** (i.e. a benefit in favour of usual care) (EQ-5D 0-1; high quality; n= 186). No clinical difference was found for short term **pain** (NRS 0-10 change score; moderate quality; n=188) and **function** (RMDQ 0-24 change score; moderate quality; n=188). No long term data were reported for QoL, pain and function. The evidence concerning **return to work** was conflicting: a lower number of days to return to work in the short term was reported in the group who received the RTW programme (low quality; n=196), however the number of persons who returned to work in the long term was higher in the usual care group (very low quality; n=57). No differences were found for the outcome of absenteeism from unpaid work (in hours) (very low quality; n=196), and different measures of **healthcare utilisation** (number of consultations with GP, duration of consultation with OP in minutes, number of physio/paramedical therapy sessions, number of visits to manual therapy) (very low quality; n=57), both in the long term.
- Lambeek 2010 reported no clinical difference at the long term in **pain** (NRS 0-10; moderate quality; n=117), however a clinical benefit in **function** (RMDQ 0-24 change score; low quality; n=117) was found in favour of usual care. No short term data were reported for pain and function. For the majority of the **healthcare utilisation** outcomes no differences were found between the RTW programme and usual care, except for the lower number of patients who visited medical specialists and physiotherapists, and who underwent diagnostic tests, which was lower in the RTW group (high to low quality; n=134).
- In contrast to the two previous studies, Whitfill 2010 found, at long term, a clinical benefit for **pain** (NRS 0-10 final score; low quality; n=141) and a higher number of persons who **returned to work** in the group who received the RTW programme (low quality; n=42). No difference could be found for **psychological distress** (BDI 0-63; moderate quality; n=141). No short term data were reported.
- **In summary** could be stated that the majority of the evidence reported no clinically important differences of RTW programmes compared to usual care.
- Not reported outcomes: adverse events, responder criteria

Mixed group and individually RTW programme

- **Patients with low back pain without sciatica**
  - **Mixed group and individually delivered RTW programme (graded activity, CBT and education) versus RTW programme (graded activity and education)**
    - **RTW programme (graded activity, CBT and education):** Multidisciplinary programmes with a specific return to work focus: 19 half-day sessions over 8 weeks in small groups of at most 5 patients, plus individual meetings with patients. 15 x 1-hour sessions of Graded Activity (operant behavioural treatment, increasing activity by quota systems with positive reinforcement) plus workplace visit + 3 sessions of back education/lifting instructions. Occupational therapist treated patients individually for 30 minutes/week, applying graded activity to personally relevant activities e.g. work, housekeeping and leisure-time activities; multi-disciplinary return to work plan. Problem-Solving therapy (CBT): behaviour therapists. Duration 8 weeks.

- **RTW programme (graded activity and education):** Same multidisciplinary programme as above, only CBT has been replaced by group education: 10 x 90-minute sessions in which issues relating to back and back pain were discussed: physio, occupational therapist and psychologist used protocolised manual. Duration 8 weeks.
- Only results for the outcome 'number of persons who **returned to work**', at long term, are reported: no clinical difference between the two RTW programmes was found (low quality; n=76).
- Not reported outcomes: QoL, pain, function, psychological distress, adverse events, healthcare utilisation, responder criteria

- **Patients with low back pain with sciatica**
  - No evidence found for this patient group
- **Mixed population (low back pain with or without sciatica)**
  - **Mixed group and individually delivered RTW programme versus usual care**
    - **RTW programme:** Multidisciplinary programmes with a specific return to work focus. RTW focused study: part of the Bergen Study: Back to work trial. 6-h sessions, 5 days per week including physical treatment (group morning exercise, body awareness, relaxation training, stretching, cardiovascular training, exercises in heated pool, work training, individually based medical training therapy, exercise), CBT (improving coping skills and changing illness behaviour to health-related behaviour; encouraged to take responsibility for own health/lifestyle; behavioural goal setting, problem-solving, self-rewards, coping strategies, reducing stress), education (anatomy, pain, physical and mental coping strategies, work and lifestyle) and workplace-based intervention (physical and psychological strains at workplace examined; telephone conference with company health service and/or work supervisor, site visit, possible re-education); neurologist, GP, psychologist, 2 nurses, 4 physiotherapists. Followed up with individual advice at 2, 6 and 10 months at clinic and telephone contacts at 2 weeks and 4 and 8 months. Duration 4 weeks.
    - No clinical difference between the RTW programme and usual care was found for the outcome '**return to work** at greater than 4 months' (moderate quality; n=223).
    - Not reported outcomes: QoL, pain, function, psychological distress, adverse events, healthcare utilisation, responder criteria

Economic evidence

- Three economic evaluations were identified on the comparison of RTW programme versus usual care (Hlobil 2007 (NL), Lambeek 2010 (NL), Steenstra 2006 (NL)):
  - One cost–utility analysis (Lambeek 2010) found that a return to work intervention was cost effective compared to usual care for treating low back pain (with or without sciatica) (ICER: £3,011 per QALY gained). This analysis was assessed as partially applicable with potentially serious limitations.
  - One cost-utility analysis (Steenstra 2006) found that usual care was dominant (less costly and more effective) compared to return-to-work interventions for the management of low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations
  - One cost–consequence analysis (Hlobil 2007) found that a return to work intervention was less costly and more effective than usual care for low back pain (without sciatica) (saves £60 per patient, pain [VAS]: 0.20 lower, disability [RMDQ] 0.06 lower). This analysis was assessed as partially applicable with potential serious limitations.
  - Costs from an employer perspective (i.e. the cost of lost productivity to the employer). When interpreting productivity costs based on days taken off work there are a number of issues to consider including:
    - The **actual productivity loss** to the employer will not necessary equate to the number of sick days taken by the employee. Time taken off work may be compensated for in some way: for example, another colleague may be able to undertake the tasks the absent employee would have been doing or the employee may be able to make up the time off when back at work within their contracted hours. The ability to compensate will depend on the type of work.
    - Employees who return to work may **not necessarily be fully productive** if still suffering symptoms.

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:**
  - Critical outcomes were return to work, health-related QoL, pain severity, function, psychological distress. Return to work was noted as reported by included studies, including number of people returned to work as well as number of days absent from work to capture all of the available evidence informing this outcome relevant to work participation.
  - Important outcome were responder criteria for pain and function, adverse events and healthcare utilisation
  - No evidence was found for responder criteria or adverse events.
- **Trade-off between clinical benefits and harms**
  - **Low back pain population without sciatica:** Some clinical benefit of an individually delivered unidisciplinary programme with return to work focus was seen compared to usual care in terms of quality of life and return to work (number of people on sick leave for greater than 8 weeks during a 3 month intervention period). The return to work intervention programme consisted of counselling sessions delivered by an occupational physician with work place visits/assessments. No clinical difference was seen in pain, function or healthcare utilisation outcomes (with the exception of an increase in physiotherapy and paramedical therapy) when an individually delivered multidisciplinary return to work programme was compared to usual care. No clinical difference was seen in either pain or function when an individually delivered programme with focus on return to work was compared to a combination of interventions, or in return to work outcome when compared to a different return to work programme.

    The GDG discussed that the evidence from Van der Hout 2003 comparing two mixed group and individually delivered return work programmes was not very informative on the benefit of a return to work focussed programme, as it had a return to work element in both intervention arms. Rather it demonstrated a clinically important benefit of having a cognitive behavioural therapy element on the outcome return to work at 12 months in a low back pain population.
  - **Mixed population (low back pain with or without sciatica):** The majority of evidence included in this review reported no clinically important difference of individually delivered, multidisciplinary programmes with a specific return to work focus when compared to usual care. There was also some evidence reporting **clinically important differences in favour of the comparator intervention** in terms of quality of life and function, and **mixed evidence of benefit and harm in terms of return to work** (number of people returning to work; number of days to return to work for a sick-listed population during an 8 week intervention period). Some evidence of benefit was seen in healthcare utilisation outcomes at 12 months follow-up. No clinical difference was seen in return to work when a mixed group and individually delivered programme with a specific return to work focus was compared to usual care.
  - **Summary:** The GDG considered that many people with low back pain will return to work following a period of sick leave without an intervention with a specific focus on occupational health. However, there was no known evidence to support the use of a tool to predict the need for a return to work intervention. Therefore any return to work programme eventually offered would need to be available to all people with low back pain unable to undertake their usual activities. The GDG accepted this may not be feasible. It was noted that most of the included studies used **tailored intervention programmes that were too intensive to be relevant to the UK healthcare context**. Two of the studies were from the Netherlands however, and the GDG considered that this is a comparable population in terms of sick leave rates. Of these, it was considered that the study featuring a programme delivered by a single practitioner consisting of individual counselling and a workplace visit by an occupational physician, would be most relevant to the UK healthcare setting. The GDG discussed that although the evidence from the review was not compelling, there was some evidence of benefit from certain programmes suggesting a need for treatment programmes to be tailored to the individual. The GDG were also aware of a government research report suggesting that returning to work has many benefits for people. The benefits of returning to work for those who were away due to sickness or disability included promoting recovery and rehabilitation, better health outcomes, improved quality of life and a reduction in the harmful physical and mental long-term side effects of absence. For these reasons the GDG agreed that **facilitation of returning patients to work, where applicable, should be encouraged** and this should be considered in consultation with people with low back pain to suggest this as one of the goals of treatment. However, they felt that **specific return to work programmes separate from other clinical interventions should not be recommended for the NHS**. The GDG also considered whether to make a recommendation that employers should consider providing such interventions. However, they felt that while the goals and benefits to employers were much more clear-cut, the evidence they had considered for specific programmes was still not sufficiently compelling to make such a recommendation.

- **Trade-off between net clinical effects and costs**
  - Three cost-utility analyses were identified for comparison of RTW programme versus usual care. All evaluated different return to work interventions but overall the evidence about cost effectiveness relevant to an NHS (health care cost) perspective was **mixed**; one study showed little difference in costs or health outcomes (although mean differences suggested a cost saving and health improvement, the magnitude of effect was small and there was uncertainty with the confidence interval crossing the line of no effect). Another study showed a return to work intervention to be cost effective while a different study showed usual care to be more cost effective than the return to work interventions.
  - Evidence was also presented from an employer's perspective to allow the GDG to consider whether a recommendation for employers might be appropriate. In line with the NHS perspective, Lambeek 2010 found a saving in terms of productivity costs, while Hlobil 2007 reported possible savings but high uncertainty with a wide confidence interval spanning no difference. The results from Steenstra 2006 were also uncertain with confidence intervals spanning no difference. The limitations in the assessment of productivity costs were also noted.
  - The GDG concluded that it was **difficult to come to a conclusion regarding the cost effectiveness** of return to work interventions (from either an NHS or employer perspective) based on this evidence. The GDG decided **not to recommend specific return to work programmes separate from other clinical interventions as they may not be cost effective**; however they considered that encouraging people who are absent from work due to their low back pain and/or sciatica to return to work or usual activities could be done **as part of usual care** and therefore unlikely to incur additional costs to the NHS, therefore this would be cost effective and should be recommended.
- **Quality of evidence**
  - Evidence from 8 RCTS, quality ranged from high to very low, mainly downgraded for high risk of bias due to lack of appropriate blinding and high number of drop-outs.
  - Evidence for individually delivered programmes with specific return to work focus versus usual care had high quality GRADE ratings for the outcomes quality of life at up to 4 months in a low back pain with or without sciatica population, and healthcare utilisation over 4 months in both people with low back pain without sciatica with or without sciatica. High quality GRADE rating was also seen in evidence for mixed group and individually delivered programmes with specific return to work focus versus usual care for the outcome return to work at longer term follow-up in a low back pain with or without sciatica population.
  - The design of the study by Anema 2007 was discussed. The GDG noted that this study had two randomisation stages; the first randomisation took place for all the sick-listed participants into either the return to work programme or usual care arm. The second randomisation at 8 weeks was only for those participants who still hadn't returned to work. The second randomisation split participants into 4 arms; return to work programme, return to work programme with a graded activity programme, usual care and usual care with a graded activity programme. Most of the results from the second randomisation were presented as pooled outcomes of both the return to work arms and both the usual care arms, and therefore could not be included in this review. However, where separated, data for people who had not switched groups was reported. This places uncertainty in the reliability of the results from the longer term follow-up (post second randomisation) as not all of the randomised participants are included in the analysis.
  - The economic evidence was assessed as partially applicable with potentially serious limitations.
- **Other considerations**
  - When setting out the protocol for this review the GDG highlighted a priori the difficulty isolating 'return to work' interventions and their effect given that many general rehabilitation programmes will address peoples individual goals which might include returning to work although this may not be explicitly specified or the primary goal of the intervention. As such they felt it should be clear that a **lack of evidence from this particular review does not negate the importance of returning to work** per se as they felt this was well-established to be valued by people with low back pain and the general population. The GDG discussed that although the aim of returning to work was of importance to a large proportion of the population suffering with low back pain, there was equally a large proportion would not be working, either due to not being of working age, or for other reasons such as caring for a child, or family member, disability, amongst others. It was noted that these people also should be considered and **return to usual activities was equally important**, the recommendation was drafted to take this into account.

- It was noted that there are different types of programmes which would not be included by this evidence review, such as **'stay at work' programmes**. The GDG are unable to comment on these programmes from this evidence review. The GDG were also aware that recently the Department for Work and Pensions is introducing a scheme called Fit for Work with the aim of helping people on long-term sick leave return to work. People can be referred by their GP if they have been off work for 4 weeks or more. Once referred, they are assessed by an occupational health professional and will receive a plan to help them return to work. While this is not low back pain specific the GDG felt it was important that GPs knew about and were confident to refer into this existing service.
- The GDG were aware of existing NICE public health guidance for Managing long-term sickness and incapacity for work (**https://www.nice.org.uk/guidance/ph19**) which, while not directly relevant to this review, should also be considered in those who are unable to return to work for a prolonged period.
- **Due to the lack of evidence for a specific intervention or programme that could be recommended to enable people to return to work and the existing services available, alongside the broader evidence highlighting benefits of enabling people to return to work or their usual activities, the GDG agreed that a consensus recommendation should be made for this to be encouraged as part of all treatment for people with low back pain and/or sciatica.**

NICE draft recommendations on imaging (March 2016)

29. Promote and facilitate return to work or normal activities of daily living for people with non-specific low back pain with or without sciatica. .

Belgian GDG considerations mentioned in the Lime survey in October 2016

Agreement with the content of the NICE recommendation 31: 14 Yes, 0 No, 0 no opinion, 0 out of competence, 0 no answer, 0 not completed

- **Comments from those who do not agree:** No comments
- **Other comments:**

Couldn't we replace "ou" by "et" ?

Strength of the recommendation 31 on RTW programmes: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	There was some evidence of benefit from certain programmes suggesting a need for treatment programmes to be tailored to the individual. The GDG agreed that facilitation of returning patients to work, where applicable, should be encouraged and this should be considered in consultation with people with low back pain to suggest this as one of the goals of treatment. However, they felt that specific return to work programmes separate from other clinical interventions should not be recommended for the NHS
Quality of evidence	High to very low
Values and preferences	Due to the lack of evidence for a specific intervention or programme that could be recommended to enable people to return to work and the existing services available, alongside the broader evidence highlighting benefits of enabling people to return to work or their usual activities, the GDG agreed that a consensus recommendation should be made for this to be encouraged as part of all treatment for people with low back pain and/or sciatica.
Costs (resource allocation)	It was difficult to come to a conclusion regarding the cost effectiveness of return to work interventions. The GDG decided not to recommend specific return to work programmes separate from other clinical interventions as they may not be cost effective.

Agreement with the strength of the NICE recommendation 31: 7 strong, 6 weak, 1 no opinion, 0 no answer, 4 not completed

- **Comments for a weak recommendation**
  - Balance between desirable and undesirable effects
- **Comments for a strong recommendation**

- Returning to normal activities of daily living (including return to work if possible) should be one of the top priorities in the management of LBP (with or without radicular pain). So promoting and facilitating this, should be strongly recommended

Belgian GDG comments during the GDG meeting on the 14th December 2016

- Overall agreement on findings in NICE review: lack of evidence on intervention programmes hampers the formulation of a clear recommendation but the aspect of returning to work or usual activities was found important for all GDG members.
- No changes in the formulation of the recommendation were suggested.

Conclusion: recommendation NICE 2016 unchanged

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30th November 2016)

Evidence behind the recommendation

- Arthritis Research UK: Promote and facilitate return to work: this is rather vague and would be strengthened by incorporating evidence for return to work outcomes in back pain, drawing the attention of the reader to the nature of **effective interventions** that result in better work outcomes.

  Reply NICE: Programmes with a specific focus on return to work have been evaluated in the review leading to this recommendation. The GDG agreed that although the evidence reviewed was not strong, that it was important to highlight the importance of return to work and therefore the recommendation from CG88 was maintained. We are unable to make this recommendation more specific as there was no evidence for which interventions would produce the best outcomes.
- Homerton University Hospital NHS Foundation Trust/ Primary Care Rheumatology Society: **Occupational therapists** provide valuable input into the management of chronic pain within specialist pain teams. It may be beneficial to advise GPs to consider suggesting referring chronic low back pain patients to see an occupational health therapist if no better within 6 months. This would reduce the risk of conflict between the GP and the patient whilst also acting as a break on longterm Fitnotes and an incentive to motivating the patient to return to work

  Reply NICE: The proposed GDG composition was previously consulted on and agreed during the scoping phase of the guideline. A co-opted expert for the topic of return to work was recruited and attended a GDG meeting to help the group developing the protocol and understanding the evidence for this review. NICE guidelines are evidence based, and therefore the GDG are unable to make recommendations where the evidence has not been reviewed.
- Chartered Society of Physiotherapy: We welcome this recommendation. Return to work is a key area where physiotherapy can impact, and we are supporting our members to consider how they can facilitate people to return to work, including people with low back pain.

  Reply Nice: Thank you for your comment.
- Association of NHS Occupational Physicians*:* Occupational Risk – should be assessed by Occupational Health – as appropriate work adjustments (short and long term) may enhance ability to cope, reduce employment risk and increase personal and employer productivity. Some jobs are inherently risky – e.g ambulance front line, tractor driving, nurses etc. Work is an important part and has been completely missed.

  Reply NICE: The importance of work in the context of back problems has been acknowledged in chapter 18 (return to work programmes).

Current practice in UK

- Faculty of Pain medicine: To return people to work requires trained negotiators in vocational rehabilitation working in collaboration with NHS practitioners. Currently such services do not exist or only in small pockets. The workforce outside general practitioners needs to understand what it takes to achieve this as it is often work conditions that prevent return to work rather than the individual per se and stigmatisation of the person with back pain often occurs. The new Fit4work service whilst admirable in its intentions does not achieve this as there is insufficient on the ground collaboration between NHS clinicians dealing with back pain and such agencies.

  Reply NICE: Your comments will be considered by NICE where relevant support activity is being planned.
- Homerton University Hospital NHS Foundation Trust: A pilot program of a specialist occupational therapist helping patients' return to work was successful at Homerton. This enabled face to face discussion with MSK outpatient physiotherapists and chronic pain therapists who were able to focus their rehabilitation so that patients could achieve the function required to return to work or remain in work. Unfortunately substantive funding was not available for this post.

Reply NICE: thank you for your comment.

- Guy's and St Thomas NHS Foundation *Trust:* Physiotherapists are already present in occupational health Continued support nationally for return to work programmes and mandating within work support services is needed to combat the variability of work place support**.**

  Reply NICE: Thank you for this information.

Research recommendations

- Society of Back Pain Research: The term "Promote and facilitate return to work": this is not clear. It would help the user if some guidance on what the clinician should offer in the way of advice/support, and what outcomes should be measured. Work Focused Healthcare is a better term than "promote and facilitate return to work.
  - what it is important is that the principle of promoting and facilitating return to work should be accepted as part of routine clinical practice (which is supported by current guidance and government policy – see below).
  - We are not sure it would be helpful for the guidelines to be prescriptive about what clinicians should offer/measure
  - We suggest to refer to the existing guidance and policy, e.g. guidance for GPs on the importance of work to health, and on how they should advise their patients to encourage work participation rather than incapacity.

    Burton AK, Waddell G, Kendall N: Developing guidance for workplace and clinic - *Work & Health* (guidance leaflet for professionals in and around the workplace). London: The Stationery Office [ISBN 9999072399] (www.tsoshop.co.uk/gempdf/Work_and_Health_Leaflet_1.pdf) *Health & Work* (guidance leaflet for GPs and other healthcare professionals). London: The Stationery Office [ISBN 0-11-703772-4] (www.dwp.gov.uk/docs/hwwb-health-work-gp-leaflet.pdf) and *Tackling musculoskeletal problems: a guide for the clinic and workplace - identifying obstacles using the psychosocial flags framework. London: The Stationery Office* (www.tsoshop.co.uk/flags). This guidance was sent to all GPs in 2010 to coincide with the introduction of the Fit Note which replaced traditional incapacity certification (http://www.dwp.gov.uk/docs/fitnote-gp-guide.pdf) and was incorporated into the related National Education Programme for GPs, run by the Royal College of General Practitioners in 2010-11. The imminent launch of the Fit for Work Service (which means that GPs, individuals and employers can refer into a tele-occupational health case management service) will in essence assist clinicians in terms of 'what to do'.
  - Current policy calls for 'work-focused healthcare' (which may be a better term than 'promote and facilitate return to work) and the evidence informing this can be found within the government's Health, Work and Wellbeing Strategy 2010-2015. Although this isn't specific to LBP, much of the evidence comes from LBP populations as this is a leading cause of sickness absence and work disability, and it is suggested that the same principles should be applied across all common, work-relevant health conditions.

  EVIDENCE:
  - There is a wealth of robust evidence, but it doesn't lend itself to clinical trials methodology or the program focuses on 'stay at work', and therefore wouldn't be deemed eligible evidence here. The RCTs that have been included suffer from the same issue as much of the other clinical evidence included – small effect sizes, largely because most people recover and return-to-work, and they do not need intensive/clinical intervention. This kind of research is essentially social research, and outcomes are generally seen as long-term, public health benefits.
  - This does then beg the question as to whether return-to-work should have been included in these guidelines, but seeing as though work disability due to LBP is a global health concern then it seems right to. The guidelines do acknowledge this and the policy evidence in this area, and I would agree that this should stay as is. This issue also then has implications for the following suggested recommendations:

  SUGGESTED RESEARCH RECOMMENDATION: Given the importance of work for people's health this is an important research topic.
  - What is the clinical and cost effectiveness of return to work programmes for people with non-specific low back pain with or without sciatica?

    Studies would have to incorporate some kind of stratification as most people do recover and return to work - current evidence suggests that most people do not need intensive, expensive return-to-work programs.
  - What are the different needs of unemployed vs employed people with non-specific low back pain with or without sciatica, in return to work?

This is an important distinction to make, but the term 'return to work' isn't usually appropriate when applied to unemployed populations as the term is only relevant to people who are already employed and taking sickness absence. It is only relevant to make this distinction in the clinical domain if people have become unemployed due to ill-health. I would be hesitant to make this a specific research recommendation due to the other issues outlined, and the social complexity involved when dealing with unemployed populations – it would mean that the term 'needs' would have to be very clearly defined, and presumably would only be related to clinical/health needs. Additionally, there is separate NICE guidance on long-term sickness absence and incapacity.

- Implementation research is needed – we know enough about what works (in the clinic and other settings), and the clinical and cost-effectiveness of keeping people at work can be measured at a societal level, e.g. less dependence on health and welfare services, but we know less about how the evidence can be implemented, or the barriers to implementing it in practice. I would put this forward as a suggestion for further research.

Reply NICE: The GDG agreed that facilitation of returning patients to work, where applicable, should be encouraged. However, they felt that specific return to work programmes separate from other clinical interventions should not be recommended for the NHS. The GDG prioritised other areas for research recommendations as they believed there was existing evidence for return to work programmes.

- Arthritis Research UK: Whilst we agree with the recommendations that specific return to work programmes should not currently be recommended for the NHS, we would argue that this is due to there being no evidence either supporting or refuting the use of return to work programmes and would suggest therefore that a research recommendation is made specifically on this point.

  Reply NICE: The GDG did not feel there was enough evidence to recommend specific return to work programmes separate from other clinical interventions for the NHS. Other areas have been prioritised for research recommendations.

- Arthritis Research UK: If it is accepted that work may be beneficial to patients and is an important outcome for patients (pg 743 lines 20-21), a view that is supported by reports such as "Is work good for your health and wellbeing?" Waddell and Burton (2006), "Working for a healthier tomorrow" Black (2008), Health at work - an independent review of sickness absence" Black and Frost (2011), then we would argue that it is in the interests of patients and clinicians to conduct research that tests optimum methods for supporting patients with back pain to remain in or return to work.

  References: Waddell, G. & Burton, A.K. 2006. Is work good for your health and wellbeing? London: *The Stationary Office;* Black C. 2008. Working for a healthier tomorrow. London: *The Stationary Office;* Black C & Frost D. 2011. Health at work - an independent review of sickness absence. London: *Department for Work and Pensions*

  Reply NICE: As stated in section 9.5 of the NICE manual (Developing NICE guidelines: the manual, November 2012), it would not be feasible for the GDG to draft research recommendations for every area of uncertainty. Therefore the GDG selected key research recommendations that are likely to inform future decision-making for inclusion in the guideline. Decisions about the inclusion of a research recommendation were based on factors such as the importance to patients or the population, national priorities, potential impact on the NHS and future NICE guidance, ethical and technical feasibility. The GDG took all of these factors into account when determining which areas warranted recommendations for future research and agreed the 7 topics in the full guideline were the most appropriate. From these, as per the NICE guidelines manual, only 5 are prioritised in the short version of the guideline, which are those considered to be most important to informing future updates of the guideline.

NICE final recommendations on imaging (November 2016)

31. Promote and facilitate return to work or normal activities of daily living for people with low back pain with or without sciatica.

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

A proposition of adding "as soon as possible" within the recommendation is suggested and accepted.

KCE 2017 final recommendations on return to work programme (February 2017)

11. Promote and facilitate return to work or normal activities of daily living as soon as possible for people with low back pain with or without radicular pain. (consensus-based experts opinion)

7.14. Pharmacological interventions

Pharmacological interventions in patients with low back pain ± radicular pain

NICE search question

"What is the clinical and cost effectiveness of pharmacological treatment in the management of non-specific low back pain?

7.14.1. General issues

Introduction based on the draft version of NICE guideline (March 2016)

- Sciatica was included in the definition of radicular pain in the NICE clinical guideline for pharmacological management of neuropathic pain (CG173) which covered oral and topical pharmacological management of sciatica. Therefore this review focused on pharmacological management of back pain with or without sciatica. The management of sciatica with injections and surgery are covered by other reviews in the NICE guideline.

- The main drug treatments used for non-specific low back pain are: Paracetamol, non-steroid anti-inflammatory drugs (NSAIDs), opioids, antidepressants, anticonvulsants, skeletal muscle relaxants, vitamin D and antibiotics.
  - **Paracetamol** has a spectrum of action similar to a weak NSAID. It inhibits COX-1 and COX-2 through metabolism by the peroxidase function of these isoenzymes. The mode of action of paracetamol is unclear. Its main effects appear to be exerted by interaction with neurotransmitters in the central nervous system, although it may act in part by inhibiting prostaglandin synthesis in peripheral tissues.

  - **NSAIDs** inhibit the activity of both cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). It is thought that inhibiting COX-2 leads to the anti-inflammatory and analgesic effects. NSAIDs and selective COX-2 inhibitors may be regarded as a single drug class of 'NSAIDs' as they have been within this review, although it is noted there are different side effect profiles
    - *According to the CBIP/BCFI, NSAIDS categories are:*
      - *Dérivés arylacétiques/Arylazijnzuurderivaten (Acéclofénac/Aceclofenac,* ***Diclofénac/Diclofenac,*** *Kétorolac/Ketorolac)*
      - *Dérivés arylpropioniques/Arylpropionzuurderivaten (Dexkétoprofène/dexketoprofen,* ***Ibuprofène/Ibuprofen****, Kétoprofène/Ketoprofen,* ***Naproxène****/Naproxen, Oxaprozine/Oxaprozine)*
      - *Dérivés indoliques/Indoolderivaten (****Indométacine/indometacine****, Proglumétacine/Proglumetacine)*
      - *Oxicams/Oxicams (Méloxicam/meloxicam,* ***Piroxicam/piroxicam****,* ***Ténoxicam/Tenoxicam****)*
      - *AINS COX-2 sélectifs/Cox-2-selectieve NSAIDs (****Célécoxib/Celecoxib****,* ***Étoricoxib/Etoricoxib****, Parécoxib/Parecoxib)*
      - *Nabumétone/nabumeton*

  - **Opioids** include natural and synthetic alkaloid derivatives of poppy plant resin. The principle mode of action on pain relief is by binding to opioid receptors in the central and peripheral nervous system. Opioids vary in potency and side-effects, based on the relative activation of different receptors and pathways. The effect of opioids on non-cancer pain is limited by tolerance (decreasing effectiveness of a given dose with repeated use), side-effects (typically constipation, nausea), dependence and addiction.
    - *In the CBIP/BCFI lists, there are they are categorised in:*
      - *Analgésiques morphiniques peu puissants/weinig krachtige analgetica:* ***codéine/codeïne****, dihydrocodéine/dihydrocodeïne,* ***tramadol****.*
      - *Analgésiques de puissance modérée/matig krachtige analgetica: pentazocine, péthidine/pethidine, tilidine.*
      - *Analgésiques puissants/krachtige analgetica:* ***buprénorphine/buprenorfine****, fentanyl, hydromorphone/hydromorfon, méthadone/methadon****, morphine/morfine, oxycodone/oxycodon****, piritramide,* ***tapentadol.***

- **Antidepressants** are used for treating chronic and neuropathic pain; separate from their antidepressant actions. The precise mechanism of analgesic action of antidepressants is unknown. Antidepressants, such as amitriptyline, elevate synaptic concentrations of neurotransmitters such as serotonin and noradrenaline, and indirectly affect opioid pathways. They also bind to other receptors that may be important for therapeutic effects and side effects. Antidepressants are not currently licenced for chronic low back pain or sciatica, but are prescribed off-license for these conditions. The NICE review looked at selective serotonin reuptake inhibitors (SSRIs), selective noradrenaline reuptake inhibitors (SNRIs) and tricyclic antidepressants (TCAs).
  - *According to the CBIP/BCFI : « Les antidépresseurs sont subdivisés en fonction de leur structure chimique et/ou de leur mode d'action. La sélectivité n'est cependant jamais tout à fait spécifique»/De antidepressiva worden onderverdeeld in functie van hun chemische structuur en/of hun werkingsmechanisme. De selectiviteit van het werkingsmechanisme is echter nooit volledig. Categories are:*
    - *Les inhibiteurs de recapture sélectifs/Selectieve heropnameremmers:*
      - *Les inhibiteurs sélectifs de la recapture de la sérotonine/Selectieve serotonine-heropnameremmers (SSRI's)* ***(****Citalopram****,*** *Escitalopram****,*** ***Fluoxétine/Fluoxetine,*** *Fluvoxamine****, Paroxétine/Paroxetine,*** *Sertraline****)***
      - *Les inhibiteurs sélectifs de la recapture de la noradrénaline/Selectieve noradrenaline-heropnameremmers (Reboxetine)*
    - *Les inhibiteurs de recapture non sélectifs/Niet-selectieve heropnameremmers*
      - *Les antidépresseurs tricycliques (ATC) et apparentés/tricyclische antidepressiva (TCA's) en aanverwanten (Amitriptyline, Clomipramine, Dosulépine/Dosulepine, Doxépine/doxepine, Imipramine, Maprotiline,* ***Nortriptyline****)*
      - *Les inhibiteurs de la recapture de la noradrénaline et de la sérotonine/Noradrenaline- en serotonine-heropnameremmers (****Duloxétine/Duloxetine****, Venlafaxine)*
      - *Les inhibiteurs de la recapture de la noradrénaline et de la dopamine/Noradrenaline- en dopamine-heropnameremmers (Bupropione/Bupropion)*
      - *Les inhibiteurs des monoamines oxydases/Monoamineoxidase (MAO)-inhibitoren (Phénelzine/Fenelzine, Moclobémide/Moclobemide)*
      - *Les antidépresseurs agissant directement sur les neurorécepteurs/Antidepressiva direct werkend op de neuroreceptoren (Agomélatine/Agomelatine, Miansérine/Mianserine, Mirtazapine,* ***Trazodone/Trazodon****)*
      - *Le millepertuis/Sint-janskruid*
      - *Les médicaments des troubles bipolaires/middelen bij bipolaire stoornissen (sels de lithium/Lithiumzouten)*

- **Anticonvulsants** are used for treating chronic and neuropathic pain; separate from their anticonvulsant actions. The precise mechanism of analgesic action of anticonvulsants is unknown. Anticonvulsants have diverse pharmacological properties including binding to sodium and calcium ion channels and decreasing the release of neurotransmitters in the brain and spinal cord. The principle drugs in this class are gabapentin and pregabalin, which are anticonvulsants that are licenced for the treatment of neuropathic pain. In UK, other anticonvulsants are not currently licenced for chronic low back pain or sciatica, but are prescribed off-licence.

- **Skeletal muscle relaxants** are used for treating chronic muscle spasm, which may also be painful. These drugs bind to different receptors and exert their effect on muscles by central nervous system mechanisms, and are distinct from the peripherally acting muscle relaxants used during general anaesthesia. Centrally acting muscle relaxants include **diazepam**, **tizanidine** and methocarbamol. **Orphenadrine** is an anticholinergic with central and peripheral actions on skeletal muscles. Diazepam, tizanidine and orphenadrine are not currently licensed for chronic low back pain or sciatica, but are prescribed off-licence.
  - *According to the CBIP/BCFI, les medicaments des états spastiques/middelen bij spasticiteit are: Baclofène/Baclofen, Cannabinoïdes/Cannabinoïden, Toxine botulique/Botulinetoxine, Dantrolène/Dantroleen, Tizanidine. L'Orphénadrine n'est pas reprise dans le répertoire/Orfenadrine is niet opgenomen in het repertorium. Le Diazepam est une Benzodiazépine, classées dans les Hypnotiques, sédatifs, anxiolytiques. Diazepam is een benzodiazepine, geklasseerd onder de Hypnotica, sedativa, anxiolytica.*
  - *According to the Belgian GDG, le Tetrazepam ou Myolastan a été retiré du marché belge (effet secondaire ++)*

- **Vitamin D** is term that covers a range of steroid-like compounds. Studies have linked low vitamin D levels to back pain, but the evidence of causation not clear.

- **Antibiotics** have been used to treat chronic low back pain. However, it is not known whether it is the antimicrobial or anti-inflammatory properties of antibiotics that are important clinically for this purpose.

PICO used by NICE (March 2016)

Population	• People aged 16 years or above with non-specific low back pain. • People aged 16 or above with sciatica *Note: Pharmacological therapies for management of sciatica will not be covered by this guideline*
Interventions	Pharmacological treatment (oral/sublingual, rectal, intra-muscular and transdermal but not intravenous): • Non-opioid analgesics (including paracetamol) • Non-steroidal anti-inflammatories • Opioid analgesics (including codeine, tramadol, tapentadol, fentanyl) • Muscle relaxants • Anti-depressants 1. SSRIs 2. SNRIs 3. Tricyclic antidepressants • Anticonvulsants 1. Gabapentinoids 2. Others • Antibiotics • Vitamin D
Comparisons	• Placebo/Sham/Attention control • Usual care/waiting list • To each other • Any other non-invasive interventions in the guideline • Combination of interventions: any combination of the non-invasive interventions in the guideline
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland-Morris disability questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BPI, BDI, STAI) **Important** • Responder criteria (>30% improvement in pain or function)

	• Adverse events: 1. morbidity 2. mortality • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

Single and combined interventions are presented separately.

- **Single intervention**: Fifty five studies were included in the review. Randomised controlled trial evidence for pharmacological treatments compared to other non-invasive interventions was found and has been reported in other chapters, comparing NSAIDS to acupuncture (chapter 13) and NSAIDs to manipulation/mobilisation (chapter 16). A further search for cohort studies on antidepressants, anticonvulsants, muscle relaxants, paracetamol, antibiotics and vitamin D was carried out due to insufficient randomised trial evidence. One cohort study was identified for anticonvulsants compared to usual care, however no relevant studies comparing the other pharmacological interventions against placebo or usual care were found.

  Paracetamol versus placebo

  - **Mixed population (low back pain with or without sciatica):**
    - Evidence from 1 study concerned new episode of acute low back pain with or without leg pain (radicular pain 20%), at least moderate-intensity pain. No clinical benefit with paracetamol (two times 665 mg modified-release paracetamol tablets 3 times a day) was found or any of the reported outcomes at 4 weeks – pain (low quality; n = 1011), function (low quality; n = 1007), quality of life (low quality; n = 495) or adverse events (very low quality; n = 1065).
    - No data were available for psychological distress, nor for the comparison with usual care.

  NSAIDs versus placebo

  - **Mixed population (low back pain with or without sciatica)**:
    - Evidence from 2 studies suggested a small clinical benefit of etoricoxib compared to placebo in terms of pain severity and function at both analysed doses (60 and 90mg during 12 weeks; MID for pain 60mg -1.13 [95%CI -1.57, -0.70]; MID for pain 90 mg -1.02 [95%CI -1.45, -0.59]; Difference in least-squares for function 60 mg -2.64 [95%CI -3.61, -1.67] ; Difference in least-squares for function 90 mg -2.23 [95%CI -3.19, -1.26]; low to moderate quality; n = 427 and 422). There was also a clinical benefit for quality of life on the physical subscale of the SF- 12 at both doses but this was not seen for the mental subscale (moderate quality; n = 427 and 422). The included population in both studies consisted on patients aged 18-75 years, with low back pain for at least 3 months, used an NSAID or paracetamol for treatment of their low back pain regularly (at least past 30 days).
  - **Low back pain population without sciatica**:
    - Evidence from 4 studies showed no clinical difference of etoricoxib, piroxicam, diclofenac or indomethacin in the rate of adverse events (low quality; n = 1344).
    - Further evidence from a single study found a potential benefit of ibuprofen (max 6x200 mg/day 7 days) or diclofenac (max 6x12,5 mg/day 7 days) compared with placebo for pain intensity at short-term (7 days) (MID Ibuprofen -1.13 [95%CI -1.85, -0.41], MID diclofenac -1.09 [95%CI -1.83, -0.35] low quality; n = 195 and 200). This study included patients aged 18 to 60 years with untreated acute low back pain without sciatica and onset within 2 days.
    - Another single study focused on tenoxicam 20 mg (one intramuscular injection followed by 20 mg oral, during 15 days) in patients with acute LBP (<2 weeks) and showed no difference on pain intensity at 15 days compared to placebo (low quality; n = 68). However, this study was old (1994) and encompassed as concurrent care, 7 days of bed rest followed by 7 days light activity at home.
    - No data were available for psychological distress, nor for the comparison with usual care.

Opioids versus placebo

- **Low back pain population with sciatica**: A single study reported only results for adverse events and no clinical differences were found between oxycodone/codeine (10 or 20mg every 12h) and placebo.
- **Low back pain population without sciatica**:
  - Evidence from 1 study (low quality, n = 389) demonstrated a clinical benefit **favouring opioids** (Oxycodone Xtampza ER ≥40 to ≤160 mg oxycodone HCL equivalents daily), for physical component (MID 3.90 [95%CI 1.95, 5.85] but **favouring placebo** for mental quality of life score (MID -3.22 [95%CI -5.37, -1.07] at 12 weeks. Results were also beneficial for responder criteria for improvement in pain severity (>30% improvement in pain intensity on NRS scale MID 1.48 [95%CI 1.16, 1.90]; (>50% improvement in pain intensity on NRS scale MID 1.57 [95%CI 1.16, 2.12]. The population consisted in male and non-pregnant females, aged 18 to 75, with a clinical diagnosis of moderate-to-severe CLBP (ie. pain intensity score of ≥5 to ≤9 on an 11-point pain intensity-numerical rating scale [PI-NRS]) for a minimum of 6 months before the screening visit.
  - Consistent evidence across a large number of studies suggested that there was no clinically important benefit in terms of pain (12 studies; moderate quality; n = 3268) or function (7 studies; moderate quality; n = 1510) for opioids compared with placebo but a clinically important harm in terms of increased adverse events with opioids (7 studies; very low quality; n = 1804). The included drugs were mainly tramadol (200-400 mg/day), oxycodone (20-80mg) and morphine 15 mg. All patients had chronic low back pain (at least 3 months duration)
  - No data were available for psychological distress, nor for the comparison with usual care.

Antidepressants versus placebo

- **Low back pain population without sciatica**: SSRIs versus placebo: One study of high risk of bias using benztropine mesylate was analysed but not reported in the results.
- **Mixed population (low back pain with or without sciatica):**
  - No clinically important difference was observed for any of the reported critical outcomes (pain, function and psychological distress) for SSRIs (Fluoxetine 100 ng/mL (low, n=14), 200 ng/mL (medium, n=14), 400ng/mL (high, n=15), duration 12 weeks or Paroxetine 20 mg, duration 56 days) or TCAs (Nortriptyline, dose escalation: 25 mg for 3 days; 50 mg for 4 days; 75 mg for 3 days; 100 mg for 4 days, duration 8 weeks) or Trazodone (50 mg tablets: 1 tablet a day for 3 days, 1 tablet 2 times a day for 3 days, 1 tablet 3 times a day for 3 days, then continue increasing dose by 1 tablet every 3 days on a 3-times-a-day schedule, barring significant side effects, to a maximum of 4 tablets 3 times a day (600 mg/day), average daily dose: 201 mg, duration 6 weeks) compared with placebo (1 or 2 studies; very low to moderate quality; range of n = 53-162).
  - Similar results were observed for SNRIs (Duloxetine 20 or 60 or 120 mg/day, duration 12 or 13 weeks) compared with placebo, where no difference was observed in terms of pain (3 studies; moderate quality; n = 1004) and function (3 studies; moderate quality; n = 1004). However, a high proportion of patients reported more than 30% reduction of pain with SNRI (2 studies; n = 630; low quality; RR 1.22 [95%CI 1.05, 1.43]). For quality of life, results were conflicting (no difference on SF-36 (1 or 2 studies; low and moderate quality; range of n = 162-588), but a benefit of SNRIs on EQ-5D in (2 studies, moderate quality; n = 742). One study (moderate quality; n = 357) showed fewer healthcare utilisation (at least one treatment for adverse events) in favour of placebo.
  - In terms of adverse events, a clinically important harm of both SSRIs (Risk ratio 3.22 [95%CI 1.04, 10.01], 1 study; very low quality; 11 n = 69) and SNRIs (Risk ratio 1.39 [95%CI 1.17, 1.65], 3 studies; n = 1041; low quality) was seen compared with placebo.
  - The included population in all studies encompassed adult patients with chronic LBP (at least 6 months).
  - No data were available for the comparison with usual care.

Anticonvulsants versus placebo or usual care

- **Low back pain population with sciatica**:
  - Gabapentinoids versus placebo: There was inconsistent evidence for the impact of gabapentinoids on pain intensity. Evidence from 1 randomised, placebo-controlled RCT with gabapentinoids (dosage increasing from 300 mg to 1200 mg per day over a period of 6 weeks) demonstrated no clinical benefit (low quality; n = 65) in pain intensity at 6 weeks (unclear duration of pain). RCT evidence also demonstrated a clinically significant harm with gabapentinoids in terms of increased risk of adverse events (Risk ratio 1.60 [95%CI 0.96, 2.67], (low quality; n = 65).

- Gabapentinoids versus usual care: One observational study on chronic LBP patients with pregabalin (mean (SD) dose 189.9 (141.7) mg/d, duration 12 weeks) demonstrated a clinically important improvement at 12 weeks on pain intensity (MID -1.40 [95%CI -1.81, -0.99]) and responder criteria (pain reduction>50%: Risk ratio 1.66 [95%CI 1.30, 2.12]) (very low quality; n = 683). Evidence from the observational study showed also no clinical benefit for depression or anxiety and a clinical harm for quality of life on SF-12 (MID for physical health 3.90 [95%CI 2.21, 5.59], MID for mental health score 5.30 [95%CI 3.71, 6.89], very low quality; n = 683).

- **Mixed population (low back pain with or without sciatica):**
  - Topiramate versus placebo: One further RCT compared topiramate (titrated at 50 mg/week to a dose of 300 mg/day in the sixth week and then remained constant, duration 10 weeks) with placebo in adults with chronic LBP with or without leg pain for at least 6 months. Evidence showed a clinically important benefit at 10 weeks of topiramate for pain severity (MID -11.40 [95%CI -12.16, -10.64]) and, no clinically important difference for function but a harm in terms of increased rate of adverse events (risk ratio 1.80 [95%CI 0.93, 3.49], low and moderate quality; n = 96). For quality of life, results should be verified.

Muscle relaxants versus placebo or usual care

- The majority of the evidence was for tizanidine, with old single studies for diazepam, baclofen and orphenadrine citrate, and no data were available for quality of life, function or psychological distress.
- There was conflicting evidence in relation to pain intensity on tizanidine:
  - Evidence from 2 placebo controlled studies showed no clinical benefit with tizanidine 4 mg three times a day, duration 7 days (moderate quality; n = 193) in acute LBP population with or without sciatica;
  - However,1 study comparing tizanidine (2 mg + aceclofenac 100 mg fixed dose, duration 7 days) with usual care found clinical benefit on pain severity (MID -2.11 [95%CI -2.72, -1.5], low to very low quality; n = 185) in adults with acute low back pain without sciatica of at least moderate severity and of recent onset.
- Conversely, there was evidence of a clinically relevant increased incidence of adverse events in the groups treated with muscle relaxants compared with placebo (3 studies; moderate quality; n = 412), but not compared with usual care (1 study; very low quality; n = 197).

Antibiotics versus placebo

- There was evidence from 1 RCT of the use of antibiotics (amoxicillin-clavulanate (500mg/125 mg) three times a day) in people with MRI confirmed disc prolapse. This evidence suggested an improvement in health care utilisation (doctor consultation for back pain, risk ratio 0.56 [95%CI 0.34, 0.92], but also an increase in adverse events (risk ratio 2.78 [95% 1.79, 4.32]) (low and moderate quality; n = 162).
- No data were available for quality of life, pain severity, function or psychological distress, nor for the comparison with usual care.

Head-to-head comparisons

- Limited data were available. A clinical harm in terms of increased adverse events (sedation, dry mouth and vertigo) with anticonvulsant (pregabalin 75mg twice daily for 2 weeks, followed by 150mg twice daily for 4 weeks then 300mg twice daily) compared with antidepressants TCA (amitriptyline 12.5mg for 2 weeks, followed by 25mg for 4 weeks and increased to 50mg) was demonstrated at 14 weeks in evidence from a single study (low quality; n = 200) in chronic LBP patients with or without sciatica.
- A further study suggested antidepressants TCA (amitriptyline 150mg daily) to be clinically beneficial compared with paracetamol (2000mg daily) for improving pain intensity at 5 weeks (MID -1.83 [95%CI -3.66, 0.00], moderate quality; n = 39), but no clinical difference for psychological distress was observed (low and moderate quality; n = 39). The population of this second study encompassed acute and chronic LBP (max 6 months) with or without sciatica.

- **Combined interventions:** Two studies looking at combinations of non-invasive interventions (with pharmacological therapy as the adjunct) were also included in this review.

Combinations of drugs versus placebo: The only available evidence for combinations of pharmacological therapies was for opioids combined with paracetamol.

- **Low back pain population without sciatica:**
  - Evidence was inconsistent: some results suggested a CIB at short term for pain in favour of the combination opioids (tramadol) and paracetamol vs placebo in acute & chronic LBP (VAS; MID -1.55 [95%CI -2.47, -0.63]; 1 study; low and moderate quality; n = 327 while other results showed a CIB at short term for **placebo** regarding pain in acute LBP (meaningful pain relief: HR 1.57 [95%CI 1.05, 2.35; 1 study; low quality, n = 277). Concerning the other outcomes, a CIB in favour of placebo was observed for the SF-36 domains of bodily pain, general health, physical function, and physical role (low and moderate quality; n = 327) and no clinical difference for pain on the McGill score, function and other SF-36 items.
  - There was a clinical harm for increased adverse events (2 studies; moderate quality; n = 613).
- **Mixed population (low back pain with or without sciatica)**:
  - A CIB was suggested at short term with a combination tramadol plus paracetamol for responder criteria (pain reduction >30%; RR 1.4 [95%CI 1.03, 1.91]; 1 study; moderate quality; n=175) but a CIB in favour of placebo for some measurement of quality of life (general health, physical function, physical role, social function and vitality; 1 study; low and moderate quality; n = 170) and no difference for other measurements of quality of life and for function. Both studies concerned patients with chronic LBP.
  - There was a clinical harm for increased adverse events (2 studies; high quality; n = 295).

Combination of drugs versus other drugs

- **Low back pain population without sciatica:**
  - One study compared opioid (tramadol) plus paracetamol versus opioid alone and did not find a CIB in adverse events at short term (1 study; moderate quality; n=119)
  - Another study compared opioid (codeine) plus paracetamol versus NSAID (ketorolac) in acute low back pain and showed no difference in pain outcomes at less than 4 months, but adverse events were more common with the combination codeinel + paracetamol (1 study; high quality; n=121).
- **Low back pain population with sciatica**:
  - One study compared a combination of opioids (tramadol) plus paracetamol versus an anticonvulsant (pregabalin 75 mg). This study only reported adverse events in older patients WITH sciatica (and not WITHOUT as mentioned in the NICE guideline) and showed no clinical difference between the groups (moderate quality; n = 60).

Combinations of non-invasive interventions – pharmacological adjunct

- **Low back pain population with sciatica:**
  - There was evidence from one RCT showing that when pharmacological therapy (not specified NSAIDs) were combined with manual therapy (massage) there was a clinical benefit for pain (MID VAS -1.16 [95%CI -2.31, -0.01] in the short-term, compared to manual therapy (massage) alone (very low quality, n=54). However, no difference was observed for function measured in RMDQ or ODI.
  - Another RCT compared a combination of NSAID (Valdecoxib 20 mg) plus exercise (biomechanical) versus acupuncture in chronic LBP and showed no difference in pain (very low quality, n=60). There was no evidence available for any of the other outcomes.

Economic evaluation

- One economic evaluation was identified that compared **anticonvulsants (pregabalin) to usual care**. This cost–consequence analysis found that care including pregabalin was less costly and more effective than care excluding pregabalin for low back pain with sciatica (£68 more per patient, pain (BPI): MID -1.40, quality of life (SF-12 physical summary score): MID 3.90, quality of life (SF-12 mental summary score): MID 5.30, psychological distress (HADS - anxiety): MID -1.80 and psychological distress (HADS - depression): MID -1.90 per patient). This analysis was assessed as partially applicable with potential serious limitations.
- Another economic evaluation (Wielage 2013) compared various pharmacological treatments (head to head studies): **duloxetine (SNRI), two NSAIDs (celecoxib and naproxen), pregabalin and four opioid analgesics.** This cost-utility analysis model found that **duloxetine** was dominant (less costly and more effective) compared to pregabalin, celecoxib, oxycodone/paracetamol**,** oxycodone, tapentadol and tramadol for treating low back pain (with or without sciatica) post paracetamol. It also found

that duloxetine was **not cost effective compared to naproxen** treatment (ICER: £41,521 per QALY gained). This analysis was assessed as partially applicable with potential serious limitations.

- In addition, one cost-effectiveness analysis comparing paracetamol to ibuprofen found that **paracetamol** was dominant (less costly and more effective) compared to ibuprofen for acute low back pain (without sciatica). This analysis was assessed as partially applicable with potential serious limitations
- *No relevant economic evaluations were identified that included muscle relaxants, SSRI antidepressants, tricyclic antidepressants, non-gabapentinoid anticonvulsants, antibiotics or vitamin D as a comparator.*
- *One economic evaluation relating to NSAIDs, opioid analgesics and muscle relaxants was identified but was selectively excluded due to a combination of applicability and methodological limitations.*
- *One economic evaluation relating to duloxetine (SNRI), two NSAIDs, two opioids, amitriptyline (tricyclic antidepressant) and pregabalin (gabapentinoid anticonvulsant) was excluded due to limited applicability.*

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:** The NICE GDG agreed that health related quality of life, pain severity, function and psychological distress were the outcomes that were critical for decision making. Responder criteria (for pain and function), adverse events and healthcare utilisation were also considered as important. In this review, antidepressants were the only intervention studies that had evidence for all the critical and important outcomes, whereas there was no evidence for any of the critical outcomes for diazepam. The available evidence comparing combinations of pharmacological therapies to placebo reported time to pain relief as well as pain severity as a continuous variable. The GDG agreed that the time taken until pain relief was achieved was of less importance than whether or not any change in pain had occurred and therefore considered that this was of less value for decision making.
- **Trade-off between clinical benefits and harms**
  - The evidence for pharmacological agents for low back pain is discussed below; note that pharmacological management for sciatica is covered by the NICE neuropathic pain guideline CG173.
  - **Paracetamol**: There was no clinical benefit observed in any of the reported outcomes, for the single study included in the analysis. Moreover the NICE GDG noted:
    - The treatment period in the RCT was only of 4 weeks duration whereas the follow-up period analysed in the NICE review was at 12 weeks. At the 12 week time point, the GDG felt it would be unlikely to expect benefits to remain after a short course of treatment.
    - The study did include outcomes for pain and function at 4 weeks, and Kaplan-Meier curves for sustained recovery by treatment group, adjusted for baseline pain score, which did not show any significant differences in recovery over time between the groups receiving paracetamol or placebo. This data was only reported graphically so could not be included in the review, but the GDG agreed it was important to note.
    - Despite having large numbers of participants at 12 weeks for the assessment of pain severity and function, the number of participants analysed for the health related quality of life outcomes had more than halved in number across both arms.
    - In conclusion, the GDG acknowledged that the evidence only considered the short-term efficacy of paracetamol, however, the GDG felt that there was no evidence to support paracetamol for the management of acute low back pain. In addition, the GDG felt that a recommendation not to use paracetamol long-term was justified given the lack of evidence of clinical benefit.
  - **NSAIDs**: The included evidence was for piroxicam, etoricoxib, diclofenac, ibuprofen and indomethacin as oral preparations and tenoxicam by intramuscular injection. NSAIDs were pooled for analysis and no heterogeneity was observed. Short-term effectiveness in terms of pain severity and function was demonstrated. Two studies (and not one as mentioned by NICE) of etoricoxib analysed 2 doses (60 and 90mg). The NICE GDG noted that although there was a clinical benefit at both doses for pain and quality of life, function was only improved at the 60mg dose (but it is suspected that it was for both doses and an error in the presentation of NICE results). Further evidence demonstrating benefit of pain was seen when NSAIDs (not specified) were combined with massage, however this was from a single small study. The GDG agreed there was sufficient evidence of benefit of NSAIDS on which to base a recommendation. Although this evidence review did not demonstrate any increase in adverse events in those receiving NSAIDs, the GDG noted that the side-effect profile of NSAIDs varied between drugs, and therefore although the efficacy could be considered similar across the class, the side effect profile should be considered when determining which drug was most appropriate for the individual. The GDG were aware of the considerable toxicity of NSAIDs and that the randomised controlled trials reviewed were not likely to pick up long term complications, toxicity due to co-morbidities or drug interactions.

- **Opioids:** The review protocol defined that opioids would be pooled unless heterogeneity was observed. Therefore strong and weak opioids were combined within this review. It was noted that there was no heterogeneity in the pooled data. It was noted that all the evidence was drawn from people with chronic low back pain. The evidence therefore suggests that there was no reason to believe different strength opioids would have different clinical effectiveness in a population with chronic low back pain. There was some evidence of a small benefit in terms of pain and function versus placebo, but these effects were not judged to be clinically important. The GDG noted that the meta-analysis included a large number of trials, and the effects were very consistent across these trials. Evidence from 1 study reported clinical benefit for opioids in physical component scores of the quality of life measure SF-12 (NICE quoted also mental health). There was no evidence found for the use of opioids in acute low back pain or for the management of acute episodes of low back pain and therefore the effectiveness of opioids alone for the management of acute low back pain could not be determined from this review. There was an increase in adverse events observed in those receiving opioids as a single agent. The GDG concluded that the potential harms of opioid treatment for chronic low back pain when used as a single agent outweighed the benefits and agreed a recommendation that opioids should not be used in the management of chronic low back pain. The GDG considered making a research recommendation regarding the use of opioids without paracetamol in acute low back pain, however did not do so because they were aware of an ongoing placebo-controlled trial in this population.
- **Antidepressants**: No clinically important difference was observed for any of the reported outcomes for SSRIs versus placebo with the exception of adverse events which were seen to increase in the intervention group. Similar results were observed for TCAs where no difference was observed in terms of pain, psychological distress or adverse events, and SNRIs where there was no difference for any of the outcomes except for an increase in adverse events in the intervention group and a benefit of SNRIs on EQ-5D. The GDG considered that consistent evidence from these RCTs for each of the antidepressant classes reviewed was sufficient to warrant a recommendation to advise against the use of SSRIs, SNRIs and TCAs in this population.
- **Anticonvulsants:** The only available evidence for gabapentinoids versus placebo or usual care was from 1 small placebo controlled RCT (n=65) and 1 observational cohort study which compared gabapentinoids to usual care. Both studies included people with low back pain with sciatica. It was agreed that this should be included to inform treatment for low back pain, in the absence of evidence from a population without sciatica. It was noted that the population in the cohort study had a low mean baseline value on the HADs scale, indicative of a 'non-anxious' population. The GDG highlighted that changes in this scale were not of clinical relevance in this population as there was no scope for improvement. A clinically important improvement in pain was observed in the intervention group, however, this was not consistent with the RCT evidence which indicated no clinically important difference in any outcome apart from an increase incidence of adverse events in the intervention group. The GDG agreed this conflicting evidence in 2 studies was insufficient to base a recommendation on. The cohort study had a large sample size but was considered at high risk of bias in part due to being an un-blinded study. The only available evidence for other anticonvulsants was 1 RCT comparing topiramate and placebo. The GDG considered that although there were differences that could be considered clinically important for both function and pain severity for topiramate, this is a drug that is not commonly used for low back pain and has a significant side effect profile, and therefore did not consider this sufficient evidence to recommend for people with low back pain.
- **Muscle relaxants:** Evidence identified was for tizanidine, baclofen and orphenadrine citrate. The only outcome that could be assessed was pain severity and occurrence of adverse events. There was conflicting evidence in relation to pain with one study versus placebo showing no clinical benefit and one study versus usual care showing clinical benefit. There was evidence of an increased incidence of adverse events in the group treated with muscle relaxants compared to placebo. The GDG agreed that this was sufficient evidence to recommend that muscle relaxants should not be used for the management of non-specific low back pain. The GDG highlighted that it was surprising the only available evidence for diazepam, which is widely prescribed for people with low back pain, was from 1 small RCT (n = 76) in 1978, which only reported change in muscle spasms. The GDG were aware of an RCT published in German which was not included in this review due to being a non-English language study. It was noted that even had this study been included, it would remain a very weak evidence base for a drug that is widely used. The GDG were also aware of the potential for dependence and the risk of toxicity such as drowsiness and impairment of driving ability. Therefore it was considered important to write a research recommendation for the use of diazepam in the management of non-specific low back pain.
- **Antibiotics**: There was evidence from 1 RCT of the use of antibiotics in people with MRI confirmed disc prolapse, subsequent vertebral end plate oedema and chronic low back pain of more than 6 months duration. Although evidence indicated an improvement in health care utilisation, there was also an increase in adverse events. Data were only reported as median and interquartile range for pain, function and quality of life and therefore conclusions on the efficacy based on these outcomes could not be made with any degree of certainty. The GDG considered the external validity of this trial, specifically due to the recruitment. The study reported very limited detail of how participants were recruited, and the GDG expressed concern that the population included within this trial was highly selected and very specific and consequently may not be a representative sample. It was agreed that no recommendation could be based on this single study.

- **Combinations of drugs**: The only available evidence for combinations of pharmacological therapies was for opioids combined with paracetamol. There was some evidence suggesting a clinically important benefit of a strong opioid plus paracetamol for the critical outcome pain severity when compared to placebo. However, as this was based on a single study, the GDG agreed that this was not enough evidence to base a recommendation on. Evidence from the same study reported clinical benefit for placebo for some quality of life domains of the SF-36 and no difference between treatments in some domains as well as in function. Evidence from another study comparing Codeine + Paracetamol with ketorolac in acute low back pain showed no difference in pain outcomes at less than 4 months, but adverse events were more common in the combination group. The GDG discussed that there was a need to provide an alternative treatment for people with acute back pain where an NSAID could not be used, or had been ineffective or poorly tolerated, and therefore agreed on this basis that this study provided sufficient evidence of equivalent effect of weak opioid with or without paracetamol to NSAID, despite the adverse event profile, to base a recommendation on for this specific group of people. There was also evidence available for opioid plus paracetamol compared to an anticonvulsant, however the only outcome data available was for adverse events (which showed no clinical difference between the groups). Due to the lack of effectiveness data the GDG were unable to weigh up the benefits and harms of this comparison, and therefore agreed that there was not enough evidence to make a recommendation.

- **Trade-off between net clinical effects and costs:** Three economic evaluations of pharmacological interventions for low back pain were included and unit costs of a selection of commonly prescribed pharmacological treatments were presented to the GDG.
  - One cost-utility analysis found that naproxen (NSAID) was cost effective compared to **duloxetine (SNRI), celecoxib (NSAID), pregabalin (gabapentinoid anticonvulsant) and four opioid analgesics** in the management of low back pain post first line treatment with **paracetamol**. This analysis was partially applicable with potentially serious limitations.
  - A cost-effectiveness analysis found that paracetamol was dominant (less costly and more effective) compared to ibuprofen (NSAID). This analysis was assessed as partially applicable with potentially serious limitations. The GDG considered both studies and although they conflicted with regards to the cost-effectiveness of NSAIDs, the GDG agreed that, when considering the limitations of these analyses, the unit cost of NSAIDs and the clinical evidence for etoricoxib (NSAID), NSAIDs were likely to be cost-effective for the treatment of non-specific low back pain. Although the clinical evidence did not report an increase in adverse events, the GDG noted that the side-effect profile should be considered when determining which drug was most appropriate for the individual.
  - The economic evidence for **opioids** (Wielage et al 2013) indicated that these were not cost-effective for the management of low back pain. As with the clinical evidence, this study was based on clinical evidence of people with chronic low back pain. The GDG agreed to not offer opioids for this particular population. No economic or clinical evidence for opioid use for the management of acute low back pain was identified and so the GDG were not able to make any recommendations on this topic.
  - The GDG considered Wielage et al 2013 study alongside the clinical evidence for antidepressants, which demonstrated a lack of clinical benefit and increase in adverse events, and agreed to not offer SSRIs, SNRI or TCAs for the management of non-specific low back pain.
  - One cost-consequence analysis demonstrated that there was uncertainty regarding the costs and effects of a gabapentinoid anticonvulsant (pregabalin) when compared to usual care. This analysis was partially applicable with potentially serious limitations. The GDG considered that both the economic and clinical evidence was insufficient to make a recommendation for the use of anticonvulsants in the management of low back pain.
  - No economic studies were found for muscle relaxants however there would of course be a cost associated with providing this drug and given the conclusion of lack of clinical benefit and increased incidence of adverse events observed in the clinical evidence the GDG agreed to not offer muscle relaxants for the management of non-specific low back pain.
- **Quality of evidence:**
  - For the majority of evidence in this review, the quality ranged from a GRADE rating of moderate to very low. This was due to the high number of drop outs in some of the included studies, resulting in a high risk of bias rating, as well as the imprecise nature of the results extracted and analysed in this review. Evidence for opioid plus paracetamol versus placebo in a low back pain with or without sciatica population had a high quality GRADE rating for the adverse events outcome and opioid plus paracetamol versus NSAIDs in a low back pain only population had a high quality GRADE rating for the pain severity and adverse events outcome. The high quality GRADE rating for these outcomes was due to the low risk of bias in the study outcomes and the precision of the results.

- **Other considerations**
  - The studies included in this review varied considerably in terms of allowed concomitant treatment and rescue medication, and the reporting of use of these treatments was poor. The GDG noted that this should be a consideration in interpreting the evidence, but is a confounding factor that applies to the majority of evidence in this condition.
  - The pharmacological interventions reported critical and important outcomes in the short term (less than or equal to four months) but no studies reported outcomes or adverse events beyond four months.
  - The populations for pharmacological interventions were drawn from both those with acute and those with chronic low back pain, and the data was not analysed separately on this basis.
  - It was noted that although some of the included evidence has populations with low back pain and sciatica, these pharmacological recommendations apply to the management of low back pain only. For the pharmacological treatment of sciatica, NICE clinical guideline 173: Neuropathic pain – pharmacological management: The pharmacological management of neuropathic pain in adults in non-specialist settings should be followed.
  - The GDG considered at what point in the treatment pathway NSAIDs should be offered to patients. Given the evidence from placebo controlled trials and the relatively low cost of the intervention it was concluded that NSAIDs were an appropriate first line treatment option and suitable for use throughout the treatment pathway for patients with low back pain. The GDG considered they were appropriate for use as-needed for chronic low back pain, subject to considering toxicity and drug interactions. The GDG were aware of the guidance in the British National Formulary (BNF) that cautioned that NSAIDs should be used at the lowest effective dose for the shortest possible period of time. The GDG agreed to reflect the BNF guidance by recommending that health professionals take into account the differing toxicity of different NSAIDs and the person's risk factors, including age, when choosing an agent. The GDG were aware of the recommendations to withdraw NSAIDs in patients presenting with upper gastrointestinal bleeding (NICE Guideline on acute upper gastrointestinal bleeding CG141) and the recommendation to regularly monitor renal function in people taking NSAIDs (NICE Guidelines on chronic kidney disease CG182). The GDG agreed to adapt the recommendations regarding the use of NSAIDs from the NICE Osteoarthritis Guideline (CG177) and incorporated the advice to consider the use of gastro-protective agents and to use the lowest dose of an NSAID for the shortest possible period of time to reduce the risk of toxicity.
  - The GDG were also aware that there were a limited number of studies looking at the effect of opioids on acute low back pain. The GDG noted there was only one study including codeine with paracetamol, one of the most commonly prescribed analgesics in England. With the known side effects of NSAIDs, the GDG acknowledged the need for an alternative treatment option for people with contraindications to NSAIDS use. The GDG therefore decided, on consensus to consider offering codeine (with or without paracetamol) alongside a research recommendation.
  - The GDG agreed that the British National Formulary (BNF) guidance should be followed for all pharmacological recommendations, including considerations for pregnant women, and therefore did not consider that separate recommendations were required for pregnant women.

Nine clinical recommendations and 2 research recommendations are formulated (see below).

KCE additional information

According to the BCFI/CBIP, in June 2016:

- *En cas de douleur aiguë, on essaie d'abord d'identifier la cause et de la traiter, mais cela ne doit pas retarder l'instauration d'un traitement antalgique adéquat. / Bij acute pijn tracht men eerst de oorzaak te achterhalen en te behandelen, maar dit mag geen uitstel geven voor adequate pijnstilling.*
- *Le paracétamol est en général envisagé comme première étape dans la prise en charge de la douleur aiguë. La place exacte de l'acide acétylsalicylique, des AINS, de la codéine, du tapentadol, du tramadol et de la tilidine dans la douleur aiguë est peu étayée et leur plus-value éventuelle par rapport au paracétamol n'est pas claire. Les associations sont en principe à éviter. / Bij acute pijn tracht men eerst de oorzaak te achterhalen en te behandelen, maar dit mag geen uitstel geven voor adequate pijnstilling. Paracetamol wordt bij acute pijn algemeen als eerste stap beschouwd. De juiste plaats van acetylsalicylzuur, NSAID's, codeïne, tapentadol, tramadol en tilidine bij acute pijn is weinig onderbouwd en hun eventuele meerwaarde ten opzichte van paracetamol is onduidelijk. In principe zijn combinatiepreparaten te vermijden.*
- *Il existe peu d'études contrôlées concernant la prise en charge de la **douleur aiguë musculo-squelettique** et traumatique. On utilisera si possible en premier lieu le paracétamol qui est l'analgésique mineur le plus sûr. / Er bestaan weinig gecontroleerde studies over musculoskeletale en traumatische acute pijn. Men gebruikt zo mogelijk eerst paracetamol als veiligste mineur analgeticum.*

- *La **douleur chronique** doit toujours faire l'objet d'un diagnostic précis, d'une évaluation biopsychosociale et de réévaluations périodiques. Le traitement médicamenteux ne représente qu'un seul aspect de la prise en charge globale de la douleur et doit s'intégrer dans une approche pluridisciplinaire. / Bij chronische pijn zijn altijd precieze diagnostestelling, bio-psychosociale evaluatie en periodieke herevaluatie noodzakelijk. Medicamenteuze behandeling is slechts één aspect van de globale pijnbenadering en moet geïntegreerd worden in een multidisciplinaire aanpak.*
- *Dans la **douleur chronique**, l'administration d'analgésiques se fait de préférence selon un schéma fixe, sans attendre que la douleur ne réapparaisse. Ici aussi, on utilise si possible en premier lieu le paracétamol, jusqu'à 3 à 4 x 1 g par jour chez l'adulte en bonne santé, à une dose moindre chez les adultes très maigres (< 50 kg), les personnes très âgées et en cas d'alcoolisme, de malnutrition chronique, d'insuffisance hépatique ou rénale [voir Folia d'avril 2011]. / Bij chornische pijn is het gebruik van pijstillers volgens een vast tijdsschema te verkiezen : men wacht niet tot de pijn opnieuw optreedt. Ook hier gebruikt men zo mogelijk eerst paracetamol, tot 3 à 4 x 1g per dag bij de gezonde volwassene, minder bij zeer magere volwassenen (<50kg), bij hoogbejaarde personen en bij alcoholisme, chronische ondervoeding, lever- of nierinsufficiëntie.*
- *Les associations sont en principe à éviter. Chez certains patients, l'association de codéine et de paracétamol peut toutefois être utile, éventuellement sous forme d'une association fixe; la dose de codéine doit être suffisamment élevée (chez l'adulte, 30 mg de codéine ou plus par prise). / In principe zijn combinatiepreparaten te vermijden. Bij sommige patiënten kan associëren van codeïne aan paracetamol echter nuttig zijn, eventueel in een vaste associatie; de dosis codeïne dient hoog genoeg te zijn (voor een volwassene 30mg codeïne of meer per dosis).*
- *La relation entre l'utilisation chronique d'analgésiques et l'apparition d'une néphropathie reste controversée. / Of chronisch gebruik van analgetica aanleiding geeft tot nefropathie blijft controversieel.*
- *L'utilisation d'analgésiques morphiniques puissants dans la prise en charge de la douleur chronique chez les patients non cancéreux est controversée. Dans ce contexte spécialement, un bilan biopsychosocial approfondi, un suivi médical rapproché et des réévaluations périodiques s'avèrent nécessaires./ Gebruik van krachtige narcotische analgetica voor chronische pijn bij niet-oncologische patiënten is controversieel. Zeker hier zijn een grondig bio-psychosociaal bilan, nauwkeurige medische opvolging en periodieke herevaluaties noodzakelijk.*
- *Dans les douleurs neuropathiques chroniques, on utilise aussi certains antidépresseurs tricycliques et la duloxétine ainsi que des antiépileptiques (carbamazépine, gabapentine et prégabaline) [voir Fiche de transparence "Prise en charge des douleurs neurogènes"]. Bij chronische neuropathische pijn worden ook bepaalde tricyclische antidepressiva en duloxetine en anti-epileptica (carbamazepine, gabapentine en pregabaline) gebruikt [zie Transparantiefiche "Aanpak van neuropathische pijn"].*
- *En préparation magistrale, l'acide acétylsalicylique, le paracétamol, la codéine, le phosphate de codéine et la caféine, associés entre eux ou prescrits séparément, sont remboursés dans le traitement de la douleur chronique, après autorisation du médecin-conseil de l'organisme assureur. Une procédure de remboursement identique est également d'application pour certaines spécialités à base de paracétamol (symbole en regard du conditionnement). Enfin, une intervention particulière dans le coût de certaines spécialités à base de paracétamol (ou à base de paracétamol + codéine) est octroyée aux patients atteints de douleurs chroniques persistantes, après autorisation du médecin-conseil de l'organisme assureur [voir Folia d'octobre 2012]: il s'agit uniquement de certains conditionnements à usage oral sous forme solide (mention "Chr" en regard de ces conditionnements). In magistrale bereiding worden acetylsalicylzuur, paracetamol, codeïne, codeïnefosfaat en coffeïne, onderling geassocieerd of afzonderlijk voorgeschreven, vergoed voor behandeling van chronische pijn, mits toelating van de adviserend geneesheer van de verzekeringsinstelling. Eenzelfde terugbetalingsregeling geldt ook voor sommige specialiteiten op basis van paracetamol. Ten slotte kunnen voor sommige specialiteiten op basis van paracetamol (of op basis van de associatie paracetamol+codeïne) patiënten met chronische persisterende pijn een bijzondere tussenkomst bekomen in de kostprijs, na toelating van de adviserend geneesheer: het gaat enkel om bepaalde verpakkingen van vaste vormen voor oraal gebruik.*

7.14.2. Specific points of discussion for NSAIDs

NICE draft recommendations on NSAIDs (March 2016): 3 clinical recommendations

19. Offer oral NSAIDs for managing non-specific low back pain taking into account potential differences in gastrointestinal, liver and cardio-renal toxicity and; the person's risk factors, including age.

20. When prescribing oral NSAIDs for non-specific low back pain, think about appropriate assessment, ongoing monitoring of risk factors, and the use of gastroprotective treatment.

21. Use oral NSAIDs at the lowest effective dose for the shortest possible period of time.

Belgian GDG considerations on NSAIDs mentioned in the Lime survey at the beginning of September 2016

NICE draft recommendation 19. Offer oral NSAIDs for managing non-specific low back pain taking into account potential differences in gastrointestinal, liver and cardio-renal toxicity and; the person's risk factors, including age

Agreement with the content of the NICE recommendation 19: 10 Yes, 1 No, 0 no opinion, 0 out of competence, 0 no answer, 6 not completed

- **Comments from those who do not agree:**
  - I would rather state "consider" because not every type of LBP needs pharmacological support and there isn't always an inflammatory component.
- **Other comments:**
  - 'short term (i.e. weeks and not months)' could be added. Ibuprofene and naproxene should be named as with best benefit/risk profiles.
  - only on the shortest period possible... this recommendations needs more précisions!!!

Strength of the recommendation 19: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	There was sufficient evidence of benefit of NSAIDS (Short-term effectiveness in terms of pain severity and function). Although this evidence review did not demonstrate any increase in adverse events in those receiving NSAIDs, the NICE GDG noted that the side-effect profile of NSAIDs varied between drugs, and therefore although the efficacy could be considered similar across the class, the side effect profile should be considered when determining which drug was most appropriate for the individual. The GDG were aware of the considerable toxicity of NSAIDs and that the randomised controlled trials reviewed were not likely to pick up long term complications, toxicity due to co-morbidities or drug interactions.
Quality of evidence	Low-Moderate evidence
Values and preferences	The GDG considered at what point in the treatment pathway NSAIDs should be offered to patients. Given the evidence from placebo controlled trials and the relatively low cost of the intervention it was concluded that NSAIDs were an appropriate first line treatment option and suitable for use throughout the treatment pathway for patients with low back pain. The GDG considered they were appropriate for use as-needed for chronic low back pain, subject to considering toxicity and drug interactions. The GDG were aware of the guidance in the British National Formulary (BNF) that cautioned that NSAIDs should be used at the lowest effective dose for the shortest possible period of time. The GDG agreed to reflect the BNF guidance by recommending that health professionals take into account the differing toxicity of different NSAIDs and the person's risk factors, including age, when choosing an agent. The GDG were aware of the recommendations to withdraw NSAIDs in patients presenting with upper gastrointestinal bleeding (NICE Guideline on

	acute upper gastrointestinal bleeding CG141) and the recommendation to regularly monitor renal function in people taking NSAIDs (NICE Guidelines on chronic kidney disease CG182). The GDG agreed to adapt the recommendations regarding the use of NSAIDs from the NICE Osteoarthritis Guideline (CG177) and incorporated the advice to consider the use of gastroprotective agents and to use the lowest dose of an NSAID for the shortest possible period of time to reduce the risk of toxicity
Cost (resource allocation)	Conflicted results from two analysis partially applicable with potentially serious limitations: from one, Naproxen (NSAID) cost effective compared to duloxetine (SNRI), celecoxib (NSAID), pregabalin (gabapentinoid anticonvulsant) and four opioid analgesics in the management of low back pain post first line treatment with paracetamol (one). According to the other, Paracetamol was dominant (less costly and more effective) compared to ibuprofen. The NICE GDG considered both studies and agreed that, when considering the limitations of these analyses, the unit cost of NSAIDs and the clinical evidence for etoricoxib (NSAID), NSAIDs were likely to be cost-effective for the treatment of non-specific low back pain.

Agreement with the strength of the NICE recommendation 2: 9 strong, 3 weak, 0 no opinion, 0 no answer, 7 not completed

- **Comments for a weak recommendation**
  - Balance between clinical benefits and harms
- **Comments for a strong recommendation**
  - Suggest to remove Dantrolene for the treatment of spasticity. This product is no longer available in Belgium in the oral formulation. It has limited effect, which is directly on the striped muscles this opposed to the action of baclofen that inhibits the mono- and polysynaptic reflex transmission in the afferent nerves on spinal level, which is more effective, in relation to the hepatotoxicity
  - 'short term (i.e. weeks and not months)' could be added. Ibuprofene and naproxene should be named as with best benefit/risk profiles.

NICE draft recommendation 20. When prescribing oral NSAIDs for non-specific low back pain, think about appropriate assessment, ongoing monitoring of risk factors, and the use of gastroprotective treatment.

Agreement with the content of the NICE draft recommendation 20: 9 Yes, 2 No, 0 no opinion, 0 out of competence, 0 no answer, 6 not completed

- **Comments from those who do not agree:**
  - Gastroprotective treatment should not be needed for short term in low risk patients (majority).
  - Evaluation a priori of risk factors**;** No systematic prescription of gastro-protector
- **Other comments:**
  - Maagbescherming met PPI in de Belgische context uitgesloten bij coxib gebruik

Nice draft recommendation 21. Use oral NSAIDs at the lowest effective dose for the shortest possible period of time.

Agreement with the content of the NICE draft recommendation 21: 11 Yes, 0 No, 0 no opinion, 0 out of competence, 0 no answer, 6 not completed

- **Other comments:**
  - Ibuprofene and naproxene should be cited.
  - I agree totally

Belgian GDG comments on NSAIDS during the GDG meeting on the 15th September 2016

NICE recommendation 19. Offer oral NSAIDs for managing non-specific low back pain taking into account potential differences in gastrointestinal, liver and cardio-renal toxicity and the person's risk factors, including age.

- The GDG agrees with the recommendation but proposes to change the strength from a strong to a weak recommendation.
- Pro:
  - Paracetamol is considered as the first choice in pain management for a lot of GDG members.
  - A strong recommendation could wrongly suggests that a medication is always indicated in LBP such as a standard.
- Contra:
  - A recent systematic reviews (Cochrane 2016, Machado 2015) does not confirm the paracetamol efficacy in low back pain (and another chronic pain). It appears that a change is ongoing in many guidelines (and there is a current discussion within the CBIP/BCFI on this topic).
  - There is in Belgium an overconsumption of paracetamol although an overestimated benefit.
  - If a lot of precautions are added (age, risk factors, appropriate dose and duration) or stressed (see recommendations 20 & 21), a strong recommendation could be acceptable.
- The GDG stresses the need to review recent publications on this topic before deciding.

⇨ The NICE recommendation 19 will be re-proposed in the lime survey 4, with a summary of the recent publication on paracetamol efficacy for LBP.

NICE recommendation 20. When prescribing oral NSAIDs for non-specific low back pain, think about appropriate assessment, ongoing monitoring of risk factors, and the use of gastro protective treatment.

- The GDG emphasises that gastro protective treatment is not always needed. It is depending of the kind of NSAIDS (not for coxib), the treatment duration (not in short term), and the patient characteristics. The French translation was unclear and will be changed to take into account the concept of "think about".
- The term "non-specific" should be removed.

⇨ The NICE recommendation 20 is accepted with a minor change

NICE recommendation 21. Use oral NSAIDs at the lowest effective dose for the shortest possible period of time.

- The GDG is not convinced by the terms "the lowest effective dose" and "the shortest possible period of time." It is confusing: Is it meaning that we have to start with a lower dose than recommended or start with a standard dose to be decreased as soon as possible? There is a risk of prescribing a lower dose because of adverse events.
- A footnote with a warning on reasonable lowest effective dose (= not an ineffective dose) and shortest duration will be added.

⇨ The NICE recommendation 21 is accepted with a minor change

Additional information on NSAIDS proposed to the GDG after the meeting (September 2016)

Beside the analysis regarding the place of NSAIDs in the management of LBP, two additional reviews were identified by the GDG:

- A systematic review of systematic reviews by the Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration published by Wong et al in the European Spine J in 2016
- A Cochrane review 2016 by Enthoven et al focusing on chronic LBP without sciatica.

Table 38 – Clinical effectiveness of NSAIDS in low back pain: three systematic reviews.

Sources	NICE 2016	Wong 2016		Enthoven Cochrane 2016
Included study	7 RCTs on NSAIDs vs placebo • But Nadler 2002, not analysed because outcomes presented only as graphs. 2 RCTs with combination of non-invasive interventions	In acute LBP without sciatica, 3 systematic reviews with a low risk of bias (Kuijpers 2010, Roelofs 2008, Keller 2007) including 32 studies. In acute LBP with sciatica, 6 systematic reviews with a low risk of bias (Shaheed 2014, Roelofs 2008, Luijsterburg 2007, Pinto 2012, Hahne 2010, Keller 2007) included 15 studies.	In chronic LBP, 3 systematic reviews with a low risk of bias (Kuijpers 2010, Roelofs 2008, Keller 2007) included 14 studies investigating NSAIDs for persistent LBP.	In chronic LBP without sciatica, 13 RCTs
Population	• Acute or chronic LBP • With or without sciatica	• Recent-onset LBP • With or without radiculopathy	• Chronic LBP (> 6 months) • With or without radiculopathy	• Chronic LBP (> 3 months) • Without radiculopathy
Intervention	• NSAIDs (Ibuprofen, Etoricoxib, piroxicam, diclofenac, indomethacin or tenoxicam)	• NSAIDs	• NSAIDs	• NSAIDs
Comparator	• Placebo in 6 studies (Dreiser 2003, Szpalski 1994, Birbara 2003, Pallay 2004, Goldie 1968, Amlie 1987. • NSAIDs combined with massage compared to manual therapy alone (Majchrzycki 2014) • Combination of NSAID (Valdecoxib 20 mg) plus exercise (biomechanical) versus acupuncture (Shankar 2011)	• Placebo in 2 studies (Bakshi 2008, Goldie 1968) • Other NSAIDS in 6 studies (Orava 1986, Pohjolainen 2000, Schattenkirchner 2003, Videman 1984, Ximenes 2007, Yakhno 2006) • Muscle relaxant (in a factorial design with a placebo comparison) in 1 study (Bakshi 2008) • One study compared NSAID with bed rest to bed rest alone (Szpalski 1994)	• Placebo in 4 studies (Berry 1982, Birbara 2003, Coats 2004, Pallay 2007) • Paracetamol (Hickey 1982) • Reference treatment (Doloteffin) (Chrubasik 2003) • Three studies compared two different NSAIDs (Berry 1982, Matsumo 1991, Zerbini 2005).	• Placebo in 6 studies (Allegrini 2009; Berry 1982, Birbara 2003, Coats 2004, Katz 2011, Kivitz 2013) • Two small RCTs compared two types of non-selective NSAIDs (Driessens 1994, Videman 1984) and 1 RCT (Zerbini 2005) compared a non-selective NSAID with a COX-2 inhibitor. • Three heterogeneous studies compared NSAIDs vs other drugs (Hickey 1982 for diflunisal vs paracetamol, O'Donnell 2009 for celecoxib vs tramadol and Romanò 2009 comparing celecoxib with pregabalin. • Finally, one RCT (Shirado 2010) compared NSAIDs with 'home-based exercise'.

Rescue medication	Paracetamol in 3 RCTs	Not reported	Not reported	Paracetamol only allowed
Risk of bias	• Moderate to very low quality	• Twenty-three studies had important methodological limitations • Nine studies (with 19 treatment arms) had a low risk of bias	• Six studies had important methodological limitations. • Eight studies (with 17 treatment arms) had a low risk of bias	• Three included RCTs were considered high risk of bias. Even in the 10 other RCTs with low risk of bias other methodological shortcomings were present, such as o no clear description of the randomization procedure, o high drop-out rates and o low or unclear compliance in the trial groups (risk of under- and overestimation. • The level of evidence, using the GRADE approach, was low due to similar issues. The most common reasons for downgrading evidence were 'risk of bias' and 'imprecision' for the included trials. • Most trials had a follow-up period of at least four weeks, • NSAIDs are usually used for a short period of time. This short follow up period might not have consequences on the results, since effects are expected shortly after the start of the NSAIDs. Although it is difficult due to this short follow-up period to assess adverse events. • Included RCTs had different trial population sizes; four trials included • less than 50 participants and may lack statistical power to detect differences in effects. Pooling may overcome this problem. • However, the most important question is whether the effect is clinically relevant. The main finding that NSAIDs are more effective than placebo on pain intensity was based on a meta-analysis that showed a mean difference of 3.30 on a 0

				to 100 scale. Although statistically significant, one could argue that this effect is too small to be clinically relevant. • A sensitivity analysis with a moderate quality of evidence showed • that the positive effect of NSAIDs compared to placebo was reduced and no longer statistically significant when only RCTs with low risk of bias were included in the analysis.
Study length	From 7 days to 12 weeks	From 3 days to 6 weeks	From 14 days to 12 weeks	From
Results	**LBP without sciatica** • **Potential benefit** of ibuprofen (max 6x200 mg/day 7 days) or diclofenac (max 6x12,5 mg/day 7 days) compared with placebo for pain intensity at short-term (7 days) (MID Ibuprofen -1.13 [95%CI -1.85, -0.41], MID diclofenac -1.09 [95%CI -1.83, -0.35]; low quality; n = 195 and 200). This study (Dreiser 2003) included patients with untreated **acute low back pain without sciatica**, pain at least 50 on the VAS (0-100) and on a 4-point pain intensity scale and onset within 2 days. **LBP with no information on sciatica** • No difference on pain intensity at 15 days with tenoxicam 20 mg (one intramuscular injection followed by 20 mg oral, during 15 days) vs placebo in patients with **acute LBP** (<2 weeks) (1 study, low quality; n = 68). However, this study was old (Szpalski 1994) and encompassed as concurrent care, 7 days of bed rest followed by 7 days light activity at home. **Mixed LBP**	**LBP without sciatica** • Similar outcomes (pain reduction or global improvement) between oral NSAIDs (Indomethacin or Diflunisal) to placebo (2 studies, low risk of bias). • Similar outcomes (pain or range of motion) between oral NSAID (tenoxicam) combined with bed rest leads to placebo with bed rest (1 studies, low risk of bias). • Similar improvements between: NSAID, muscle relaxant, and NSAID combined with muscle relaxant (1 studies, low risk of bias). • Conflicting results for comparison between different oral NDAIDs: o Similar outcomes (pain, disability, or satisfaction) in 4 studies with a low risk of bias (Diflunisal vs Indomethacin; Piroxicam vs Indomethacin; Valdecoxib vs Diclofenac; Aceclofenac vs Diclofenac).	• Oral NSAIDs more effective than placebo (4 studies with a low risk of bias): statistically significant differences in pain reduction favoring: (1) Naproxen over placebo; (2) Etoricoxib over placebo; (3) Valdecoxib over placebo (also clinically significant. • Statistically significant outcomes in satisfaction for NSAID (Diflunisal) over paracetamol (one study with a low risk of bias) • Neither clinical nor statistical significance reported for NSAID vs reference treatment (Doloteffin). • Similar outcomes for different oral NSAIDs (3 studies): o Ketoprofen vs Diclofenac;	• NSAIDs are more effective than placebo in pain intensity score (MID VAS 0-100 scale from baseline: -6.97 [95% CI −10.74 to −3.19]; low quality evidence; 6 studies) with a median follow-up of 56 days (interquartile range (IQR) 13 to 91 days). • NSAIDs are more effective than placebo on disability (MID RMDQ 0-24 from baseline: −0.85 [95% CI −1.30 to −0.40]; low quality evidence; 4 studies) with a median follow-up of 84 days (IQR 42 to 105 days). • When only RCTS at low risk of bias were included, differences in effect between NSAIDs and placebo were reduced. • All six placebo controlled studies also reported adverse events, and suggested that adverse events are not statistically significant more frequent in participants using NSAIDs compared to placebo (RR 1.04, 95% CI 0.92 to 1.17). Due to the relatively small sample size and relatively short follow-up in most included trials, it is likely that the proportion of patients experiencing an adverse event is underestimated. • Two studies compared different types of non-selective NSAIDs, namely ibuprofen versus diclofenac and piroxicam versus

- Small clinical benefit of etoricoxib vs placebo in terms of pain severity and function at both analysed doses (60 and 90mg during 12 weeks) in chronic mixed LBP (at least 3 months), (2 studies (Birbara 2003 & Pallay 2004); low to moderate quality; n = 427 and 422).
- Also a clinical benefit for quality of life on the physical subscale of the SF- 12 at both doses but this was not seen for the mental subscale (moderate quality; n = 427 and 422). The patients used an NSAID or paracetamol for treatment of their low back pain regularly (at least past 30 days).
- Four studies (Goldie 1968, Amlie 1987, Dreiser 2003 & Pallay 2004) showed no clinical difference of etoricoxib, piroxicam, diclofenac or indomethacin in the rate of adverse events (low quality; n = 1344).
- Further evidence demonstrating benefit of pain (MID VAS -1.16 [95%CI -2.31, -0.01], very low quality, n=54) in the short-term was seen when NSAIDs were combined with massage, however this was from a single small study in patients with pain lasting longer than 7 weeks and no difference wes observed for function.
- Another RCT compared a combination of NSAID (Valdecoxib 20 mg) plus exercise (biomechanical) versus acupuncture in chronic LBP and showed no difference in pain (very low quality, n=60.
  - Statistically significant differences favoring: Lornoxicam over Diclofenac for pain reduction; Nimesulide over Ibuprofen (for improving disability; no statistically significant differences for pain reduction) in 2 studies.

LBP with sciatica

- Inconsistent evidence on the effectiveness of oral NSAIDs vs placebo (5 studies with a low risk of bias).
  - Similar outcomes (pain, recovery, or sick leave) for NSAID (Piroxicam, Phenylbutazone, or Diclofenac) vs placebo tablets (3 studies with a low risk of bias) whereas two studies
  - NSAID (Diclofenac) more effective than placebo in reducing pain (2 studies).
  - Oral Meloxicam, Diclofenac, Lornoxicam, and Proquazone equally effective in improving pain or recovery (4 trials with a low risk of bias);
  - Statistically significant differences in pain reduction between Dipyrone and Diclofenac (with intramuscular administration), favoring Dipyrone (1 study)
  - Naproxen vs Diflunisal;
  - Etoricoxib vs Diclofenac

.

LBP with sciatica

None of the included studies with a low risk of bias addressed persistent low back pain with radiculopathy.

indomethacin. The trials did not find any differences between these NSAID types, but both trials had small sample sizes. One trial reported no differences in pain intensity between treatment groups that used selective or non-selective NSAIDs. One other trial compared diflunisal with paracetamol and showed no difference in improvement from baseline on pain intensity score. One trial showed a better global improvement in favour of celecoxib versus tramadol.

- One included trial compared NSAIDs with 'home-based exercise'. Disability improved more in participants who did exercises versus participants receiving NSAIDs, but pain scores were similar

Authors' conclusions	• The GDG agreed there was sufficient evidence of benefit of NSAIDS on which to base a recommendation. • Although this evidence review did not demonstrate any increase in adverse events in those receiving NSAIDs, the GDG noted that the side-effect profile of NSAIDs varied between drugs, and therefore although the efficacy could be considered similar across the class, the side effect profile should be considered when determining which drug was most appropriate for the individual. The GDG were aware of the considerable toxicity of NSAIDs and that the randomised controlled trials reviewed were not likely to pick up long term complications, toxicity due to co-morbidities or drug interactions.	• Oral NSAIDs are not more effective than placebo for recent-onset LPB without radiculopathy. • Inconsistent evidence on the effectiveness of NSAIDs vs placebo for recent-onset low back pain with radiculopathy. • The high-quality systematic reviews lacked detailed information on the nature and frequency of adverse events related to NSAIDs	• Oral NSAIDs are more effective than placebo for persistent LBP. • Different oral NSAIDs lead to similar outcomes for neck and low back pain with or without radiculopathy. • The high-quality systematic reviews lacked detailed information on the nature and frequency of adverse events related to NSAIDs.	• Six of the 13 included RCTs showed that NSAIDs are more effective than placebo regarding pain intensity. NSAIDs are slightly more effective than placebo regarding disability. • However, the magnitude of the effects is small, and the level of evidence was low. • When we only included RCTs at low risk of bias, differences in effect between NSAIDs and placebo were reduced. • We identified no difference in efficacy between different NSAID types, including selective versus non-selective NSAIDs. • Due to inclusion of RCTs only, the relatively small sample sizes and relatively short follow-up in most included trials, we cannot make firm statements about the occurrence of adverse events or whether NSAIDs are safe for long-term use.

Results showed that:

- **For acute LBP without sciatica**, unclear results regarding oral NSAIDs vs placebo (potential benefit of ibuprofen or diclofenac in NICE but similar outcomes for indomethacin or diflusal in Wong).
- For **acute LBP with sciatica,** there is inconsistent evidence on the effectiveness of oral NSAIDs versus placebo (NICE and Wong).
- For **persistent/chronic LBP,** evidence suggests that oral NSAIDs are more effective than placebo (NICE and Enthoven); and oral NSAIDs may be more effective than paracetamol (Enthoven).

In conclusion, all systematic review included different primary studies. However, efficacy of NSAIDs is unclear in acute LBP and is suggested by low quality evidence for chronic LBP but the effect appeared to be small. No type of NSAIDs showed clearly superiority to other in term of efficacy. All reviews acknowledged that the lack of sufficient data preclude firm statements about adverse events.

Belgian GDG comments on NSAIDS during the GDG meeting on the 12th October 2016

During the brief presentation of the literature review on NSAIDs and paracetamol, one GDG member highlights that the doses of celecoxib used in the studies (400 mg/day) was often a maximal dose according to the CBIP/BCFI[e]. In the opposite, paracetamol was sometimes clearly under-dosed. This should make us very cautious in the interpretation of the results.

[e] 200 à 400 mg p.j. en 1 à 2 prises

NICE recommendation 19. Offer oral NSAIDs for managing non-specific low back pain taking into account potential differences in gastrointestinal, liver and cardio-renal toxicity and the person's risk factors, including age.

- A major proportion of the participants in the Lime survey suggested a change in the strength of the recommendation (from strong to weak). The GDG confirms the need of this change.
- The term "non-specific" should be removed (and this is the case for almost all the recommendations below).
- The terms "taking into account potential differences in…" are questioned by the KCE. It suggests a potential difference between NSAIDs (some NSAIDs have mostly a gastro-intestinal toxicity, other a cardio-renal… and should be selected according each patient's risk factors) but this could be clarified by adding the words "between NSAIDs".
- Since a medication is not always needed in low back pain, the terms "If a medication is required" should be added.
- The recommendations on pharmacological interventions (not only the 19) do not specify if it concerns LBP with and without sciatica or LBP alone. It is possible that NICE deemed the terms "LBP with and without sciatica" too heavy to be inserted in each recommendation. This will be verified within the new version of the NICE guideline. The Belgian GDG agrees that the recommendations focusing on pharmacological interventions are applicable also for LBP with radicular pain.

⇨ **The NICE recommendation 19 will be changed as following:**
⇨ **"**If a medication is required for managing low back pain, consider oral NSAIDs taking into account potential differences between NSAIDs in gastrointestinal, liver and cardio-renal toxicity and the person's risk factors, including age."

NICE recommendation 20. When prescribing oral NSAIDs for non-specific low back pain, think about appropriate assessment, ongoing monitoring of risk factors, and the use of gastro protective treatment.

- The GDG emphasises that gastro protective treatment is not always needed. It is depending of the kind of NSAIDS (not for coxib), the treatment duration (not in short term), and the patient characteristics. The French translation was unclear and will be changed to take into account the concept of "think about".
- The term "non-specific" should be removed.
- The terms « risk factors » is discussed. Should we monitor risk factors or adverse events? The GDG understands that we have to monitor risk factors because NSAIDs are frequently used, even by patients with high blood pressure or renal failure. For example, in patient with cardio-renal risk, the development of oedema should be monitored because it can occur (in link or not with the NSAIDs and effect on the renal function). The French and Dutch translations of the recommendation 20 will take this aspect into account (i.e. in French "surveillance continue de l'évolution des facteurs de risque"; in Netherlands "continue herevalueren van de evolutie van de risicofactoren").

⇨ **The NICE recommendation 20 is accepted with a minor change in the English version and two small amendments in the French and Dutch versions.**

NICE recommendation 21. Use oral NSAIDs at the lowest effective dose for the shortest possible period of time.*

- Given the "Consider oral NSAIDs" in the recommendation 19, the recommendation 21 is now too strong. The terms "When prescribing oral NSAIDs for low back pain" will be added
- Moreover, the GDG had asked during the GDG meeting of October to formulate a footnote with a warning on reasonable lowest effective dose (= not an ineffective dose). A KCE proposition is presented and discussed. "**The lowest effective dose means the lowest dose that has an effect according to each individual patient. The Belgian GDG stressed the risk of under- or over-dose and suggested to start with a recommended dose and to test a decrease of this dose*."
- In practice, it appears that physicians prefer to prescribe the NSAID they well know or the NSAID that is the patient's preference (already used and tolerated by him or her). The prescription is done for a limited duration (about 1 week). The physicians usually start with a recommended dose and decrease the dose in case of improvement some days later (decreasing adaptation) because medication is only one part of the management of LBP. In some cases however, due to the patient's risk factors, the

clinicians start with a lower dose than recommended and increase it if not sufficiently effective but well tolerated (increasing adaptation). In other situations, it is also possible to prescribe a medication as needed rather than a fixed dose.

⇨ **The NICE recommendation 21 is accepted with a minor change and a footnote. A new formulation of the footnote will be submitted by e-mail to the GDG**
⇨ "When prescribing oral NSAIDs for low back pain, use oral NSAIDs at the lowest effective dose for the shortest possible period of time.*"
⇨ *The lowest effective dose means the lowest dose that has an effect according to each individual patient. The Belgian GDG stressed the risk of under- or over-dose and suggested to start in most situations with a recommended dose and in case of improvement to test a decrease of this dose.

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30 November 2016)

General comment

- Arthritis Research UK: The guideline does not give clinicians much to offer patients in terms of medications. There is great inter-individual variability in response to analgesic medications, and mean pain reduction from RCTs conducted on highly selected but at the same time heterogeneous patients with LBP do not predict response in an individual patient. There is little or no good evidence to guide analgesic choices in patients with acute / chronic LBP and consequently we should expect failure of trial medications with this in mind (See Moore A et al BMJ 2013:346;f2690). We therefore feel it would be more useful to point out the lack of good evidence to guide choices and give guidance about trialling analgesics in individual patients (including how / when to stop them in the absence of effectiveness) who are struggling to engage in self-management / rehabilitation without them - or at least suggest that specialist assessment is required prior to offering antidepressants / anticonvulsants / muscle relaxants / opioids in chronic LBP. Reference: Moore A, Derry S, Eccleston C, Kalso E. Expect analgesic failure; pursue analgesic success. BMJ 2013; 346; f2690. **NICE reply**: The recommendations are based on the evidence reviewed and the GDG agreed that it was appropriate to recommend against treatments where there was no evidence of benefit and therefore do not agree that other pharmacological treatments should be recommended. (p17/111)

Problem with evidence

- British Institute of Musculoskeletal Medicine**: Outcomes** of RCTs are all short-term effects on pain and function while taking the drug. In chronic NSLBP that may be useful but in acute first attacks or relapses the use of any drug should surely test the expectation of patient and clinician that it may hasten recovery. This SH suggested a research recommendation on effects on rate of recovery of acute episodes of back pain, rather than short-term symptom levels during drug-use with NSAIDs vs placebo. This would be to test the often-stated rationale for analgesia that it facilitates mobilisation into otherwise painful activities thereby accelerating recovery. There are strong rational arguments and some experimental evidence against confronting pain barriers during activity as a means of hastening recovery. **NICE reply: T**he recommendation for NSAIDs has been revised to 'consider' rather than 'offer' to reflect the evidence base. However, the GDG did not consider that this area is a priority for further research given that there is existing evidence available.(p56/222)
- Spondyloarthritis GC: One SH speculated that the **patient populations** in the evidence underpinning the recommendation of NSAIDs could include participants with unrecognised inflammatory back pain, which may account for some of the apparent effectiveness of NSAIDs. However, there does not appear to be any discussion around this point. Was it considered by the committee? Are the included studies' eligibility criteria sufficiently robust to exclude people with inflammatory back pain? **NICE reply: T**he populations included in each of the included trials were carefully checked by the technical team and then by the GDG when reviewing the evidence reviews to ensure they did not involve inflammatory forms of back pain along with other exclusion criteria for this guideline and for each specific review.(p197/222)

Soften the strength of the recommendation

- Royal College of General Practitioners: Should be "CONSIDER offering non-steroidal…" because NSAIDS kill a lot of patients. They should not be used simply because a guideline says so. **NICE reply:** On reconsidering stakeholder comments and the evidence, this change has been made to the recommendation.(p213/222)

Acute or chronic pain?

- Are the GDG recommending NSAIDS in chronic pain? YES. Where the chronicity of the LBP has not been specified in the recommendation, the recommendation applies to both acute and chronic LBP. (p17/111)

- Homerton University Hospital NHS Foundation Trust: NSAIDS are quite effective for the acute flare up or acute non-specific low back pain as long as not contraindicated (which is stated). The guidelines do not appear to be differentiating between acute and chronic non-specific low back pain so the recommendations are correct. Although they do mention not to offer paracetamol alone it is not clear that recommendation is to add it to NSAIDs. 1.2.21 should be swapped with 1.2.20 to follow some sort of order. **NICE reply**: It was agreed a priori that evidence would be pooled unless there was heterogeneity, in which case chronicity of pain would be considered for subgroup analysis (please see appendix c). We have considered the recommendation order, but believe they should remain in the order stated.(p213/222)

Kind of NSAIDS? Royal College of General Practitioners: Can a specific non-steroidal anti-inflammatory review recommended as being more effective than other non-steroidals? **NICE reply**: The evidence review for pharmacological interventions separated different classes of drugs, however within-class comparisons were not considered (see appendix C for review protocol). Therefore NSAIDs were not compared against each other to consider effectiveness of one over the other.(p214/222)

Topical NSAIDS?

- GSK is concerned that the proposed guidelines make no reference to the potential role of topical NSAIDs in the management of this. Most cases of non-specific low back pain do not result from serious pathology, but are frequently due to minor sprains, strains or injuries of low back muscles and may be triggered by posture (sitting or standing), awkward movement, lifting incorrectly or overuse of muscles; resulting in symptoms such as pain, soreness, stiffness and muscular tension. Many sufferers may choose to self medicate mild to moderate pain symptoms before presenting to their general practitioner or other healthcare access point; many experienced sufferers may choose to self-medicate their symptoms along with other management strategies. Non prescription products provide sufferers of low back pain useful self medication options. Topical NSAIDs are used for the treatment of local musculoskeletal conditions specifically for the local symptomatic relief of pain and discomfort in trauma of tendons, ligaments, muscles and joints due to sprains, strains or bruising. Topical NSAIDs may be a useful self medication treatment option for patients with acute low back pain where oral NSAIDs are either not chosen or may not be appropriate, for example due to well-documented gastrointestinal, liver and cardio-renal adverse events or in patients in whom use of oral NSAIDs is contraindicated such as gastrointestinal bleeding, renal impairment and cardiovascular disease. A number of studies have demonstrated the benefit of topical NSAIDs for the treatment of pain… In light of the evidence, GSK suggests that NICE consider acknowledging the role of topical NSAIDs for the management of non specific low back pain. **NICE reply**: Topical NSAIDs were included within the protocol and search for the review, however no evidence was found and therefore no recommendation could be made specifically for topical NSAIDs. The Cochrane review mentioned in your comment was not considered in the review as it included studies with chronic musculoskeletal pain, and was not restricted to non-specific low back pain. (p51/111)
- The PCR Society requests that NICE consider topical NSAIDs as first line in those whom you have GI or cardiovascular concerns with and before the use of opioids. Whilst topical NSAIDs RCTs did not include low back pain specifically they are used commonly in General Practice for low back pain with or without sciatica. Oral opioids have also typically not been assessed per se for low back pain. Topical NSAIDs are typically safer and are not considered to be placebos in comparison to many rubefacients. The use of placebo rubefacients should not be promoted but topical NSAIDs clinical usefulness should be acknowledged, especially in providing effective pain relief without the associated equivalent GI and CVS risk compared to oral NSAIDs. (It is noted that studies that have been done appear to indicate that opioids should not be used for low back pain). As such it appears to be an omission to not consider topical NSAIDs especially where oral NSAIDs are rejected. The omission of topical NSAIDs from the guidelines may put patients at inappropriate clinical risk from use of less safe or effective medications. **NICE answered as above** that topical NSAIDs were included in the search however, no evidence was found that met the review criteria; therefore no recommendations for topical NSAIDs could be made. (p60/111)

Proton pump inhibitor?

- Royal College of General Practitioners: Previous has advised that a proton pump inhibitor should be taken with non-steroidal anti-inflammatories for people over the age of 45 years but this is not present in this guidance. **NICE reply:** Since evidence for proton pump inhibitors were not reviewed in this guideline, the GDG cannot make such a recommendation. However the recommendation does include taking into account 'gastrointestinal toxicity' and 'the person's risk factors, including age'.(p214/222)

NICE changes in the final version of the guideline (November 2016):

In the literature review, 16.3.1.2 Combinations of interventions – pharmacological adjunct:

Ten Cochrane reviews were identified but could not be included for the following reasons:

- The stratification of the population, i.e. low back pain only, low back pain with or without sciatica and low back pain with sciatica, did not match that of the review protocol.

- The population did not meet the requirement of the review protocol; included people with sciatica, osteoarthiritis, included people with non-cancer and breakthrough pain but not limited to the low back.
- The review focussed on vitamin E as the intervention.

However the studies included in the Cochrane reviews were individually assessed and included if they matched the review protocol criteria.

Within the recommendations, a general recommendation was added and the first recommendation on NSAIDS was reformulated:

20. For recommendations on pharmacological management of sciatica, see NICE's guideline on neuropathic pain in adults.

In other considerations, some words were changed:

The GDG discussed at what point in the treatment pathway NSAIDs should be considered (and not offered such as in the draft version).

NICE final recommendations on NSAIDs (November 2016)

21. Consider oral non-steroidal anti-inflammatory drugs (NSAIDs) for managing low back pain, taking into account potential differences in gastrointestinal, liver and cardio-renal toxicity, and the person's risk factors, including age.

22. When prescribing oral NSAIDs for low back pain, think about appropriate clinical assessment, ongoing monitoring of risk factors, and the use of gastroprotective treatment.

23. Prescribe oral NSAIDs for low back pain at the lowest effective dose for the shortest possible period of time.

Belgian GDG comments on the last formulation during the meeting on 24 January 2016

The recommendations on NSAIDs are considered acceptable also for people with radicular pain.

KCE 2017 final recommendations on NSAIDs (February 2017)

12. If a medication is required for managing low back pain with or without radicular pain (e.g. due to severity of the pain and patients' preferences), consider oral NSAIDs taking into account potential differences between NSAIDs in gastrointestinal, liver and cardio-renal toxicity and the person's risk factors, including age.

(weak recommendation based on moderate to very low evidence from RCTs)

- When prescribing oral NSAIDs for low back pain, think about appropriate assessment, ongoing monitoring of the evolution of risk factors, and the use of gastro protective treatment*;

* The Belgian GDG emphasises that gastro protective treatment is not always needed. It depends on the kind of NSAIDS (usually not for coxib), the treatment duration (usually not in short term), and the patient characteristics.

- When prescribing oral NSAIDs for low back pain, select the lowest effective dose for the shortest possible period of time.**

**The lowest effective dose means the lowest dose that has an effect according to each individual patient. The Belgian GDG stresses the risk of under- or over-dose and suggests to start in most situations with a recommended dose, to assess the result and in case of improvement to test a decrease of this dose.

7.14.3. Specific points of discussion for paracetamol

NICE draft recommendation on paracetamol (March 2016)

22. Do not offer paracetamol alone for managing non-specific low back pain.

Belgian GDG considerations on paracetamol mentioned in the Lime survey at the beginning of September 2016

Agreement with the content of the NICE recommendation 22: 9 Yes, 2 No, 0 no opinion, 0 out of competence, 0 no answer, 6 not completed

- **Comments from those who do not agree:**
  - What do they mean with "alone"? I think the results are based on the PACE trial. Looking at the in- and exclusion criteria, this trial doesn't cover all types of LBP (for instance moderate pain intensity). So you can't make a general conclusion. Finally, the fact that there is not a difference in time to recovery compared to placebo, doesn't mean that paracetamol is useless in LBP.
  - **T**o start pharma**co**logical intervention as a first step, **I** prefer paracetamol. If it is not helping enough than I prescribe NSAID.
- **Other comments:**
  - If we precise for chronic pain.

Strength of the recommendation 22 (According to NICE formulation, it is a strong recommendation)

GRADE Factors proposed in the Lime survey	
Balance between desirable and undesirable effects	No clinical benefit observed in any of the reported outcomes (pain intensity, function, quality of life and adverse events) at short term in acute LBP, for the single study included in the analysis. At the 12 week time point, the GDG felt it would be unlikely to expect benefits to remain after a short course of treatment.
Quality of evidence	One study, low to very low
Values and preferences	The NICE GDG acknowledged that the evidence only considered the short-term efficacy of paracetamol, however, the GDG felt that there was no evidence to support paracetamol for the management of acute low back pain. In addition, the GDG felt that a recommendation not to use paracetamol long-term was justified given the lack of evidence of clinical benefit.
Cost (resource allocation)	A cost-effectiveness analysis found that paracetamol was dominant (less costly and more effective) compared to ibuprofen (NSAID).

Agreement with the strength of the NICE recommendation 22: 3 strong, 6 weak, 0 no opinion, 0 no answer, 8 not completed

- **Comments for a weak recommendation**
  - Weak recommendation – based on the Cochrane review: “We found that paracetamol does not produce better outcomes than placebo for people with acute LBP, and it is uncertain if it has any effect on chronic LBP”.
  - Many patients are treated with paracetamol regarding contra-indications or inefficacity of other medications.
  - Quality of evidence
- **Comments for a strong recommendation**
  - Because in chronic condition, only medication is not sufficient!!

Belgian GDG comments on paracetamol during the GDG meeting on the 15th September 2016

NICE recommendation 22: Do not offer paracetamol alone for managing non-specific low back pain.

- The strength of the recommendation is discussed because the results of the Lime survey suggested to change from a strong to a weak recommendation. The GDG members confirm that the NICE recommendation sounds too hard.
- Reasons are:
  - Recommendation is based on 1 single trial on patients with moderate pain (not applicable in all cases).
  - The findings are not in line with the current clinical practice (paracetamol as first choice).
- Adding "routinely/always" is suggested but without consensus.
- The GDG stresses the need to check the recent publications previously quoted before deciding.
- In the analysis, we should take into account the characteristics of the included population (chronic LBP only? Pain of at least moderate intensity as in the PACE study of Williams 2014…)

⇨ The NICE recommendation 22 will be re-proposed in the lime survey 4, with a summary of the recent publication on paracetamol efficacy for LBP.

Additional information on paracetamol proposed to the GDG after the meeting (September 2016)

Beside the NICE analysis regarding the place of paracetamol in the management of LBP, two additional reviews were identified by the GDG:

- The Cochrane review by Saragiotto et al in 2016
- The meta-analysis by Machado et al published in the BMJ in 2015

Table 39 presented a comparison of the results from the 3 reviews and stressed that the PACE trial was the major source of data for the 3 reviews. Two primary studies were quoted both by Saragiotto and Machado:

- Nadler et al 2002 compared the efficacy of continuous low-level heat wrap therapy (40 C, 8 hours/day) with that of ibuprofen (1200 mg/day) and paracetamol (4000 mg/day) in subjects with acute nonspecific low back pain. They found a higher efficacy for the heat wrap in Day 1 pain relief and in extended mean pain relief (Days 3 to 4) than for ibuprofen or paracetamol. This study was not analysed by NICE because pain outcome only presented graphically.
- Wetzel 2014 who studied the efficacy of a single dose of 1 g intravenous paracetamol in chronic LBP and showed no effect on pain at immediate-term FU. This study was not analysed by NICE because retracted at one author's demand.

Table 39 – Clinical effectiveness of paracetamol in low back pain: three systematic reviews.

Sources	NICE 2016	Saragiotto Cochrane 2016		Machado 2015
Included study	1 study for acute LBP: • Williams 2014 ((PACE) study) Nadler 2002 not analysed because pain outcomes only presented graphically	2 studies for acute LBP: • Williams 2014 • Nadler 2002 (but not meta-analysed)	1 study for chronic LBP • Wetzel 2014 (retracted at one author's demand)	13 RCTs but 3 for LBP: • Williams 2014, Nadler 2002 for acute & Wetzel 2014 for chronic
Population	• New episode of acute LBP (<6 weeks' duration and preceded by 1 month of no pain),	See beside for Williams For Nadler • Acute LBP	• Chronic LBP (> 6 months) • Intensity ≥4 on a 0 to 10 NRS scale • N=40	Spinal pain (acute and chronic) but also osteoarthritis of the hip or knee

	• With or without leg pain (radicular pain 20 %) • At least moderate-intensity pain during the preceding 24hours (measured by an adaptation of item 7 of the SF-36). • N=1097 • In 181 general practitioners, 50 pharmacists, and four physiotherapists) across Sydney, Australia	• At least moderate pain intensity (2 or more on a 6-point scale), • N=371, randomly assigned to heat wrap (n = 113), paracetamol (n = 113), or ibuprofen (n = 106) for efficacy evaluation, or to oral placebo (n = 20) or unheated back wrap (n = 19) for blinding. • 11 sites, ambulatory status, US	• Pain clinic at Vienna University Hospital • Austria	
Intervention	• In the regular group: Paracetamol (2X665mg)X3/day • In the group 2: Paracetamol 'as required' up to 4 g/day; Both group, daily paracetamol until recovered, up to a max of 4 weeks	• See beside for Williams • In Nadler: continuous low-level heat wrap therapy (40 C, 8 hours/day)	• Paracetamol 1g IV one single dose	Paracetamol oral or IV
Comparator	Placebo	Paracetamol 1gX4/day or Ibuprofen (1200 mg/day)	Placebo	Placebo
Rescue medication	Naproxen 250 mg 2 day (2 tablets initially, then 1 tablet every 6-8 hours as needed Wide range of concomitant medicine and treatment allowed			
Risk of bias	Low-very low quality level • No raw data provided on number of participants experiencing outcome (sustained recovery). • No attrition information provided. • No formal statistical test to assess calibration.	High quality level for Williams 2014 (sponsored study but negative trial outcome & free of other sources of bias (allocation, blinding, outcome data, reporting) Unclear for Nadler 2002 (selective reporting-not data reported for the placebo group, unclear allocation, unclear blinding).	Low quality level Selective reporting, unclear allocation, no clear exact length of the follow-up; either weak or potent opioids at least four months before the intervention; trial retracted;	High quality level for LBP
Study length	4 weeks	4 weeks for Williams; 4 days for Nadler		

Results	No diff at 4 wks for pain, function, QoL or AE.	No diff at 1, 2, 4 & 12 wks for pain, disability, fct, sleep quality, QoL*, No diff for global impression of recovery, patient adherence, use of rescue medication & AE	No effect on pain at immediate-term FU	Ineffective for reducing pain intensity and disability or improving QoL in the short term in people with LBP. Minimal short term benefit on pain and disability for people with hip or knee osteoarthritis.
Authors' conclusions	The GDG acknowledged that the evidence only considered the short-term efficacy of paracetamol, however, the GDG felt that there was no evidence to support paracetamol for the management of acute low back pain. In addition, the GDG felt that a recommendation not to use paracetamol long-term was justified given the lack of evidence of clinical benefit.	Paracetamol does not produce better outcomes than placebo for people with acute LBP.	It is uncertain if paracetamol has any effect on chronic LBP.	Paracetamol is ineffective in the treatment of low back pain and provides minimal short term benefit for people with osteoarthritis. These results support the reconsideration of recommendations to use paracetamol for patients with low back pain and osteoarthritis of the hip or knee in clinical practice guidelines.

A quick search in Medline allowed us to find one additional primary study by Bedaiwi 2016 comparing Celecoxib and paracetamol in chronic LBP.

- This RCT included 50 patients from a back pain clinic in a tertiary hospital in Canada. Included patients had chronic non-specific LBP (>3 months) without sciatica and with moderate intensity pain (VAS score ≥4 of 10 in the past week). Patients treated with celecoxib for 4 weeks showed a greater improvement in pain scores as well as disability compared with the patients treated with paracetamol. In addition to the numerical change, the frequency of patients who had achieved the therapeutic target with at least 50% improvement in nocturnal back pain and Oswestry Disability Index was also greater in the group of patients treated with celecoxib. Celecoxib treatment demonstrated that 40% of patients reached therapeutic targets on defined outcome measures, whereas paracetamol achieved the targets in less than 10%. However the posology of the paracetamol was particularly low (500 mg twice daily) compared to celecoxib (200 mg twice daily).

In conclusion, main results were provided by the PACE study and concerned acute LBP, of at least moderate intensity, in mixed population (with and without sciatica)**.** This study did not demonstrate efficacy of paracetamol alone in acute LBP.

Belgian GDG comments on paracetamol during the GDG meeting on the 12th October 2016

Paracetamol: one clinical recommendation as single medication and another recommendation in combination with opioids.

NICE recommendation 22. Do not offer paracetamol alone for managing non-specific low back pain.

- The strength of the recommendation is discussed because the results of the Lime survey suggested to change from a strong to a weak recommendation. The GDG members confirm that the NICE recommendation sounds too hard and that "routinely" should be added. The arguments for this change are:
  - Paracetamol may be effective in some patients (even if it is only a placebo effect).
  - Paracetamol may be the single option if NSAIDs or opioids are contra-indicated (e.g. elderly patients with risk factors).
  - The risk of harm/adverse events is not so important with the paracetamol.
  - The lack of efficacy of paracetamol vs placebo in LBP is demonstrated by a single study (Williams 2014) in patients with pain of moderate intensity, since a mean duration of 10 days. This is not generalizable for all patients with LBP.

- The Belgian clinicians used to start analgesic treatment by paracetamol and there is a risk of high resistance in front of a strong recommendation.

- The word “alone” is not clear.
  - Is it meaning “as single medication” or “as single treatment”?
  - Is it useful for us? Given that the NICE recommendation is strong, the word “alone” was needed to open the door for a potential use of combination with paracetamol. Since we soften the recommendation in Belgium, the word alone is maybe not useful.
  - If we remove the word “alone”, according to some GDG members, we do not provide the suggestion to use it in combination with other medication such as opioids or NSAIDs.
  - However, for other GDG members, if the words “alone” or “as single medication” remain, we suggest to use paracetamol always in combination.
  - **Finally, it is decided to wait the new version of the NICE guideline, hoping that it will provide an explanation of the presence of the word “alone” (if this word remains).**

⇨ **The NICE recommendation 22 will be softened with the addition of “routinely”. The word alone could be changed on “as single medication” or will be removed from the recommendation depending on the new version of the NICE guideline.**

⇨ **“**Do not routinely offer paracetamol (as single medication) for managing low back pain.”

Stakeholders’ comments and replies from NICE team on draft of March 2016 (edited the 30 November 2016)

Problems with some evidence:

- GSK stressed that the first study, Nadler 2002, is not a paracetamol vs. placebo controlled study. This study compared the efficacy of continuous low level heat wrap therapy (40°C, applied for 8 hours/day) with that of ibuprofen (1200 mg/day) and paracetamol (4000 mg) day in subjects with acute nonspecific low back pain. **NICE answered** that Nadler 2002 included 5 arms; heat wrap, paracetamol, ibuprofen, placebo and unheated wrap. As heat wrap and unheated wrap are not interventions in the protocol for this review, only the three relevant arms were extracted and presented in the guideline.(p52/111)
- GSK noted that the single large placebo-controlled study (Williams et al; Lancet 2014) reviewed in the GDG’s dataset did not measure simple analgesia, ie pain relief shortly after taking paracetamol, but rather the ability of paracetamol to shorten episodes of back pain defined as ≥7 days with absent or near absent pain. Paracetamol is recommended as a first line pharmacological treatment for the management of acute low back pain in the majority of existing guidelines (Koes et al. An updated overview of clinical guidelines for the management of non-specific low back pain in primary care. Eur Spine J 2010; 19: 2075–94). GSK suggests that in developing these guidelines, NICE acknowledge the extensive experience and existing recommendations on the place of paracetamol in the management of lower back pain and does not conclude that a lack of recent evidence from RCTs confirming a benefit means a lack of effect. **NICE reply**: Although the GDG recognise the wide spread use of paracetamol, however the recommendations drafted must reflect the evidence available. As detailed in section 16.6 of the guideline, the GDG were unable to recommend paracetamol due to the very limited evidence available, 1 RCT, which showed no clinical benefit for paracetamol in any of the outcomes reported. (p53/111)
- GSK**:** This recommendation contradicts other guidelines: The draft guideline currently recommends that paracetamol alone should not be offered for non-specific acute low back pain, due to lack of evidence. This recommendation contradicts other treatment guidelines (Koes BW et al. An updated overview of clinical guidelines for the management of non-specific low back pain in primary care. Eur Spine J 2010; 19: 2075–94). GDK stressed that paracetamol is indicated and recommended for its analgesic effects in the treatment of mild to moderate pain in various pain types. Given the extensive experience and long history of use, the evidence base in this clinical setting has not changed over time (few RCTs or real world studies have been conducted). While acknowledging the limited high quality randomised control trial data, GSK recommends that, based on the long experience of use in addition to existing evidence, NICE acknowledge the contribution of paracetamol as a useful self medication treatment option for patients who choose to self medicate mild to moderate pain symptoms before presenting to their general practitioner or other healthcare access point. Experienced sufferers may choose to self-medicate their symptoms along with other management strategies. Non prescription products provide sufferers of low back pain useful self medication options. **NICE reply:** Although the GDG recognise the wide spread use of paracetamol, however the recommendations drafted must reflect the evidence available. As detailed in section 16.6 of the guideline, the GDG were unable to recommend paracetamol due to the very limited evidence available, 1 RCT, which showed no clinical benefit for paracetamol in any of the outcomes reported. We are unable to comment on the over-the counter use of paracetamol as these guidelines apply to settings in which NHS care is delivered or provided only.(p52/111)

Meaning of “alone”:

- MPP: I imagine this will be quite a controversial recommendation in practice. Would it be possible to give additional information on what to do with patients currently being managed on paracetamol alone? Given the wording of the rec – is it acceptable for people to receive paracetamol in combination with any other analgesic, or just weak opioids (as per rec 1.2.21). This change will be a challenge in practice and people will need to be informed on why the recommendation has changed, and how to manage existing patients. **NICE reply**: It is important to include this recommendation as there was no evidence of benefit of paracetamol alone and it is widely used so this is important to highlight. People currently being managed on paracetamol should consider other treatment options in the guideline. Recommendations 1.2.20 clearly states that weak opioids can be given with or without paracetamol, therefore there can be no confusion regarding which analgesic is being considered in combination with paracetamol. Whereas the draft recommendation for osteoarthritis was based on potential harms of paracetamol, in this guideline recommendation 1.2.21 is based on a lack of effects seen as well potential harms and we believe it is important to include. Detail on why this recommendation has been made is included in the 'evidence and link to recommendations' table of the full guideline.(p212/222)

Option if NSAIDs not tolerated or contra-indicated:

- GSK: Paracetamol provides a useful treatment option, especially for patients who do not tolerate oral NSAIDs or for whom NSAID use in either contra-indicated or not appropriate. **NICE reply:** The GDG recognised the need for a pharmacological treatment option for those in whom NSAIDs are contradicted and have therefore included a recommendation to consider weak opioids with or without paracetamol for that specific population.(p53/111)

Risk with NSAIDs:

- NHS North Derbyshire CCG: Paracetamol has long been a first line analgesic for many different causes of pain and our feeling is that this should still be considered for patients who haven't already tried it. Although the evidence is less than convincing local feedback from GPs is that they have many patients who are successfully managed on paracetamol and this reduces the need to prescribe NSAIDs. There is a large placebo effect for analgesia which may make it difficult to show a benefit in short-term RCTs but this does not mean that paracetamol is not working for individual patients. Paracetamol is cheap and relatively safe and, as low back pain is not a life threatening condition it would seem a reasonable management strategy to try paracetamol first and then progress to other drugs if the patient does not gain benefit. The alternative is that most patients will receive NSAIDs which are well known to be drugs associated with hospital admissions – heart failure, renal dysfunction, AKI and GI bleeds are all well-known issues. Many CCGs have been working hard to reduce the prescribing of NSAIDs and this would seem contrary to that aim. Also, the evidence base for NSAIDs doesn't seem to be that much better than the paracetamol evidence – the trials considered are all short-term (and so take little account of long-term side effects) and although the results are often statistically significant their clinical significance would appear to be questionable. Prescribing more NSAIDs would also lead to increased prescribing of PPIs, again increasing the patient's medication burden and the risk of side effects. The comment from our GPs is that they will ignore that bit of the guideline and continue to prescribe paracetamol, which begs the question what other bits of the guideline will they choose to ignore if their confidence in the advice has been reduced. **NICE reply**: Although the GDG recognise these concerns, the recommendations drafted for this guideline are based on the evidence available. As detailed in section 16.6 of the guideline, the GDG were unable to recommend paracetamol due to the very limited evidence available; 1 RCT, which showed no clinical benefit for paracetamol in any of the outcomes reported. (p60/111)

Risk with opioids:

- The PCR Society (PCR) welcomes the NICE draft guidelines on low back pain and sciatica. The PCR agrees with the concerns about inappropriate prescribing and over medicalization of back pain. In particular we agree that Paracetamol and Opioids should not be first line medications. The PCR is concerned that Paracetamol is ineffective and has associated clinical risks making it effectively a clinically dangerous placebo for the majority of patients- see Appendix of OA NICE guidelines (2015). The recent data from the National institute of Health (NIH) in America has highlighted that significant numbers of patients become addicted to opioids from prescription drugs and there is an associated rise in mortality from the inappropriate use of these drugs. **No answer from NICE**.(p60/111)

NICE changes in the final version of the guideline (November 2016)

In the Trade-off between net clinical effects and costs, one part of and one sentence were added**:**

No economic evidence for opioid use for the management of acute low back pain was identified and so the GDG decided not to recommend them as a first line option for this group. However, the GDG discussed the possible alternative for people with acute back pain that cannot use NSAIDs and agreed that weak opioids (with or without paracetamol) could be a cost effective option as they would provide pain relief at an acceptable cost.

NICE final recommendations on paracetamol (November 2016)
Do not offer paracetamol alone for managing low back pain.

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017
The recommendation on paracetamol is considered acceptable also for people with radicular pain

KCE 2017 final recommendations on paracetamol (February 2017)
15. Do not routinely offer paracetamol (as single medication) for managing low back pain with and without radicular pain.
(weak recommendation based on low to very low evidence from RCTs)

7.14.4. Specific points of discussion for opioids

NICE draft recommendations on opioids (March 2016): 3 clinical and 1 research recommendations
23. Do not routinely offer opioids for managing acute non-specific low back pain.
24. Consider weak opioids (with or without paracetamol) for managing acute non-specific low back pain only where a NSAID is contra-indicated, not tolerated or has been ineffective.
25. Do not offer opioids for managing chronic non-specific low back pain.
Research recommendation 2. What is the clinical and cost-effectiveness of codeine with and without paracetamol for the acute management of non-specific low back pain?
(Codeine, often in combination with paracetamol, is commonly prescribed in primary care to people presenting with acute low back. This is often the case for people who are intolerant of NSAIDs or for whom there are contra-indications to these medications. Whilst there is evidence that opioids are not effective in chronic low back pain, there are relatively few studies that look at the acute low back pain scenario that is commonly experienced in primary care. In addition it is not known whether the addition of paracetamol to codeine has a synergistic effect in the treatment of back pain.)

Belgian GDG considerations on opioids mentioned in the Lime survey at the beginning of September 2016
NICE recommendation 23. Do not routinely offer opioids for managing acute non-specific low back pain.
Agreement with the content of the NICE recommendation 23: 11 Yes, 0 No, 0 no opinion, 0 out of competence, 0 no answer, 6 not completed

- **Comments from those who do not agree: NONE**
- **Other comments:**
  - Can be stronger formulated, cfr US CDC guidelines & recommendations JAMA, April 2016.

Strength of the recommendation 23: According to NICE formulation, it is a weak recommendation

GRADE Factors	
Balance between desirable and undesirable effects	There was no evidence for the use of opioids in acute low back pain or for the management of acute episodes of low back pain.
Quality of evidence	NA
Values and preferences	

Cost (resource allocation)	No economic or clinical evidence for opioid use for the management of acute low back pain was identified.

Agreement with the strength of the NICE recommendation 23: 7 strong, 2 weak, 1 no opinion, 1 no answer, 6 not completed

- **Comments for a weak recommendation**
  - Weak because the lack of strong evidence and the potential harmful side effects.
- **Comments for a strong recommendation**
  - Quality of evidence

NICE draft recommendation 24. Consider weak opioids (with or without paracetamol) for managing acute non-specific low back pain only where a NSAID is contra-indicated, not tolerated or has been ineffective.

Agreement with the content of the NICE draft recommendation 24: 11 Yes, 0 No, 0 no opinion, 0 out of competence, 0 no answer, 6 not completed

- **Comments from those who do not agree: NONE**
- **Other comments:**
  - Systematic associations (in the same pill) should not be encouraged.
  - In French, I would write "opioide faible" instead of "léger"

Strength of the recommendation 24: According to NICE formulation, it is a weak recommendation

GRADE Factors	
Balance between desirable and undesirable effects	There was only one study including codeine with paracetamol compared to the NSAID ketorolac. This study found no difference in pain outcomes with the combination at less than 4 months, but more adverse events.
Quality of evidence	High quality of a single study
Values and preferences	The combination codeine + paracetamol is one of the most commonly prescribed analgesics in England. With the known side effects of NSAIDs, the GDG acknowledged the need for an alternative treatment option for people with contraindications to NSAIDS use. The NICE GDG therefore decided, on consensus, to consider offering codeine (with or without paracetamol) alongside a research recommendation.
Cost (resource allocation)	No data

Agreement with the strength of the NICE recommendation 24: 2 strong, 8 weak, 0 no opinion, 1 no answer, 6 not completed

- **Comments for a weak recommendation**
  - Because of the lack of strong evidence, I would consider it as weak. Could it be interesting to make a suggestion to use preferably tramadol instead of **codeine** (worse profile: constipation, addiction...)?
  - Patients values & preferences
- **Comments for a strong recommendation: none**

NICE draft recommendation 25. Do not offer opioids for managing chronic non-specific low back pain.

Agreement with the content of the NICE draft recommendation 25: 8 Yes, 3 No, 0 no opinion, 0 out of competence, 0 no answer, 6 not completed

- **Comments from those who do not agree:**

- In selected cases (for instance nociceptive pain due to clear degeneration) it can be useful. Therefore I would rather suggest: not routinely or in selected cases.
- When you have severe complaints (e.g.: severe spondylatrosis) and other pain killers do not help enough, this may be an opportunity.
- I would accept the use of weak opioids, to a max. dose of 400 mg/d (tramadol, tilidine)

- **Other comments:**
  - Addiction problems
  - It's sure!

Strength of the recommendation 8: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	There was some evidence of a small benefit in terms of pain and function versus placebo in chronic LBP, but these effects were not judged to be clinically important by the NICE GDG. The evidence suggests that there was no reason to believe different strength opioids would have different clinical effectiveness in a population with chronic low back pain. Moreover, there was an increase in adverse events observed in those receiving opioids as a single agent. The GDG concluded that the potential harms of opioid treatment for chronic low back pain when used as a single agent outweighed the benefits and agreed a recommendation that opioids should not be used in the management of chronic low back pain.
Quality of evidence	From very low to moderate
Values and preferences	
Cost (resource allocation)	The economic evidence for opioids (Wielage et al 2013) indicated that these were not cost-effective for the management of chronic low back pain.

Agreement with the strength of the NICE recommendation 25: 3 strong, 4 weak, 1 no opinion, 0 no answer, 9 not completed

- **Comments for a weak recommendation**
  - Quality of evidence
- **Comments for a strong recommendation: none**

<u>NICE draft research recommendation 2. What is the clinical and cost-effectiveness of codeine with and without paracetamol for the acute management of non-specific low back pain?</u>

Agreement with the RESEARCH recommendation 2: 6 Yes, 2 No, 2 no opinion, 1 out of competence, 0 no answer, 6 not completed

- **Comments from those who do not agree:**
  - Systematic associations (in the same pill) should not be encouraged. Codeine is unpredictably metabolised
  - Dit is een vraag en geen aanbeveling.
- **Other comments:**
  - This is a question, not a recommendation

But at this time, the most frequent prescription concerns association tramadol and paracetamol...

Belgian GDG comments on opioids during the GDG meeting on the 15th September 2016

<u>NICE recommendation 23. Do not routinely offer opioids for managing acute non-specific low back pain</u>

- The terms “non-specific” has to be removed.
- The reference of the Alberta guideline, proposed by one respondent, does not justify a change in the recommendation.
- The word “routinely” evokes a weak recommendation. However, according to the GDG members there should be a difference between weak and strong opioids. We cannot recommend to offer strong opioids in acute LBP but it is almost not possible to avoid codeine and tramadol in the management of some patients.
- With the word “routinely” it is allowed to prescribe weak opioids if necessary. Moreover the recommendation 24 confirms this option.

⇨ The NICE recommendation 23 is accepted with a minor change

NICE recommendation 24. Consider weak opioids (with or without paracetamol) for managing acute non-specific low back pain only where a NSAID is contra-indicated, not tolerated or has been ineffective.

- The GDG discusses the potential difference in adverse events between codeine and tramadol and does not reach a consensus. The side effects is more patient’s dependent than substance dependent.
- However, codeine should not be prescribed at first line given its characteristics and the existence of rapid and poor metabolizers.
- By the way, a fixed association “paracetamol tramadol” is not recommended by the CBIP/BCFI: “L'association fixe de paracétamol + tramadol n’a pas beaucoup de sens: le tramadol est difficile à doser et les deux constituants ont une demi-vie très différente/De vaste associatie van paracetamol + tramadol heeft weinig zin: men kan tramadol moeilijk titreren en de halfwaardetijd van de twee bestanddelen is sterk verschillend.” This should be mentioned in the text of the guideline.
- The terms “non-specific” should be removed.

- The NICE recommendation 24 is accepted with a minor change

NICE recommendation 25: Do not offer opioids for managing chronic non-specific low back pain.

- The GDG discusses the utility of opioids in chronic LBP (sometimes useful) and the strength of the NICE recommendation (strong is too hard). The lack of differentiation between weak and strong opioids is a weakness in this recommendation.
- Adding “routinely” is suggested since strength of opioids was no specified.
- Adding “At shortest duration possible, lowest effective dose possible” is also proposed to decrease some risks (adverse effect but also addiction).
- But the risk profile is not the same for NSAIDS (risk at short term) and for opioids (more long term).
- For strong opioids, the recommendation could be accepted but it is less clear for weak opioids.
- Finally a detailed analysis of the NICE review and some recent publications is needed to support the GDG decision.

⇨ The NICE recommendation 25 will be re-proposed in the lime survey 4, with a summary of the recent publication on paracetamol efficacy for LBP.

NICE research recommendation 2. What is the clinical and cost-effectiveness of codeine with and without paracetamol for the acute management of non-specific low back pain?

- The GDG emphasises the use of the combination tramadol + paracetamol in Belgium rather than codeine + paracetamol as quoted by the NICE GDG and decides not to support the NICE research recommendations 2.
- A research on tramadol + paracetamol is mentioned but finally not retained given the lack of consensus.

- The NICE research recommendation 2 will be not included in the Belgian guideline

Additional information on opioids proposed to the GDG after the meeting (September 2016)

Besides the NICE analysis regarding the place of opioids in the management of LBP, two additional reviews were identified by the GDG (see tabe 34):

- The Cochrane review by Chaparro et al in 2013
- A review by Abdel Shaheed et al published in the JAMA Intern Med in 2016

Table 40 – Clinical effectiveness of steroids for low back pain: three systematic reviews

Sources	NICE 2016	Chaparro Cochrane 2013	Shaheed 2016
Included study	**For chronic LBP**, 12 RCTs • Weak opioids vs placebo o Tramadol: alone (Schnitzer 2000; Vorsanger 2008) or the combination tramadol/paracetamol (Ruoff 2003; Peloso 2004**; Lasko 2012; Hyup lee 2013; Schiphorst preuper 2014**). o Transdermal buprenorphine: (Steiner 2011). • Strong opioids vs placebo o Tapentadol (Buynak 2010). o Morphine (Chu 2012) o Oxycodone (**Hale 2005**; Webster 2006; **Vondrackov 2008; Buynak 2010; Katz 2015**). o Hydromorphone (Hale 2010) **For acute, subacute LBP or nociceptive pain**, 3 RCTS, all comparing weak opioids vs other active medication **In subacute LBP** (of at least moderate intensity without any signs of radiculopathy, for at least 10 to 42 days before enrolment), 1 RCT. o Combination Tramadol + paracetamol vs tramadol (Perrot 2006) : only adverse events quoted by NICE **In neuroceptive or neuropathic LBP,** 1 RCT: o Combination tramadol + paracetamol vs anticonvulsants Pregabalin 75 mg (Sakai 2016): only adverse events quoted,	**For chronic LBP**, 15 RCTs • Weak opioids vs placebo or celecoxib o Tramadol: alone (Schnitzer 2000; Vorsanger 2008; **O'Donnell 2009; Uberall 2012**) or the combination tramadol/paracetamol (Ruoff 2003; Peloso 2004). o Transdermal buprenorphine: (**Gordon 2010**; Steiner 2011) • Strong opioids vs placebo o Tapentadol (Buynak 2010). o Morphine (**Khoromi 2007**; Chu 2012) o Oxymorphone (**Hale 2007; Katz 2007**) o Oxycodone (Webster 2006) o Hydromorphone (Hale 2010)	**For chronic LBP**, 19 studies 1 study for subacute LBP • Weak opioids vs placebo o Tramadol: alone (Schnitzer 2000; Vorsanger 2008; Uberall 2012) or the combination tramadol/paracetamol (Ruoff 2003; Peloso 2004, Schiphorst 2013). o Transdermal buprenorphine: (Gordon 2010; Steiner 2011) • Strong opioids vs placebo o Tapentadol (Buynak 2010). o Morphine (Chu 2012) o Oxymorphone (Hale 2005, Hale 2007**;** Katz 2007) o Oxycodone (Hale 2005, Webster 2006) o Hydromorphone (Hale 2010) o Hydrocodone (**Rauck 2014**) o Combination oxycodone + naloxone (**Cloutier 2010**) • Opioids vs opioids o Transdermal fentanyl vs oral morphine **(Allan 2005)** o Transdermal buprenorphine or oxycodone vs other dosis of Transdermal buprenorphine or oxycodone **(Steiner 2011)** o Tramadol + paracetamol vs tramadol **(Perrot 2006**)

	In acute LBP with or without sciatica, 1 RCT o Combination codeine + paracetamol vs NSAID ketorolac (Innes 1998)		
Population	• For all comparison vs placebo: chronic LBP, without sciatica except 2 RCTS for Tramadol + paracetamol vs placebo carried out in LBP population with or without sciatica (Hyup lee 2013 ; Schiphorst preuper 2014). • For pain intensity: N=3268, 12 studies • For function: N=1510, 7 studies • For QoL: N=389, 1 study SF-12 or 296, 1 study SF-36 • For responder criteria ≥30% in pain intensity on NRS scale: N=389, 1 study • For responder criteria ≥50% in pain intensity on NRS scale: N=389, 1 study • For adverse events: N=1804, 7 studies For head-to-head comparisons, 1 study on acute, another on subacute LBP and a third on neuropathic and nociceptive pain.	For all: persistent pain in the low-back for at least 12 weeks, with or without radiating symptoms to the legs or prior low-back surgery syndrome). For Tramadol vs placebo: N=1378, 5 studies For Tramadol vs celecoxib: N=1583, 1 study For Buprenorphine vs placebo: N=653, 2 studies For strong opioids vs placebo: N=1887, 6 studies All RCTS conducted in US except for one in Canada (Gordon 2010) and another in Germany (Uberall 2012).	Chronic LBP patients except Perrot 2006 which focused on subacute LPB patients (and also on tramadol + paracetamol vs tramadol alone) 1 study with opioid-experienced patients (Hale 2007) Many RCTS conducted in US except for two in Canada (Cloutier 2013, Gordon 2010), one in The Netherland (Schiphorst 2013), and 2 in Germany (Uberall 2012, Perrot 2006). One RCT concerned US, Australian and Canadian centers (Buynack).
Intervention	Tramadol 100-400 mg/day, Buprenorphine 10 or 20 mcg/hour, Oxycodone 10-160 mg/day, sustained acting morphine 15 mg	Opioids to be prescribed for a period of one month or longer	In the 13 RCTs evaluating short-term efficacy, the morphine equivalent dose ranged from 40.0 mg to 242.7 mg per day.
Comparator	Placebo except for the 3 head-to-head comparisons	Placebo for all except celecoxib in 1 RCT (O'Donnell 2009).	Placebo except for 3 RCTs
Rescue medication	Paracetamol (1-2 g/day), Ibuprofen (800 mg/day), previous antidepressants; oral morphine sulphate (15mg q4-6hrs) for 1 study on oxycodone (Hale 2005), hydromorphone immediate release for 1 RCT on hydromorphone extended release (Hale 2010), immediate release oxycodone during the first 6 days for 1 RCT on buprenorphine (Steiner 2011)	Paracetamol, NSAIDs and non-opioid analgesics (antidepressants or anticonvulsants) were used in several studies; Steiner 2011 allowed paracetamol plus ibuprofen and oxycodone IR during the first six weeks of the double-blind phase, Hale 2010 allowed hydromorphone immediate release (study on hydromorphone extended release) and Katz 2007 oxymorphone immediate release (study on oxymorphone extended release)	Not quoted
Risk of bias	From very low to moderate	Ranged between "very low" and "moderate". • High drop-out rates (attrition bias)	Typically of high quality with a mean (SD) PEDro score of 7.8 (1.5).

		• Enriched enrolment design in many trials which is known to under-report adverse events • Short duration (<15 weeks) • Limited interpretability of functional improvement. • Effect sizes medium for pain and small for function. • Limited generalizability (poor description of the study population regarding duration of pain, concurrent treatments, work status, and compensation) • Poor generalizability to populations at high risk for complications.	The effects of single-ingredient and combination opioids were minimal and approximately half the20-point threshold or clinical importance. The evidence for short term efficacy was downgraded 1 level for publication bias (Egger P= .007). There were no long-term outcomes data.
Study length	From 10 days (Perrot 2006) until 12 weeks	>4 weeks but <15 weeks	From 10 days (Perrot 2006) until 12 weeks (except 13 mo for transdermal fentanyl vs oral morphine in Allan 2005)
Results	**Opioids versus placebo, in chronic LBP, mainly without sciatica** • Evidence (not quoted by NICE in the text but found in the Forest plot) showed a CIB on quality of life (SF-36) for physical role, bodily pain, emotional role and mental health in favour of a combination Tramadol + paracetamol (1 study, Ruoff 2003) • Oxycodone had a clinical benefit for physical component of QoL (MID 3.90 [95%CI 1.95, 5.85] and responder criteria for improvement in pain but results favoured placebo for mental QoL score (1 study, Katz 2015, low quality) • Not meta-analysed, Hale 2010: hydromorphone ER significantly reduced pain intensity compared to placebo (at least 30% reduction in diary NRS pain score) • No effect on pain (12 studies, moderate quality) or function (7 studies, moderate quality) • Clinically important harm in terms of increased adverse events with opioids (7 studies; very low quality)	• Tramadol was better than placebo for pain (Standardized mean difference-SMD -0.55 [95%CI -0.66 to -0.44]; low quality evidence) and function (SMD -0.18 [95% CI -0.29 to -0.07]; moderate quality evidence). • Transdermal buprenorphine (2 trials, n= 653) may make little difference for pain (SMD -2.47 [95%CI -2.69 to -2.25]; very low quality evidence), but no difference compared to placebo for function (SMD-0.14 [95%CI -0.53 to 0.25]; very low quality evidence). • Strong opioids were better than placebo for pain (SMD -0.43 [95%CI -0.52 to -0.33]; moderate quality evidence) and function (SMD-0.26 [95% CI -0.37 to -0.15]; moderate quality evidence). • Little difference between tramadol compared to celecoxib (RR 0.82 [95% CI 0.76 to 0.90]; very low quality evidence) for pain relief. • No difference between opioids and antidepressants for either pain or function (very low quality evidence). • Ten studies described one or more of 14 adverse events: People treated with opioids	• Effect of single ingredients opioids on pain at short term (MID −10.1 [95% CI −12.8 to −7.4]; 13 studies; n=3419; moderate quality evidence) and in the intermediate term (MID −8.1 [95% CI −10.2 to −6.0]; 6 studies; n=2605; high quality) • No clinically significant reduction with morphine in disability for the short term (MID −6.3 [95% CI 0.5-12.1]; 1 study; very low quality). • The combination opioïds/analgesic provided moderate quality evidence of pain relief for the intermediate term; MID −11.9 [95% CI −19.3 to -4.4]). • The combination tramadol/paracetamol provided very low quality evidence of pain relief for the short term; MID −8 [95% CI −16.2 to 0.2]). • No significant effect of the combination of tramadol-paracetamol on disability for the short term (MID −6.2 [95% CI −8.5 to 20.9]; 1 study; very low quality) and for the

	Tramadol + paracetamol vs tramadol in subacute LBP (of at least moderate intensity without any signs of radiculopathy, for at least 10 to 42 days before enrolment): • No CIB in adverse events at short term-10 days (1 study; moderate quality; n=119) **Codeine + paracetamol vs ketorolac in acute LBP (**less than 72 hours duration, of at least moderate severity) • No difference in pain outcomes at less than 4 months (at 6 hrs and 1 week), but adverse events more common with the combination tramadol + paracetamol at 1 week (1 study; high quality; n=121). **Tramadol + paracetamol vs pregabalin in neuropathic or nociceptive pain:** • No clinical difference in adverse events between the groups (moderate quality; n = 60).	had a statistically significant higher incidence of nausea (10% [95% CI 7% to 14%], dizziness (8% [95% CI 5% to 11%]), constipation (7% [95% CI 4% to 11%]), vomiting (7% [95% CI 4%to 9%], somnolence (6% [95% CI 3% to 9%]) and dry mouth (6% [95% CI 2% to 10%]) than people treated with placebo. People who received opioids had a < 5% higher incidence of headaches, pruritis, fatigue, anorexia, increased sweating and hot flushes compared to placebo. People treated with either opioids or placebo showed no differences regarding the number of people with upper respiratory tract infection or sinusitis.	intermediate term (MID −3.7 [95% CI −11.8 to 4.4; 1 study; very low quality). • The meta-regression model showed there was a significant effect of opioid dose on treatment effect, with a 12.0 point greater pain relief for every 1 log unit increase in dose (P = .046) (ie, 10 mg of morphine equivalents). The model predicts that clinically important effects are not seen within the dose range evaluated (≤240-mg morphine equivalents per day). • There was statistically significant difference in treatment outcome between different strengths of transdermal buprenorphine for both the short and intermediate term, with the 20-µg/h patch providing greater pain relief than the 5-µg/h patch. • Oxycodone, 40 mg per day, provided greater pain relief than transdermal buprenorphine, 5-µg/h, for both the short and intermediate term. • Eight trials provided details on the proportion of participants experiencing at least 1 adverse event in the run-in and/or RCT phase. Overall, the median rates (interquartile range [IQR]) of adverse events in the RCT phase were 49.1% (44.0%-55.0%) for placebo and 68.9.% (55.0%-85.0%) for treatment groups (risk ratio [RR], 1.3; P < .01).Common adverse events included central nervous system adverse events (headache, somnolence, dizziness), gastrointestinal tract adverse events (constipation, nausea, vomiting), and autonomic adverse events, such as dry mouth.
Funded	Described individually in evidence table	Pharmaceutical industry conducted and sponsored three RCTs	Pharmaceutical industry sponsored 17 RCTs

Comment			Seven of the 13 RCTs evaluating short-term efficacy used an enrichment study design whereby only the participants who responded favorably to the study medication, and tolerated the medicine in the trial run-in phase (prerandomization) were eligible to continue in the trial proper and be randomized to the study treatment. The effect of enrichment study design was not statistically significant (P = .69). Treatment effects are small, being half the threshold for clinical importance. Importantly, the observed magnitude of the treatment effect was similar to that reported for NSAIDs vs placebo in the Cochrane review of NSAIDs (Roelofs 2008). Typically, the trials' estimate of treatment effect was derived from approximately 50% of participants who initially entered the trial, with participants withdrawn mainly because they did not tolerate or respond to the medicine. Taken together, these issues suggested there would be **much lower treatment effects among unselected groups of people new to these medicines**.
Authors' conclusions	There was some evidence of a small benefit in terms of pain and function versus placebo in chronic LBP, but these effects were not judged to be clinically important. The GDG noted that the meta-analysis included a large number of trials, and the effects were very consistent across these trials. Evidence from 1 study reported clinical benefit for opioids in physical component scores of the quality of life measure SF-12. There was no evidence found for the use of opioids in acute LBP or for the management of acute episodes of low back pain and therefore the effectiveness of opioids alone for the	There is some evidence (very low to moderate quality) for short-term efficacy (for both pain and function) of opioids to treat CLBP compared to placebo. The very few trials that compared opioids to non-steroidal anti-inflammatory drugs (NSAIDs) or antidepressants did not show any differences regarding pain and function. The initiation of a trial of opioids for long-term management should be done with extreme caution, especially after a comprehensive assessment of potential risks. There are no placebo-RCTs supporting the effectiveness and safety of long-term opioid therapy for treatment of CLBP.	In people with chronic low back pain, opioid analgesics provide short and/or intermediate pain relief, though the effect is small and not clinically important even at higher doses. Many trial patients stopped taking the medicine because they did not tolerate or respond to the medicine. There is no evidence on opioid analgesics for acute low back pain or to guide prolonged use of these medicines in the treatment of people with chronic low back pain.

	management of acute low back pain could not be determined. There was an increase in adverse events observed in those receiving opioids as a single agent. The GDG concluded that the potential harms of opioid treatment for chronic low back pain when used as a single agent outweighed the benefits and agreed a recommendation that opioids should not be used in the management of chronic low back pain.	

In Cochrane http://www.cochrane.org/CD004959/BACK_opioids-for-the-treatment-of-chronic-low-back-pain

There is some evidence (very low to moderate quality) for short-term efficacy (for both pain and function) of opioids to treat CLBP compared to placebo. The very few trials that compared opioids to non-steroidal anti-inflammatory drugs (NSAIDs) or antidepressants did not show any differences regarding pain and function. The initiation of a trial of opioids for long-term management should be done with extreme caution, especially after a comprehensive assessment of potential risks. There are no placebo-RCTs supporting the effectiveness and safety of long-term opioid therapy for treatment of CLBP.

Results showed that:

- **In chronic LBP, mainly without sciatica**, conflicting results : some small benefits in NICE, Chaparro & Abdel Shaheed but no difference for pain and function in the NICE meta-analysis); The very few trials that compared opioids to non-steroidal anti-inflammatory drugs (NSAIDs) or antidepressants did not show any differences regarding pain and function.
- **In acute LBP or for the management of acute episodes of low back pain,** no evidence found for the use of opioids and therefore the effectiveness of opioids alone for the management of acute low back pain could not be determined.
- None systematic review distinguish weak and strong opioids effects in the results.
- There was an increase in **adverse events** observed in those receiving opioids as a single agent.

Moreover, Chaparro in the Cochrane review quoted 3 other SR on the same topic:

- Furlan 2011 concluded that opioids were more effective than placebo for improving both pain and function in the management of CNCP. The results were significant for both neuropathic and nociceptive pain. Subgroup analyses revealed that only strong opioids (oxycodone and morphine) were statistically more effective in reducing pain but not function when compared to naproxen and nortriptyline.
- Kuijpers 2011 evaluated opioids, antidepressants and NSAIDs for CLBP; however, they excluded patients with sciatica. Several studies included in the Cochrane review were not considered in Kuijpers 2011 due to timing of publication. Their conclusion regarding the effectiveness of opioids does not differ from the Cochrane conclusion.
- Martell 2007 included 15 studies in the literature assessing the efficacy of opioids in CLBP. Nine of the studies considered comparisons among different opioids, while another six compared opioids with placebo or other analgesics. The review authors found that opioids were ineffective in the management of CLBP when compared to the pooled sample of placebo and other analgesics.

In conclusion, several systematic reviews, including different primary studies, stressed that there is a potential effect of opioids in chronic LBP but also an important risk of adverse events that should be taken into account. No difference between strong and weak opioids was showed. There is also no sufficient data on acute LBP.

Belgian GDG comments on opioids during the GDG meeting on the 12th October 2016

NICE recommendation 23. Do not routinely offer opioids for managing acute non-specific low back pain.

- In the Lime survey results, there is a clear disagreement concerning the strength of the recommendation (6 respondents for a weak recommendation, 6 for a strong). However, none GDG members has a robust argument to change from a weak (such as NICE) to a strong recommendation.
- Should we add the word "strong" before opioids and remove the word "routinely"? No because both strong and weak opioids are encompassed in the NICE recommendation. Moreover in case of acute radicular pain, a strong opioid could be useful even if it is not a 'gold' standard.
- Thus, we keep a weak recommendation without adding strong or weak before opioids.
- The terms "non-specific" should be removed.

⇨ **The NICE recommendation 23 is accepted with a minor change**
⇨ ***"Do not routinely offer opioids for managing acute low back pain"***

NICE draft recommendation 24. Consider weak opioids (with or without paracetamol) for managing acute non-specific low back pain only where a NSAID is contra-indicated, not tolerated or has been ineffective.

- Should we remove the word "weak" before opioids given the lack of differentiation between strong and weak opioids in the literature? No because the guideline should cover the majority of the cases and not some selected cases. Strong opioids are not frequently useful for acute LBP (and mainly for radicular pain).
- The terms "non-specific" should be removed.

⇨ **The NICE recommendation 24 is accepted with a minor change**
⇨ ***"Consider weak opioids (with or without paracetamol) for managing acute low back pain only where a NSAID is contra-indicated, not tolerated or has been ineffective."***

NICE draft recommendation 25. Do not offer opioids for managing chronic non-specific low back pain.

- The respondents of the Lime survey did not agree with the NICE recommendation.
  - Some would like to add "routinely".
  - Other want to specify that only strong opioids are concerned.
  - Based on a suggestion of one respondent, the KCE proposes to formulate a recommendation 25bis: "*Consider weak opioids for managing chronic low back pain only in selected cases taking into account the potential adverse effect".*
- During the meeting, the GDG mentioned that:
  - There is no evidence pro the use of opioids in chronic LBP but there is evidence against chronic use of 'strong opioids' because of their harm.
  - The NICE recommendation is too strongly formulated if strong and weak opioids are encompassed. It is better to soften the message.
  - Why do we mention the potential adverse events here and not in other recommendations?
  - If we precise selected cases, we weaken the whole guideline (that should be cover the majority of cases). Moreover we should specify what the selected cases are.
  - The third option is the best one but should be changed: weak or strong opioids should not be mentioned and the selected cases should be replaced by "If it is clinically relevant and considering patient characteristics".

- In Belgium, opioids are used in chronic LBP, mostly weak opioids. However instead of highlighting the difference between weak and strong opioid, we should also stress the importance of the doses (e.g. tramadol OK but no 2X30mg of oxycodone).
- According to the literature review there are small benefits of opioids in chronic LBP. Thus NICE is severe when formulating the recommendation.
- Since we cannot precisely define what is hidden behind the terms "selected cases", we should avoid to use them.
- Finally, a consensus is reached for only inserting "routinely" in the recommendation 25 and not adding a recommendation 25bis on selected cases.

⇨ **The NICE recommendation 25 will be changed as following:**
⇨ **"*Do not routinely offer opioids for managing chronic low back pain*."**

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30 November 2016)

Poor argument pro and important adverse events:

- Warwick Clinical Trials Unit **is** surprised by the recommendation to consider weak opioids (with our without paracetamol) for managing acute non-specific low back pain. The GDG agreed that the efficacy of opioid for low back pain could not be determined. They then proceed to offer this as an option based on a paper by Innes where they conclude that a paracetamol/codeine combination is equivalent to ketorolac. It is not possible to conclude equivalence from this study that was designed as a superiority study. The data in the Forest plot no 948 are the differences in pain scores six hours after an initial dose of study medications. As described in the paper the pain scores improved substantially in both groups with the effects peaking around 2.5 hours. It is highly likely that there will have been little or no actual analgesic effect from either preparation at six hours. Whilst no statistically significant differences were seen in any of the short term outcomes, this study was not designed to show equivalence and cannot be interpreted as such. For this conclusion to be drawn it is necessary for an equivalence margin to have been pre-specified and a per protocol analysis performed. To conclude equivalence it is necessary to measure outcomes just on people who are exposed to the intervention. With the six hour outcomes it is likely there is insufficient drug present for any possible effects to be seen. There are some additional data included in the paper on one week outcomes not presented to the GDG. These again show no statistical difference. However, as 16 participants had withdrawn prematurely because of analgesic inefficiency it is not possible to draw any conclusion about equivalence as a per protocol analysis is not provided. We suggest that is recommendation should be withdrawn. Consequentially recommendation 22 should also be removed. That this study that provided six hour outcomes that are presented in the data synthesis as four month outcomes illustrates a possibly fatal flaw in the approach used by the GDG to assessing the short term effect on pain of analgesic medications. We suggest that this whole section needs revisiting to ascertain if there are short term benefits to be gained from analgesics. **NICE reply: T**he GDG were mindful of the limited evidence base for this recommendation, including the limitations of some of the study follow-up time points, however they acknowledged the need for a treatment option for the subset of people who are unable to take NSAIDs. The recommendation has therefore been modified to specify this and reads as follows: Where an NSAID is contraindicated, not tolerated or has been ineffective consider weak opioids (with or without paracetamol) for managing acute non-specific low back pain only. (p57/222)
- Society for Back Pain Research: The GDG have acknowledged the harmful effects of Opioid. The risk of harm is also relevant for (even weak ones) for acute LBP. We are concerned that many readers could overlook the rather weak caveats regarding opioids and suggested to amend the recommendation: "put in a caution, like for NSAID and if offered, use the lowest effective dose for the shortest possible period of time". The same SH also suggested a research recommendation: "What is the effectiveness and cost effectiveness of combinations of pain relief in people with acute, severe back pain, with or without sciatica which limits activity participation?" **NICE reply**: The GDG recognised that there will be a number of people who won't be able to take NSAIDs, and therefore there needed to be a treatment option for them. As a result of which the GDG developed the recommendation for weak opioids for this subset of people with low back pain. The recommendation has been edited to clarify this; Where an NSAID is contraindicated, not tolerated or has been ineffective consider weak opioids (with or without paracetamol) for managing acute non-specific low back pain only. Research recommendations are developed based on priority areas which the GDG identify from the evidence available for each review question. Based on the evidence, the GDG have formulated a research recommendation looking into the effectiveness of codeine with or without paracetamol for low back pain with or without sciatica. (p64/111)
- PCR Society (PCR) welcomes the NICE draft guidelines on low back pain and sciatica. The PCR agrees with the concerns about inappropriate prescribing and over medicalization of back pain. In particular we agree that Paracetamol and Opioids should not be first line medications. The recent data from the National institute of Health (NIH) in America has highlighted that significant numbers of patients become addicted to opioids from prescription drugs and there is an associated rise in

mortality from the inappropriate use of these drugs4. In the USA it has been estimated that 81.8% of unintentional deaths from all prescription drugs were due to opioids. It is highly likely that these statistics are similar in the UK. **No reply** (p60/111)

- PCR: The recent data from the National institute of Health (NIH) in America has highlighted that significant numbers of patients become addicted to opioids from prescription drugs4- medication often prescribed initially with the best of intentions. It has been shown by the NIH that this has significant negative effects on patients' mortality and morbidity. It is highly likely that the UK has a similar issue and PCR member's clinical experience is suggestive that this is a problem, especially in patients who are unemployed, from lower social classes or end-up in prisons. The North of England low back pain guidelines (on the Map of Medicine) working group have identified that opiate prescribing is a significant problem in the North of England. There appears to be poor understanding of this within the medical community given the level of opiate prescribing for low back pain. There is both a need to ensure that the new guidelines highlight more clearly the clinical risks and concerns of opiate prescribing. More importantly there is a need to consider these 'addicted' patient populations within the clinical guidelines and how best to manage them**. NICE answered** that the GDG recognise the risks associated with opioid use and factored in the potential harms of opioids when considering the evidence. Based on this, they agreed a recommendation that opioids should not be used in the management of chronic low back pain. 'Addicted' patient populations are beyond the scope of this guideline. (p62/111)
- Spine Intervention Society agrees with using the lowest effective dosage of non-steroidal anti-inflammatories. The guidelines recommend "weak" opioids if non-steroidal anti-inflammatory drugs (NSAIDs) are contraindicated. The guidelines then recommend against selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and anti-convulsants. While the evidence for the use of other medications is not convincing, strong evidence supporting opioid use to treat chronic pain lasting > 3 months is lacking. Offering only an opioid alternative may propagate further expansion of opioid use that has already resulted in accidental overdoses and deaths resulting in an opioid crisis of enormous proportions over the last two decades. In fact, the U.S. Centers for Disease Control and Prevention (CDC) guidelines for prescribing opioids emphasize that, "of primary importance, non opioid therapy is preferred for treatment of chronic pain." (http://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm) Physicians need options, and patients require effective treatment with safe therapeutic indices. The guidelines include psychotherapy in their algorithm, but discount the use of other medications for treating pain. Anticonvulsants like gabapentin and pregabalin are known to be very effective in the treatment of sciatica. Cymbalta is an SNRI shown to be effective in the treatment of musculoskeletal pain. These drugs are opioid alternatives with acceptable therapeutic indices. **NICE reply: T**he GDG agreed it was appropriate to recommend against the use of opioids for chronic pain, but did recognise the need to provide an alternative pharmacological treatment option for people with acute low back pain who were unable to take NSAIDS. They therefore agreed that weak opioids could be considered only in this context and that short term acute use only could be considered. Pharmacological treatment of sciatica is beyond the scope of this guideline and a cross-referral to NICE CG173 for Neuropathic pain is included in the recommendations. (p81/111)

Utility of the recommendation on weak opioid in acute LBP?

- MPP is not sure if this rec is slightly redundant – there will be a lot of people can't take NSAIDs (due to AEs, contraindications, other meds etc). The SH suggested losing this rec and just state in whom they can be used (1.2.21). **NICE answered** that they however believe it's important to note that opioids should not be routinely used for acute low back pain as the evidence reviewed did not support their use. The subsequent recommendation is only specific to those who can't tolerate or for whom NSAIDs are unsuitable, and is a clarification of when opioids can be considered, so the two recommendations should both be included for clarity. (p212/222)

Classification of weak opioids?

- Napp Pharmaceuticals suggested it may be useful to provide a classification of weak opioids to support the recommendation that weak opioids be considered for patients with acute low back pain that are unsuitable for NSAIDs. **NICE reply:** Weak opioids are defined in the BNF. Therefore NICE does not think this need to be specified within the recommendation.(p1/222)

Question of dose

- Grunenthal: Most pharmacological therapies have dose dependent limitations to treatment therefore it is inequitable to only highlight the limitations to opioids in this section. Furthermore there is no acknowledgement of the fact that drugs acting on opioid receptors have different side effect profiles (several references). **NICE reply:** Evidence for tapentadol was included in this guideline as a form of opioid, however the GDG did not look at within-class comparisons. Therefore tapentadol was not be directly compared to other opioids. Evidence for adverse events was sought for all pharmacological groups included in the review and highlighted where available. (p50/111)

- Grunenthal: Failing to ensure that equianalgesic doses are included in the table of the costs of analgesics results in a distorted view of the comparative annual costs of opioid therapy. The equianalgesic dose ratio of tapentadol to oxycodone is 5:1. Therefore the equianalgesic dose of 30mg oxycodone is 150mg of tapentadol per day at an annual cost of £487.08, similar to the cost of oxycodone. **NICE answered** that there was an explanation in footnote b in the table: the cost per day is calculated based on the maximum recommended dosage as described in the BNF. The costs presented in the table are only indicative as we are aware that dosages would vary for each individual patient.(p50/111)

Efficacy of tapentadol:

- Grunenthal: By excluding the pharmacological management of low back pain with sciatica and referring to the clinical guideline on neuropathic pain (CG 173) this review inadvertently excludes pertinent evidence on the use of tapentadol prolonged release (PR); the most recently introduced strong centrally acting analgesic… (several references). The above-mentioned evidence suggests that tapentadol PR exhibits an improved risk vs benefit profile and therefore provides a suitable alternative to conventional strong opioids as part of the holistic management of severe chronic low back pain, particularly in patients where a neuropathic component to their pain cannot be excluded. Given the extended remit of the revised guideline to include sciatica, consideration should be given to including evidence on the pharmacological management of low back pain with sciatica published since the neuropathic pain guideline (CG 173) in November 2013. **NICE reply:** Since CG173 was published in 2013 and updated in December 2014, and included sciatica within the conditions covered, it was agreed that pharmacological management of sciatica did not need to be included within the scope of this update (p48/111)
- Grunenthal: This evidence statement fails to capture the favourable clinical benefit of tapentadol over placebo in terms of physical quality of life (least squares mean difference in; physical component summary (2.3), physical functioning (4.1), role physical (9.9) body pain (5.5) and vitality (3.2); and the 30% and 50% responder criteria for improvement in pain severity observed in the study by Buynak et al. (46% and 43% increase in the proportion of patients experiencing a ≥ 30% and ≥ 50% improvement s respectively). **NICE answered** that the benefits of tapentadol have been captured within the evidence statements. However, since the GDG consider evidence for opioids as a whole rather than for each type of drug included in this category, the evidence statements will not specify which opioid is being referred to for the outcomes mentioned. (p50/111)

Distinction between acute and chronic LBP.

- MPP noticed that opioids is the only class of drug in which the distinction between acute and chronic back pain is made (with all other rec just referring to 'non-specific low back pain'. I assume this is because of concerns about long-term opioid use! How should patients who present with acute pain which is adequately managed with opioids be managed? Is a time limit for 'acute treatment' needed (ie no more than 4 weeks). **NICE reply:** Recommendation 25 states 'do not offer opioids for managing chronic non-specific low back pain'. In terms of acute low back pain, recommendation 23 states 'do not routinely offer opioids for managing acute non-specific low back pain'. When considering the evidence, the GDG found no evidence for the use of opioids in acute low back pain or for the management of acute episodes of low back pain and therefore the effectiveness of opioids alone for the management of acute low back pain could not be determined from this review.(p213/222)

NICE changes in the final version of the guideline (November 2016)

In the Trade-off between net clinical effects and costs, one part of and one sentence were added**:**

No economic evidence for opioid use for the management of acute low back pain was identified and so the GDG decided not to recommend them as a first line option for this group. However, the GDG discussed the possible alternative for people with acute back pain that cannot use NSAIDs and agreed that weak opioids (with or without paracetamol) could be a cost effective option as they would provide pain relief at an acceptable cost.

NICE final recommendations on opioids (November 2016)

24. Consider weak opioids (with or without paracetamol) for managing acute low back pain only if an NSAID is contraindicated, not tolerated or has been ineffective.
26. Do not routinely offer opioids for managing acute low back pain (see recommendation 24).
27. Do not offer opioids for managing chronic low back pain.

Research recommendations

2. What is the clinical and cost effectiveness of codeine with and without paracetamol for the acute management of low back pain?

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

The recommendations on opioids are considered acceptable also for people with radicular pain.

KCE 2017 final recommendations on opioids (February 2017)

13. Think about weak opioids (with or without paracetamol) for the shortest period possible for managing acute low back pain with and without radicular pain only if an NSAID is contraindicated, not tolerated or has been ineffective.

(consensus-based experts opinion)

14. Do not routinely offer opioids for managing chronic low back pain with and without radicular pain.

(weak recommendation based on moderate to very low evidence from RCTs)

7.14.5. Specific points of discussion for antidepressants

NICE draft recommendation on antidepressants

26. Do not offer selective serotonin reuptake inhibitors, serotonin–norepinephrine reuptake inhibitors or tricyclic antidepressants for managing non-specific low back pain.

Belgian GDG considerations on antidepressants mentioned in the Lime survey at the beginning of September 2016

Agreement with the content of the NICE recommendation 26: 8 Yes, 2 No, 0 no opinion, 1 out of competence, 0 no answer, 6 not completed

- **Comments from those who do not agree:**
  - I agree for SSRI's, but not for SNRI's. There are several RCT's showing a positive effect of duloxetine compared to placebo in LBP (especially if there is a neuropathic component). And what about LBP with sciatica (neuropathic component)?
  - I'm surprised that no distinction is made between acute and chronic pain. SNRIs or tricyclics (but not SSRIs), if clearly not indicated for acute low back pain, can be useful for chronic pain (where central sensitisation and/or a neuropathic component may be present).
- **Other comments: none**

Strength of the recommendation 26: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	No clinically important difference was observed compared with placebo for any of the reported critical outcomes (pain, function and psychological distress) for SSRIs, SNRIs and TCAs in chronic LBP. An increased in adverse events was observed with SSRIs and SNRIs.
Quality of evidence	From very low to moderate
Values and preferences	The GDG considered that consistent evidence from these RCTs for each of the antidepressant classes reviewed was sufficient to warrant a recommendation to advise against the use of SSRIs, SNRIs and TCAs in this population.
Cost (resource allocation)	The economic evidence for antidepressants (Wielage et al 2013) indicated that these were not cost-effective for the management of chronic low back pain.

Agreement with the strength of the NICE recommendation 26: 5 strong, 2 weak, 0 no opinion, 1 no answer, 9 not completed

- **Comments for a weak recommendation: none**
- **Comments for a strong recommendation: none**

Belgian GDG comments on antidepressants during the GDG meeting on the 15th September 2016

NICE recommendation 26. Do not offer selective serotonin reuptake inhibitors, serotonin–norepinephrine reuptake inhibitors or tricyclic antidepressants for managing non-specific low back pain.

- The GDG discusses the potential efficacy for SNRI's. Several RCT's showed a positive effect of duloxetine compared to placebo in LBP (especially if there is a neuropathic component). The FDA approved Duloxetine for chronic LBP without neuropathic and musculo-skeletical pain.
- Add 'routinely" is proposed to open the door for the use of SNRIs
- The lack of distinction between acute and chronic pain is surprising. One suggests to specify "for chronic LBP".
- Finally a detailed analysis of the NICE review and some recent publications is needed to support the GDG decision.

⇨ The NICE recommendation 26 will be re-proposed in the lime survey 4, with a summary of the recent publication on duloxetine efficacy for LBP.

Additional information on antidepressants proposed to the GDG after the meeting (September 2016)

A quick search in Medline was performed by a GDG members (PVW) and summarised by the KCE.

One systematic review and 2 RCTs were found. All concerned chronic LBP with or without sciatica:

- A systematic review from US (Chou 2016) concluded that "For chronic low back pain, effective therapies versus placebo, sham, no treatment, usual care, or wait list are NSAIDs, opioids, tramadol, duloxetine, multidisciplinary rehabilitation, acupuncture, and exercise (SOE: moderate) and benzodiazepines, psychological therapies, massage, yoga, tai chi, and low-level laser therapy (SOE: low); spinal manipulation was as effective as other active interventions (SOE: moderate). The results for Duloxetine is based on the same 3 RCTs than NICE. They highlighted the efficacy of Duloxetine on pain intensity (differences, 0.58 to 0.74 on a 0 to 10 scale i.e. MID>1!) and better function (differences, 0.58 to 0.74 on the Brief Pain Inventory Interference scale) vs. placebo**.**
- One cross-over RCT (Schukro, Anaesthesiology 2016) found significantly lower pain scores (VAS) in patients with neuropathic pain during the duloxetine phase vs placebo after 4 weeks (4.1 ± 2.9 vs 6.0 ± 2.7; P=0.001), corresponding to an average pain reduction of 32%. Adverse events were distributed equally between the duloxetine (65%) and the placebo phases (62%) (P=0.5).
- One RCT (Konno, in press, Spine 2016) focused on the comparison of duloxetine versus placebo and found significant improvement in BPI average pain at week 14 (-2.43 ± 0.11 vs -1.96±0.11) and significant improvements in secondary outcomes (e.g. least pain, pain right now, patient's global impression of improvement, clinical global impressions of severity, function). Adverse events occurred at a significant higher incidence in the duloxetine group but most of them were mild or moderate in severity and were resolved or improved. The authors concluded that duloxetine 60mg was effective and well tolerated in Japanese chronic LBP patients.

In conclusion, new evidence suggested a positive effect of fluoxetine in chronic LBP.

Belgian GDG comments on antidepressants during the GDG meeting on the 12th October 2016

NICE recommendation 26. Do not offer selective serotonin reuptake inhibitors, serotonin–norepinephrine reuptake inhibitors or tricyclic antidepressants for managing non-specific low back pain.

- The respondents of the Lime survey agreed with the recommendation but proposed to change from a strong to a weak recommendation.
- In the NICE recommendation on pharmacological interventions for neuropathic pain, NICE quoted the amitriptyline and the duloxetine among the options of initial treatment.
- Should we separate SSRI from the two other categories?
- The literature on duloxetine is recent but for TCA there are old studies.
- By adding “routinely” we open the door for the use of SNRIs and/or tricyclic antidepressants. But it is too soft given evidence against the use of SSRIs. There is an agreement for the recommendation “Do not offer” SSRIs and “do not routinely offer” TCAs and SNRIs (first choice TCA based on old literature).
- The TCAs and SNRIs should never be used in acute LBP. However if we formulate “do not routinely offer TCAs and SNRIs in chronic LBP”, there is a risk of misunderstanding (such as you cannot offer them in chronic but you can offer them in acute LBP).
- Thus, a footnote will be added specifying the situations where antidepressants are allowed.
- Each recommendation that have led to a broad discussion will be presented in the Belgian guideline with a summary of the main points of the discussion.

⇨ **The NICE recommendation 26 will be changed as following:**

⇨ **“*Do not offer selective serotonin reuptake inhibitors and do not routinely offer tricyclic antidepressants or serotonin–norepinephrine reuptake inhibitors* for managing low back pain*.”**

⇨ ***This recommendation is applicable only in chronic LBP; the use of antidepressants is not recommended in acute LBP.***

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30 November 2016)

Central sensitisation in long-term pain:

- British Pain Society: The proposal to actively recommend against any attempts with adjuvant analgesics (tricyclics and antidepressants) to alleviate chronic non-specific background pain seems to ignore clinical reality and research findings of central sensitisation in most patients with long-term pain. The review of pharmacological therapies restricts itself to only examining non-specific low back pain (i.e. excluding sciatica) whereas the remainder of the guidance considers low back pain with or without sciatica. I believe that this will be confusing to non-specialist readers. Neuropathic pain is covered in other NICE guidance, but patients with sciatica rarely present as people with just a well-defined neuropathic leg pain and most will present with accompanying back pain. In these instances the non-specialist may just recall the headlines of the NICE low back pain guidance and conclude that there are hardly any therapies that are worth trialling and patients won't be given medication that could well help (such as Amitriptyline, Duloxetine, Gabapentin and Pregabalin which NICE Guideline CG173 suggests may help). (p35/111) **NICE reply**: The recommendations made have been based on the evidence that was reviewed. It was agreed that there was no evidence of benefit of tricyclic antidepressants for low back pain, and therefore they should not be recommended. Unfortunately we were unable to cover sciatica within this review as this is already covered by the neuropathic pain guideline as you highlight. We acknowledge the concerns you raise regarding the gap that may occur for people with sciatica without well-defined neuropathic pain symptoms and have highlighted this to NICE.(p34/111)

NICE changes in the final version of the guideline (November 2016): none for antidepressants

NICE final recommendations on antidepressants (November 2016)

28. Do not offer selective serotonin reuptake inhibitors, serotonin–norepinephrine reuptake inhibitors or tricyclic antidepressants for managing low back pain.

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

The recommendation on antidepressants is considered particularly acceptable for people with radicular pain.

KCE 2017 final recommendations on antidepressants (February 2017)

16. Do not offer selective serotonin reuptake inhibitors for managing low back pain with or without radicular pain.

17. Do not routinely offer tricyclic antidepressants or serotonin–norepinephrine reuptake inhibitors for managing low back pain with or without radicular pain. This recommendation is applicable only for chronic pain; the use of antidepressants is not recommended in acute pain.

(weak recommendations based on moderate to very low evidence from RCTs)

7.14.6. Specific points of discussion for anticonvulsants

NICE draft recommendation on anticonvulsants

27. Do not offer anticonvulsants for managing non-specific low back pain.

Belgian GDG considerations mentioned in the Lime survey at the beginning of September 2016

Agreement with the content of the NICE recommendation 27: 8 Yes, 2 No, 0 no opinion, 1 out of competence, 0 no answer, 6 not completed

- **Comments from those who do not agree:**
  - I agree for LBP, but not for LBP with sciatica.
  - Same remark as for antidepressants : these drugs may be useful in chronic pain

Strength of the recommendation 8: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	• Inconsistent evidence relative to gabapentinoids versus usual care on pain but more adverse events • Clinically important for both function and pain severity for topiramate, but this drug is not commonly used for low back pain and has a significant side effect profile. • Absence of evidence from a population without sciatica.
Quality of evidence	Low and moderate
Values and preferences	
Cost (resource allocation)	One cost-consequence analysis demonstrated that there was uncertainty regarding the costs and effects of a gabapentinoid anticonvulsant (pregabalin) when compared to usual care (partially applicable with potentially serious limitations). The GDG considered that both the economic and clinical evidence was insufficient to make a recommendation for the use of anticonvulsants in the management of low back pain.

Agreement with the strength of the NICE recommendation 27: 4 strong, 3 weak, 0 no opinion, 1 no answer, 9 not completed

- **Comments for a weak recommendation: none**
- **Comments for a strong recommendation: none**

Belgian GDG comments on anticonvulsants during the GDG meeting on the 15th September 2016

NICE recommendation 27. Do not offer anticonvulsants for managing non-specific low back pain.

- The GDG discusses the potential efficacy for anticonvulsants in LBP (especially if there is a neuropathic component)).
- There is a physiological explanation of this efficacy (working action on central sensitization)
- The NICE guideline formulated so many recommendations against pharmacological interventions in low back pain that almost only NSAIDs remain as a pharmacological intervention.
- All studies concerned chronic LBP, why not added 'chronic' in recommendation?
- Adding "routinely" is suggested.
- Finally a detailed analysis of the NICE review is needed to support the GDG decision.

⇨ The NICE recommendation 27 will be re-proposed in the next lime survey

Additional information on anticonvulsants proposed to the GDG after the meeting (September 2016)

A quick search in Medline was performed by a GDG members (PVW) and summarised by the KCE.

- Taguchi T. 2015. Prospective observational study excluded by NICE for incorrect population (sciatica). Results in favour of pregabalin for chronic neuropathic pain (n=331).
- Malik KM. 2015. RCT not quoted by NICE. No difference between placebo and pregabalin in patients WITH motor or sensory neurological signs and in chronic lumbar or cervical pain (only 8 patients with lumbar pain under pregabalin vs 5 placebo).
- Takahashi N. 2014. Non randomized trial not quoted by NICE. Improvement after 3 months with NSAIDs + pregabalin vs NSAIDs alone in patients WITH leg symptoms due to lumbar spinal stenosis or degenerative spondylolisthesis and WITH motor or sensory neurological signs (n=124).
- Baron R. 2010. RCT excluded by NICE for incorrect population (sciatica). No definitive conclusion between pregabalin and placebo in chronic lumbosacral radiculopathy (n=217)
- Saldaña MT. 2010. Observational study not quoted by NICE. Subjects were refractory to previous analgesia and suffered chronic pain and with ≥4 in the questionnaire (n=1304). The pain was secondary to cervical or to lumbosacral radiculopathy. Conclusions in favour of pregabalin after 12 wks (in monotherapy or add-on).

In conclusion, this new evidence focused on LBP with sciatica, were mainly not RCTs and provided inconsistent results.

Belgian GDG comments on anticonvulsants during the GDG meeting on the 12th October 2016

NICE recommendation 27. Do not offer anticonvulsants for managing non-specific low back pain.

- The respondents to the lime survey suggested to add "routinely' or to change the recommendation on "consider gabapentinoids only in selected cases of chronic LBP and radicular pain (when there is a neuropathic component).
- The place of anticonvulsants in the management of LBP with or without radicular pain is questioned?
- A suggestion is to keep the NICE recommendation and to add "in absence of neuropathic pain"

⇨ **The NICE recommendation 27 will be changed as following:**

⇨ ***Do not offer anticonvulsants for managing low back pain in absence of a neuropathic pain component."***

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30 November 2016)

- Warwick Clinical Trials Unit asked if for recommendation 27. Might there be merit in explicitly stating the drug groups of interest here? Or, indeed, subsuming this recommendation into recommendation 26 which then becomes: "Do not offer selective serotonin reuptake inhibitors, serotonin– norepinephrine reuptake inhibitors, tricyclic antidepressants, or gabapentinoids for managing non-specific low back pain." **NICE reply: T**he drug classes included when looking at evidence for anticonvulsants were gabapentinoids and other anticonvulsants. However the only available evidence for other anticonvulsants was for topimarate. Therefore the GDG did not develop a more specific recommendation for this area to avoid confusion regarding other anticonvulsants not included in the review. It was thus considered best to have a general recommendation for anticonvulsants. (p58/222)
- Faculty of Sport and Exercise Medicine suggested the need for a research recommendations: could further study of anticonvulsants be justified on the basis of the evidence presented? **NICE answered** that since there were 3 studies included for anticonvulsants within the review with multiple outcomes, the GDG agreed that there were other areas in the guideline where research recommendations should be given priority.(p58/222)

NICE final recommendations on anticonvulsants (November 2016)

29. Do not offer anticonvulsants for managing low back pain.

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

The recommendations on opioids are considered acceptable also for people with radicular pain.

KCE 2017 final recommendations on anticonvulsants (February 2017)

18. Do not offer anticonvulsants for managing low back pain with or without radicular pain in absence of a neuropathic pain component.
(strong recommendation based on moderate and low evidence from RCTs & cohort studies)

7.14.7. Specific points of discussion for muscle relaxants

No NICE clinical recommendation but one research recommendation.

3. What is the clinical and cost-effectiveness of benzodiazepines for the acute management of non-specific low back pain?

Guidelines from many countries have advocated that muscle relaxants be considered for short-term use in patients with low back pain when the paraspinal muscles are in spasm. The evidence for this mainly comes from studies on medications that are not licenced for this use in the United Kingdom. The 2009 NICE guideline makes the recommendation to consider prescribing diazepam as a muscle relaxant in this scenario, but the evidence base to support this particular drug is extremely small. Benzodiazepines are not without risk of harm even in the short-term. **No economic studies were found for muscle relaxants however there would of course be a cost associated with providing this drug and given the conclusion of lack of clinical benefit and increased incidence of adverse events observed in the clinical evidence the GDG agreed to not offer muscle relaxants for the management of non-specific low back pain. Moreover t**here is therefore a need to determine whether diazepam is cost-effective in the management of acute low back pain.

Belgian GDG considerations on muscle relaxants mentioned in the Lime survey at the beginning of September 2016

Agreement with the content of the NICE research recommendation 2: 7 Yes, 3 No, 1 no opinion, 0 out of competence, 0 no answer, 6 not completed

- **Comments from those who do not agree:**
  - Dit is een vraag en geen aanbeveling.
  - Because of adverse events... no cost-efficacy study is necessary!
  - From clinical experience, in a lot of patients (selectively chosen on clinical basis) BDP are effective as supplementary treatment, not as monotherapy. So OK for the research question without excluding them from justifiable use as a short trial in an individual patient
- **Other comments**
  - This is a question!

Belgian GDG comments on muscle relaxants during the GDG meeting on the 15th September 2016

NICE research recommendation 3. What is the clinical and cost-effectiveness of benzodiazepines for the acute management of non-specific low back pain?

- One noticed that oral administration of dantrolen included by NICE in this chapter is not available in Belgium.
- Regarding the research recommendation its-self, no consensus is reached during the GDG meeting: for some members this research question was already outdated, whereas other members were interested in the effect on other outcomes than pain, e.g. anxiety, particularly because they are commonly used although they have a lot of side effects.
- Finally it was decided not to support the research recommendation since there is no consensus for it.

⇨ The NICE research recommendation 3 will not be included in the Belgian guideline.

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30 November 2016)

- Royal College of General Practitioners: **Diazepam and similar should be mentioned: whether to advise their use or advise against**. Diazepam is frequently prescribed for spinal spasm in both primary care and in the ED. **NICE answered** that due to a lack of evidence, the GDG made a research recommendation regarding benzodiazepines (see Chapter 16, research recommendation number 3). (p215/222)
- British Institute of Musculoskeletal Medicine: 16.1 "Skeletal muscle relaxants are used for treating chronic muscle spasm, which may also be painful. These drugs bind to different receptors and exert their effect on muscles by central nervous system mechanisms, and are distinct from the peripherally acting muscle relaxant". Although the

draft report finds no evidence for their effectiveness and does not recommend using “muscle relaxants”, it does refer to drugs by that title, suggests research into the effectiveness of benzodiazepines, and acknowledges that they are used, and so reinforces the idea that they are part of clinical practice. This ‘product placement’ should have no place in the report; better a more rational statement that people may be anxious as a result of a sudden onset of disabling back pain and have difficulty relaxing with the result that muscles involved in the problem may go into spasm. In the short term a sedative may be useful provided that, to reduce anxiety, clear prior information is given that muscle spasm pain does not signify increasing harm to any structure any more than does an attack of cramp in the calf. The mention of “chronic muscle spasm” is surprising as few clinicians seem aware of this as a clinical entity and advice is against prolonged use of these agents. What is the basic science proof of concept for describing benzodiazepines as “muscle relaxants”? Animal model work originally justifying these drugs crudely assessed motor control during ‘voluntary’ activity on rotating drums at drug levels where contemporaneous tests of spontaneous activity would suggest marked central sedation rather than any direct muscle effect [Indian J Pharmacol. 2015; 47(4): 409-13]. Is this experimental model testing a homologous phenomenon, a meaningful surrogate, for muscle spasm in acute back pain? Some patients may be anxious and find it difficult to relax in which case sedation may be useful – is this muscle relaxation? **NICE reply**: The GDG considered that this is common terminology. The BNF defines benzodiazepines as a skeletal muscle relaxant, as does a Cochrane review on muscle relaxants for nonspecific low back pain (Van Tulder, M. W., Touray, T., Furlan, A. D., Solway, S., & Bouter, L. M. (2003). Muscle relaxants for nonspecific low back pain: a systematic review within the framework of the Cochrane collaboration. Spine, 28(17), 1978-1992.). We therefore believe this wording is appropriate and should remain unchanged. (p55/222)

NICE changes in the final version of the guideline (November 2016): none for muscle relaxants

NICE final research recommendations on muscle relaxants (November 2016)

2. What is the clinical and cost-effectiveness of benzodiazepines for the acute management of low back pain?

Belgian GDG comments on the absence of recommendation on muscle relaxants during the meeting on the 24th January 2017

A recommendation against muscle relaxants is considered acceptable instead of a research recommendation.

KCE 2017 final recommendations on muscle relaxants (February 2017)

XX. Do not offer skeletal muscle relaxants for managing low back pain with or without radicular pain

7.14.8. Specific points of discussion for antibiotics

No NICE 2016 recommendation on antibiotics

There was evidence from 1 RCT of the use of antibiotics in people with MRI confirmed disc prolapse, subsequent vertebral end plate oedema and chronic low back pain of more than 6 months duration. Although evidence indicated an improvement in health care utilisation, there was also an increase in adverse events. Data were only reported as median and interquartile range for pain, function and quality of life and therefore conclusions on the efficacy based on these outcomes could not be made with any degree of certainty. The GDG considered the external validity of this trial, specifically due to the recruitment. The study reported very limited detail of how participants were recruited, and the GDG expressed concern that the population included within this trial was highly selected and very specific and consequently may not be a representative sample. It was agreed that no recommendation could be based on this single study.

Belgian GDG considerations on antibiotics mentioned in the Lime survey at the beginning of September 2016

Agreement with the absence of recommendation on antibiotics: 9 Yes, 2 No, 0 no opinion, 0 out of competence, 0 no answer, 6 not completed

- **Comments from those who do not agree:**
  - Antibiotics should not be recommended because of insufficient evidence and evidence of possible side effects.

- I would make a recommendation against use of antibiotics, given the adverse events

- **Other comments**
  - There is already an overwhelming overuse of AB. Hence, in the context of absence of real good studies this should not be encouraged.
  - Lack of recommendation... and lack of indication in a country where the control of antibiotic prescription is already a problem!!!

Belgian GDG comments on antibiotics during the GDG meeting on the 15th September 2016

No NICE recommendation given the lack of evidence.

- The GDG stresses that in Belgium there is already an overwhelming overuse of antibiotics.
- The NICE review identified a Danish study on patients with prolapsed disc which promoted the use of antibiotics. However, the authors of this study did not recommend the use of antibiotics due to its societal impact (overconsumption of antibiotics).
- If a new study promotes antibiotic in LBP, there is a risk that several practitioners will be convinced.
- In the context of absence of real good studies, societal impact of antibiotic use and real overconsumption in Belgium, antibiotics should not be encouraged.

⇨ A recommendation against antibiotic in the management of LBP is suggested

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30 November 2016). None on antibiotics

NICE changes in the final version of the guideline (November 2016): none for antibiotics

No NICE final recommendations on antibiotics (November 2016)

Belgian GDG comments on the last formulation the meeting on the 24th January 2017

A recommendation against antibiotics is considered acceptable instead of an absence of recommendation.

KCE 2016 final recommendations on antibiotics (February 2017)

X Do not offer antibiotics for managing low back pain with or without radicular pain

7.14.9. Specific point of discussion for oral methylprednisolone

Belgian GDG comments during the GDG meeting on the 12th October 2016

- One member of the GDG asked if oral methylprednisolone was sometimes used in Belgium in the treatment of LBP (for example in case of slight motor deficit).
- It is appeared not usual according to the answers of the other GDG members.
- Moreover, it was not studied by NICE.
- A KCE proposition is to include this medication in the list on "treatment not included in the Belgian guideline on LBP because not covered by NICE" (as andulation, shock waves, etc.).
- This list will be submitted to the GDG before the end of the project in order to select only the interesting (positive or negative) interventions and avoid a too long list.

⇨ **No additional search will be performed on oral methylprednisolone in LBP but the medication will be added in the list of topic not covered by the guideline.**

7.15. Spinal injections

Spinal injections for patients with low back pain ± radicular pain

NICE search question
"What is the clinical and cost-effectiveness of spinal injections in the management of non-specific low back pain?"

Introduction based on the draft version of NICE guideline (March 2016)

- There are many different types of spinal injections performed for low back pain. There are a variety of different techniques, and many are used in conjunction with other therapies, for example, fitness, stretching and exercise programmes. Many injectates can be used. Usually the injected agents aim to sooth inflamed tissue or calm excessive nerve activity, but some (sclerosants) aim to induce inflammation and stimulate healthy new tissue growth. Whilst prolotherapy and trigger point injections are not spinal injections as such, these were considered as they can also be used for low back pain. This chapter excludes epidural injections and facet joint radiofrequency denervation, which are considered elsewhere.
- Following spinal injections were considered:
    - **Facet joint injections** target the small joints linking the spinal vertebrae, known as the facet joints. Each vertebra has 2 connections below, one each side, and 2 above. Injections of local anaesthetic or steroid into selected joints are used to try to temporarily reduce or stop back pain. It is usually used in conjunction with an exercise programme. It is unlikely that the substances injected would remain for long.
    - **Medial branch blocks** are injections of local anaesthetic on to the medial branch nerves that supply the facet joints. It is usually done to define those who would respond to radiofrequency denervation of the positive tested levels.
    - **Intradiscal therapy** is aimed at treating internal disc disruption (IDD), which some therapists believe can be a cause of low back pain. Both steroids and non-steroidal anti-inflammatory drugs have been injected into the disc in an attempt to suppress inflammation and reduce pain.
    - **Prolotherapy** (also known as proliferation therapy or regenerative injection therapy) involves injecting tissue with an irritant solution. This may be a joint, ligament or tendon insertion, or injected into connective tissue or muscle.
    - **Trigger Point Injections** use various mixtures of local anaesthetics and a steroid, or botulinum toxin. A trigger point is argued to be a painful or irritable knot in a muscle. Injections are usually carried out in an outpatient setting, and repeated at intervals.
- The GDG agreed that the main area of uncertainty that this review would address was the effectiveness of various agents, rather than the route or mode of administration.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with non-specific low back pain • Populations with low back pain only and low back pain with/without sciatica will be pooled for analysis
Intervention(s)	• Agents (alone and in combination): • Steroid □ • Local anaesthetic • Sclerosants (prolotherapy, phenol, hypertonic glucose, dextrose, glycerol) • Botulinum toxin • Hyaluronans • Strata: • Image guided facet joint injections

	• Other image guided injections • Prolotherapy/sclerosants • Other non-image guided injections (for example, trigger point injections)
Comparison(s)	Interventional agents to be compared versus each other (across class comparisons) and versus other treatments below: • Sham (needle alone)/placebo/saline • Usual care • Other treatment (non-invasive and invasive treatments being considered by the guideline)
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (>30% improvement in pain or function) • Adverse events: morbidity • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

- Thirty one randomised controlled trials and 2 cohort studies were included in the review (not all studies could be reported because results were graphically reported so data was unusable). Four Cochrane reviews were identified, but were not included due to methodological reasons. The individual studies were assessed and included if they matched the review protocol.

Image-guided facet joint injections (see Table 41)

- **monotherapy**
  - Steroid vs saline
    - A single RCT (fluoroscopic guided injections of 20mg (1ml methylprednisolone mixed with 1 ml saline) at facet joints L4-L5 and L5-S1 versus 2 ml saline) reported a clinical benefit in **pain** (VAS 0-10; very low quality; n=95) and **function** (MSIP 0-100; very low quality; n=95) at long term, but not at short term.
    - Not reported outcomes: QoL, function, psychological distress, adverse events, healthcare utilisation
  - Steroid vs hyaluronans
    - A single RCT (CT-guided injections of 10 mg triamcinolone acetonide in 1 ml crystalline suspension at facet joints L4-L5, L5-S1 and L4-L3 versus 10mg sodium hyaluronate in a 1 ml buffer) reported a short term clinical benefit in **pain** (VAS 0-10; very low quality; n=59) favouring steroids but this benefit was not anymore seen at long term. Also no clinical differences were found for (different measures of) **function** (ODI 0-100; RMDQ 0-24; LBOS 0-754; low-very low quality; n=59).
    - Not reported outcomes: QoL, psychological distress, healthcare utilisation, adverse events, responder criteria

- **Combination therapy**
  - Steroid + biomechanical exercise (home stretching exercises) vs biomechanical exercise (home stretching exercises)
    - A single RCT (fluoroscopic guided injections of 1 ml 0.5% bupivacaine and 1ml of a depot corticosteroid preparation mixed with 1ml 2% lidocaine at 1-3 levels bilaterally) reported no short term clinical differences in **pain** (VAS 0-10; very low quality; n=70), **function** (MVAS 0-150; very low quality; n=70) and **responder criteria** (>50% improvement in pain or function; very low quality; n=70). No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, healthcare utilisation, adverse events
  - Steroid + anaesthetic vs biomechanical exercise (McKenzie exercises)
    - The cohort study (X-ray guided injections of 0.5ml (20mg) of methylprednisolone acetate and 0.5ml of 0.25% bupivacaine, level of injection determined by tenderness over the joint) found a clinical benefit in **pain** at both time points (VAS 0-10; very low quality; n=18), but not in **function** (ODI 0-100; very low quality; n=18).
    - Not reported outcomes: QoL, psychological distress, healthcare utilisation, adverse events, responder criteria

Table 41 – Clinical effectiveness of facet joint injections in patients with low back pain

Image-guided facet joint injections in patients with LBP				
Outcomes	**Steroid versus saline**	**Steroid versus hyaluronans**	**Steroid + biomechanical exercise versus biomechanical exercise**	**Steroid + anaesthetic versus biomechanical exercise (cohort)**
Pain	At short term (<4mo): • **VAS 0-10: no diff** (1 RCT; low; n=96) At long term (4mo-1y): • **VAS 0-10: CIB favouring steroids** (1 RCT; very low; n=95)	At short term (<4mo): • **VAS 0-10: CIB favouring steroids** (1 RCT; very low; n=59) At long term (4mo-1y): • **VAS 0-10: no diff** (1 RCT; very low; n=59)	At short term (<4mo): • **VAS 0-10: no diff** (1 RCT; very low; n=70) At long term (4mo-1y): Not reported	At short term (<4mo): • **VAS 0-10: CIB favouring steroids** (1 cohort; very low; n=18) At long term (4mo-1y): • **VAS 0-10: CIB favouring steroids** (1 cohort; very low; n=18)
Function	At short term (<4mo): • **MSIP 0-100: no diff** (1 RCT; low; n=96) At long term (4mo-1y): • **MSIP 0-100: no diff** (1 RCT; very low; n=95)	At short term (<4mo): • **ODI 0-100: no diff** (1 RCT; low; n=59) • **RMDQ 0-24: no diff** (1 RCT; low; n=59) • **LBOS 0-75: no diff** (1 RCT; very low; n=59) At long term (4mo-1y): • **ODI 0-100: no diff** (1 RCT; low; n=59)	At short term (<4mo): • **MVAS 0-150: no diff** (1 RCT; very low; n=70) At long term (4mo-1y): Not reported	At short term (<4mo): • **ODI 0-100: no diff** (1 cohort; very low; n=18) At long term (4mo-1y): • **ODI 0-100: no diff** (1 cohort; very low; n=18)

		• **RMDQ 0-24: no diff** (1 RCT; low; n=59) • **LBOS 0-75: no diff** (1 RCT; very low; n=59)		
Responder criteria			At short term (<4mo): • **>50% pain reduction: no diff** (1 RCT; very low; n=70) • **>50% function improvement: no diff** (1 RCT; very low; n=70) At long term (4mo-1y): Not reported	

CIB: clinically important benefit

Outcomes not reported: QoL, psychological distress, adverse events, healthcare utilisation

Other image-guided injections: intradiscal injections (see Table 42)

- **Monotherapy**
  - Steroid vs saline
    - Evidence from 3 studies showed a clinical benefit in terms of improving **pain** (VAS 0-10) and **function** (ODI 0-100) in the group receiving a steroid injection (CT-guided injections of 3ml bethametasone or 5mg dexamethasone) versus saline in the short term (low-very quality, n=45-80). Evidence from 2 studies also showed clinical benefit of steroid injections (betamethasone) for **pain and function in the long term** (VAS 0-10; ODI 0-100; very low quality; n=80), but this was not observed in the case of **function** when dexamethasone (low quality; n=45), or methylprednisolone acetate (fluoroscopic guided injections of 40mg in 1ml) (ODI 0-100; low quality; n=45-96), was used as injectate.
    - Not reported outcomes: psychological distress, QoL, adverse events, healthcare utilisation, responder criteria
- **Combination therapy**
  - Steroid + anaesthetic vs anaesthetic
    - Evidence from 3 studies (fluoroscopy guided injections of betamethasone at 0.15mg/ml mixed with bupivacaine at L1-L4 medical branches and L5 dorsal ramus) showed that there was no clinically important difference between treatments for all outcomes reported (**pain** NRS 0-10; moderate-low quality; n=270-248; **function** ODI 0-100; moderate quality; n=270-248; **responder criteria** >50% pain improvement; moderate-low quality; n=150) when steroid plus anaesthetic was injected compared to anaesthetic injection alone irrespective of route of administration being caudal epidural, medial branch blocks or interlaminar injections.
    - Not reported outcomes: psychological distress, QoL, healthcare utilisation, adverse events
  - Steroid + anaesthetic vs mixed modality exercise
    - Evidence from 1 study comparing steroid plus anaesthetic (image-intensifier guided perifacet injections of 80mg methylprednisolone and 1-2ml of 0.5% bupivacaine at L4/L5 and L4/S1 bilaterally) versus mixed modality exercise (self-management (back education and home exercise), biomechanical exercise (McKenzie and stability), manual therapy (manipulation/mobilisation, Maitland and mulligan), electrotherapy (ultrasound) and heat/ice) reported

no benefit of injection for **QoL** (EQ-5D 0-1; very low quality; n=36), **pain** (McGill 0-78; low quality; n=36) or **function** (ODI 0-100; low quality; n=36) in the short term.

- Not reported outcomes: psychological distress, healthcare utilisation, adverse events, responder criteria

Table 42 – Clinical effectiveness of spinal injections (intradiscal) in patients with non-specific low back pain

Spinal injections (intradiscal) in patients with LBP			
Outcomes	**Steroid vs saline**	**Steroid + anaesthetic vs anaesthetic**	**Steroid + anaesthetic vs mixed modality exercises**
QoL			At short term (<4mo): • **EQ-5D 0-1: no diff** (1 RCT; very low; n=36) At long term (4mo-1y): Not reported
Pain	At short term (<4mo): • **Betamethasone VAS 0-10: CIB favouring steroids** (2 RCTs; very low; n=80) • **Dexamethasone VAS 0-10: CIB favouring steroids** (1 RCT; low; n=45) At long term (4mo-1y): • **Betamethasone VAS 0-10: CIB favouring steroids** (2 RCTs; very low; n=80) • **Dexamethasone VAS 0-10: no diff** (1 RCT; low; n=45)	At short term (<4mo): • **NRS 0-10: no diff** (3 RCTs; moderate; n=270) At long term (4mo-1y): • **NRS 0-10: no diff** (3 RCTs; low; n=248)	At short term (<4mo): • **McGill 0-78: no diff** (1 RCT; low; n=36) At long term (4mo-1y): Not reported
Function	At short term (<4mo): • **Betamethasone ODI 0-100: CIB favouring steroids** (2 RCTs; very low; n=80) • **Dexamethasone ODI 0-100: CIB favouring steroids** (1 RCT; low; n=45)	At short term (<4mo): • **ODI 0-100: no diff** (3 RCTs; moderate; n=270)	At short term (<4mo): • **ODI 0-100: no diff** (1 RCT; low; n=36)

	At long term (4mo-1y): • **Betamethasone ODI 0-100: CIB favouring steroids** (2 RCTs; very low; n=80) • **Dexamethasone ODI 0-100: no diff** (1 RCT; low; n=45) • **Methyprednisolone acetate ODI 0-100: no diff** (1 RCT; low; n=96)	At long term (4mo-1y): • **ODI 0-100: no diff** (3 RCTs; moderate; n=248)	At long term (4mo-1y): Not reported
Responder criteria		At short term (<4mo): • **>50% pain improvement: no diff** (2 RCTs; moderate; n=150) At long term (4mo-1y): • **>50% pain improvement: no diff** (2 RCTs; low; n=150)	

CIB: clinically important benefit

Prolotherapy/sclerosants

- **Monotherapy**
  - Sclerosant vs anaesthetic
    - A single RCT (fluoroscopic-guided injections of 1 ml of 50% glycerol versus 2ml of 0.5% bupivacaine) reported only one outcome: no clinical difference was found for **pain** at short term (VAS 0-10; very low quality; n=11). No long term data were reported.
    - Not reported outcomes: QoL, function, psychological distress, healthcare utilisation, responder criteria, adverse events
- **Combination therapy**
  - Sclerosants + anaesthetic vs saline
    - Evidence from a single study demonstrated a clinical benefit favouring the injection of sclerosant plus anaesthetic (non-image guided injections of 25% dextrose, 25% glycerine, 2.5% phenol and pyrogen-free water to 100% + 0.5% plain lignocaine at L4-5 and L5-S1) compared to saline for **pain** (VAS 0-7.5; low quality; n=81) and **function** (RMDQ 0-33; moderate quality; n=81) in both the short and long term.
    - Not reported outcomes: QoL, psychological distress, healthcare utilisation, responder criteria, adverse events
  - Sclerosants + anaesthetic vs anaesthestic
    - A single RCT (fluoroscopy guided injections of 25% dextrose, 25% glycerine, 2.4% phenol and pyrogen-free water + 15ml of 0.5% lidocaine at L4-5 and L5-S1 versus 15ml of 0.5% lidocaine and 15ml saline) reported no clinical differences in long term **pain** (VAS 0-8; moderate quality; n=79) and **function** (RMDQ 0-24; moderate quality; n=79). No short term data were reported.
    - Not reported outcomes: QoL, psychological distress, healthcare utilisation, responder criteria, adverse events

Table 43 – Clinical effectiveness of prolotherapy in patients with low back pain and sciatica

Prolotherapy in patients with LBP			
Outcomes	**Sclerosant vs anaesthetic**	**sclerosant + anaesthetic versus saline**	**sclerosant + anaesthetic versus anaesthetic**
Pain	At short term (<4mo): • **VAS 0-10: no diff** (1 RCT; very low; n=11) At long term (4mo-1y): Not reported	At short term (<4mo): • **VAS 0-7.5: CIB favouring sclerosant** (1 RCT; low; n=81) At long term (4mo-1y): • **VAS 0-7.5: CIB favouring sclerosant** (1 RCT; low; n=81)	At short term (<4mo): Not reported At long term (4mo-1y): • **VAS 0-8: no diff** (1 RCT; moderate; n=79)
Function		At short term (<4mo): • **RMDQ 0-33: CIB favouring sclerosant** (1 RCT; moderate; n=81) At long term (4mo-1y): • **RMDQ 0-33: CIB favouring sclerosant** (1 RCT; moderate; n=81)	At short term (<4mo): Not reported At long term (4mo-1y): • **RMDQ 0-24: no diff** (1 RCT; moderate; n=79)

CIB: clinically important benefit

Other non-image guided injections

- **Monotherapy**
  - Botulinum toxin vs saline
    - Evidence from 1 study for the comparison of botulinum toxin (non-image guided injections of 100U/ml saline - 40 units given at each site, at L1 to L5, L2-S1) versus saline showed clinical benefit of botulinum toxin for **responder criteria** in pain (>50% pain improvement; moderate quality; n=30) at short term. No long term data were reported.
    - Not reported outcomes: QoL, pain, function, psychological distress, healthcare utillisation, adverse events
- **Combination therapy**
  - Steroid + anaesthetic vs steroid
    - Evidence from 1 study for the comparison of steroid in combination with anaesthetic (non-image guided injections of 80mg methylprednisolone + 5ml levobupivacaine + 3ml saline) versus steroid alone (80mg methylprednisolone mixed with 8ml saline) demonstrated no clinically important difference between the treatments for **pain** (first or second block) at either short or long term (VAS 0-10; NRS 0-10; very low quality; n=60).
    - Not reported outcomes: QoL, function, psychological distress, responder criteria, healthcare utillisation, adverse events

Economic evidence

No relevant economic evaluations were identified.

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:**
  - Critical outcomes were health-related QoL, pain severity, function, psychological distress
  - Important outcome were responder criteria for pain and function (>30%), adverse events and healthcare utilisation
  - Evidence was reported for all of the critical outcomes except for psychological distress and healthcare utilisation. For image guided facet joint injections, evidence was only available for pain, function, and responder criteria. For other image guided injections, evidence was only available for pain, function, quality of life (EQ-5D) and for responder criteria. Evidence for prolotherapy injections was only available for pain and function and for other non-image guided injections, evidence was found for pain and responder criteria only. The majority of outcomes described in other non-image guided stratum were in a format that rendered the data un-suitable for meta-analysis.

- **Trade-off between clinical benefits and harms**
  - **Image guided facet joint injections:** The GDG noted that the lack of short term effect with some evidence of a long term effect raised some doubt on the long term effect being solely due to the injection. The authors of the study stated that there was **no pharmacological/biological reason** for the observed effect and were **uncertain about the validity** of the results. The GDG noted that image guided facet joint injections of steroid are widely used but there is a paucity of evidence to support their ongoing use. It was noted that there was **no evidence of clinical harm** from the studies reviewed**.** It was noted that use of hyalurons may cause inflammation and therefore an increase in pain, although both groups did improve from their baseline pain levels. As there was uncertainty around the effects reported from this single trial (steroid + biomechanical exercise versus biomechanical exercise), the GDG considered that no clear conclusion could be made about the benefits of steroid injections compared to biomechanical exercise from this very low quality evidence.

    Image guided facet joint injections
    - **Steroid versus saline:** A clinical benefit in pain (VAS) was observed in the long term (greater than 4 months - 1 year) although no clinically important difference was seen short term (less than 4 months). A similar effect was also seen for function (MSIP), however, it was noted that the baseline values were very low and therefore it was unlikely that much improvement could be demonstrated from this baseline. The GDG noted that the lack of short term effect with some evidence of a long term effect raised some doubt on the long term effect being solely due to the injection. The authors of the study stated that there was no pharmacological/biological reason for the observed effect and were uncertain about the validity of the results. The GDG noted that image guided facet joint injections of steroid are widely used but there is a paucity of evidence to support their ongoing use. It was noted that there was no evidence of clinical harm from the studies reviewed.
    - **Steroid versus hyaluronans:** Very low quality evidence demonstrated that steroids were more effective at improving pain (assessed by VAS) than hyalurons in the short term although no clinically important difference between treatments was seen long term. It was noted that use of hyalurons may cause inflammation and therefore an increase in pain, although both groups did improve from their baseline pain levels. Three different measures of function were reported (ODI, RMDQ and Low Back Pain Outcome Score (LBOS)); all of which showed no clinically important difference between treatments.
    - **Steroid plus biomechanical exercise versus biomechanical exercise**: No clinically important difference in pain, function or responder criteria was observed at the short term follow ups. As there was uncertainty around the effects reported from this single trial, the GDG considered that no clear conclusion could be made about the benefits of steroid injections compared to biomechanical exercise from this very low quality evidence.
    - **Steroid plus anaesthetic versus biomechanical exercise**: Very low quality non randomised evidence for this comparison came from a very small trial and demonstrated a clinical benefit in pain (VAS) in both the short and long term although no clinically important difference was observed for function (assessed by ODI) at any time point.
  - **Other image guided injections:** This very low quality evidence at high risk of bias reported inconsistent results separately for 2 distinct populations with or without modic changes. There was concern raised by the GDG that the inpatient population set in a hospital in China was not reflective of current UK practise

and did not have confidence in the effects reported as a result. The **potential risk of harm** for intra-discal injections was also highlighted including risk of infection and risk of prolapse (although this risk is not captured by RCTs). Given the applicability issue and risk of potential harm, the GDG concluded that the evidence in this area was **inadequate to base a recommendation** on. The GDG noted that the study (steroid + anaesthetic versus mixed modality exercise) was a very small trial and that the baseline scores for all outcomes were different between groups and both groups were in the 'normal' range at baseline, and therefore it would be unlikely to observe a meaningful change over the course of the trial. It was however also highlighted that the comparator arm consisted of a 10 week intensive rehabilitation programme -is a very active intervention. The GDG discussed that the lack of a difference observed between arms could be indicative of positive evidence for both injections of steroid and anaesthetic as well as the combination of education and physiotherapy. However, the limitations of **the single small study precluded firm conclusions** being drawn.

Other image guided injections

- **Steroid versus saline:** An overall clinical benefit in pain (assessed by VAS) and function (assessed by ODI) favouring the use of steroid injected intra-discally was seen in the short term and long term. Subgroup analysis by injection agent to address heterogeneity revealed no clinically important difference in pain in the long term from low quality evidence at high risk of bias taken from 1 small trial. The results for function in the long term were more heterogeneous; subgroup analysis by injection agent showed benefit favouring steroid was only maintained in the long term in results taken from 1 trial. This very low quality evidence at high risk of bias reported inconsistent results separately for 2 distinct populations with or without modic changes. There was concern raised by the GDG that the inpatient population set in a hospital in China was not reflective of current UK practise and did not have confidence in the effects reported as a result. The potential risk of harm for intra-discal injections was also highlighted including risk of infection and risk of prolapse (although this risk is not captured by RCTs). Given the applicability issue and risk of potential harm, the GDG concluded that the evidence in this area was inadequate to base a recommendation on.
- **Steroid in combination with anesthetic versus anesthetic**: Moderate quality evidence from 3 studies showed no clinically important difference in pain (assessed by VAS), function (assessed by ODI) and responder criteria for pain improvement exceeding 50% in either the short or long term irrespective of the route of administration of the injection.
- **Steroid in combination with anesthetic versus combined treatment**: One study included assessed the effects of steroid plus anaesthetic versus a combination package of self-management (back education and home exercise), biomechanical exercise (McKenzie and stability), manual therapy (manipulation/mobilisation, Maitland and Mulligan), electrotherapy (ultrasound) and heat/ice. There was no clinical benefit seen in terms of any of the outcomes reported in this study. The GDG noted that the study was a very small trial and that the baseline scores for all outcomes were different between groups and both groups were in the 'normal' range at baseline, and therefore it would be unlikely to observe a meaningful change over the course of the trial. It was however also highlighted that the comparator arm consisted of a 10 week intensive rehabilitation programme -is a very active intervention. The GDG discussed that the lack of a difference observed between arms could be indicative of positive evidence for both injections of steroid and anaesthetic as well as the combination of education and physiotherapy. However, the limitations of the single small study precluded firm conclusions being drawn.

o **Prolotherapy:** Only 1 study demonstrated that injection of sclerosant and anaesthetic was more effective than saline in improving pain and fuction at both time points. The GDG expressed caution with the interpretation of these results as people in the intervention group received a forceful manipulation, concurrent to the injection on the first day of treatment, whereas those in the saline group received non-forceful manipulation. The GDG were unable to be certain that the clinical benefit in pain and function was directly attributable to the spinal injections.

Prolotherapy Injections

- **Sclerosant versus anaesthetic**: The only evidence identified for this comparison was from a very small trial that reported only 1 outcome relevant to the review protocol (pain assessed by VAS). This showed no difference between treatments in the short term with considerable uncertainty in the direction of the effect.
- **Sclerosant plus anaesthetic versus saline**: Evidence from 1 study indicated that injection of sclerosant and anaesthetic was more effective than saline in improving pain (assessed by VAS) and function (assessed by RMDQ) in both the short and long term. The GDG expressed caution with the interpretation of these results as people in the intervention group received a forceful manipulation, concurrent to the injection on the first day of treatment,

whereas those in the saline group received non-forceful manipulation. The GDG were unable to be certain that the clinical benefit in pain and function was directly attributable to the spinal injections.

- **Sclerosant plus anaesthetic versus anaesthetic**: No clinically important difference was seen between treatments in terms of pain (assessed by VAS) and function (assessed by RMDQ) in the long term. No data was presented for short term results.

- **Other non-image guided injections:** A clinical benefit in responder criteria for pain improvement was seen in favour of botulinum toxin compared to saline. However, as this was from a single small trial (15 patients in each arm) and was not in a critical outcome measure, the GDG felt that this was insufficient evidence to make a recommendation. The GDG expressed concern with the interpretation of the study on steroid + anaesthetic versus steroid as the description provided suggested the population may be people with sciatica although the study specifically stated it was for treatment of low back pain. In addition, the study only looked at the immediate short term effect of the diagnostic blocks up till a maximum of 24 hours which the GDG did not feel was very useful information.

  Other non-image guided injections

  - **Botulinum toxin versus saline**: A clinical benefit in responder criteria for pain improvement exceeding 50% was seen in favour of botulinum toxin in the short-term. However, as this was from a single small trial (15 patients in each arm) and was not in a critical outcome measure, the GDG felt that this was insufficient evidence to make a recommendation.
  - **Steroid plus anaesthetic versus steroid**: Evidence from 1 study demonstrated no short-term clinically important difference between treatments in terms of pain (NRS) between injections of steroid and anaesthetic or steroid alone. The evidence was from a study which stratified participants according to how many diagnostic blocks they had received, however the outcome was the same for each strata.
  - It was noted that in the studies included in this review, no data were available on adverse events. The GDG noted that they are aware of studies/clinical reports (that did not meet inclusion criteria for this review) reporting serious adverse effects of spinal injections although these were relatively rare.

- **Harms:** It was noted that in the studies included in this review, no data were available on adverse events. The GDG noted that they are aware of studies/clinical reports (that did not meet inclusion criteria for this review) reporting serious adverse effects of spinal injections although these were relatively rare.
- **Overall** the GDG agreed that there was **no consistent good quality evidence to recommend the use of spinal injections** for the management of non-specific low back pain. There was **minimal evidence of benefit** from injections, and reason to believe that there was **a risk of harm**, even if rare. The GDG consequently agreed that it was appropriate to **recommend against the use of spinal injections** for people with non-specific low back pain.

- **Trade-off between net clinical effects and costs**
  - **No economic evaluations** were identified from the published literature. Use of injections for low back pain will be associated with costs relating to the drugs, consumables and equipment (e.g. imaging) used and the personnel time required to deliver the therapy. Intervention costs will also depend on the number of injections given. If effective, upfront intervention costs may be offset by downstream cost savings due to reduced healthcare utilisation or may be justified due to the benefits to the patient. However, given the GDG's conclusions that there was a lack of evidence of clinical benefit for injections (for any of the agents or modalities reviewed), intervention costs were not considered justified.
- **Quality of evidence**
  - **Overall quality:** 31 RCTs, ranged from very low to moderate quality due to risk of bias
  - **Image guided facet joint injections:** Low to very low quality evidence for this stratum came from 4 studies of which 2 reported data graphically and the third was a small trial comparing steroid and hyaluronan. The weight of evidence rested on 1 main RCT, in which Mean Sickness Impact Profile (MSIP) was used to assess improvement in function. However, the GDG were unclear as to what magnitude of change could be considered meaningful and therefore were unable to place much significance on this outcome.
  - **Other image guided injections:** The evidence for this stratum was rated as low or very low quality, mainly due to risk of bias (and sometimes due to additional imprecision). The results reported were often inconsistent and there was concern that the study population wouldn't be entirely representative of the guideline population, however the GDG agreed that the same response would be expected in either case. There was concern that the results reported in this study had

not been reproducible in other similar studies and whilst they may be clinically important, there was considerable doubt regarding their validity. The applicability of this study to a UK setting was also questioned as this study population were all in-patients.

The GDG did not consider the study Manchikanti 2007 to be suitable for inclusion in the image guided facet joint strata despite the study classifying the injections as facet joint injections. This was because the agents were administered to the medial branches at L1-L4 levels and L5 dorsal ramus which the GDG did not feel qualified as a facet joint injection. The study was therefore included in the 'other image guided injections' strata. The small study population received numerous injections during the study period which further compromised the quality of the outcomes reported; the GDG did not feel they could make accurate judgement of clinical importance for these reasons.

- **Prolotherapy:** The majority of evidence in this stratum was of low quality as there was serious imprecision attached to all the effects reported. One trial reported the inclusion of forceful manipulation in the treatment arm which the GDG considered to be a risk of bias affecting interpretation of the evidence. They did not feel they could make accurate judgement of clinical importance from this evidence as the manipulation could have compromised the clinical benefit shown for the combination treatment for both the outcomes pain and function in the short and long term periods.
- **Other non-image guided injections:** Overall low quality evidence for this stratum reported came from 2 studies. One of these trials had a very small sample size which made judging clinical importance for the outcome responder criteria pain (VAS) exceeding 50% improvement difficult for the GDG. There was also considerable polarity of opinion in the GDG regarding the second trial. One concern was that the study might include sciatica patients as some included patients had nerve compression and also reported 2 diagnostic blocks for each group with short follow up of 6, 12 and 24 hours. The GDG felt that this trial was largely irrelevant and did not have much confidence in the outcomes reported.

- **Other considerations**
  - The GDG noted that many sclerosants were not licensed as injection agents for the treatment of low back pain in the UK but were licensed for other indications, however they did not agree that there was evidence to recommend these injections for low back pain.
  - The GDG were aware of existing NICE interventional procedure guidance for Therapeutic endoscopic division of epidural adhesions (IPG333) recommending special arrangements for clinical governance, consent, audit and research. This procedure was therefore excluded from this review and if its use is considered for people with non-specific low back pain, existing guidance should be followed.

NICE 2016 draft recommendations: 1 clinical recommendation (March 2016)

30. Do not offer spinal injections for managing non-specific low back pain.

*KCE note: The recommendation is based on a majority of studies that included LBP patients with at least 6 months pain complaints and after failure of conservative treatments. Few studies included also patients with LBP for at least 3 months pain. The older studies (1990 and older) did not mention clearly the minimum duration of the LBP. Adding "chronic" to the recommendation could be an option, however, this could suggest a potential benefit in acute LBP (for which no evidence was found).

Belgian GDG considerations mentioned in the Lime survey at the end of September 2016

Agreement with the content of the NICE recommendation 35: 6 Agree, 5 Disagree, 0 no opinion, 2 out of competence, 1 no answer, 4 not completed

- **Comments from those who do not agree:**
  - Despite the literature, we do see patients who have a good result (especially pain) after facet joint injection with cortiosteroids. There is need for differentition in subgroups in LBP patients. The use of local anaesthetic injection on the facet may be important (patients with pain relief may benefit subsequently a steroid injection?)
  - Medial branch blocks/facet joints injections can have a place, as first line, after conservative treatment and before eventual denervation. Low cost, few harms, with a positive signal in the literature, even if quality of evidence is low. One important problem is the patient selection. More discussed in the very interesting review: Cohen SP et al, Nat Rev Rheumatol 2013;9,101-16[18].

- I agree except for the facet joint injections. According the cited papers in the NICE guideline and adding the paper of Lakemeier 2013[19] (cfr. infra) I would suggest: Consider facet joint injections with steroids for managing LBP with suspected facet joint pain when non-surgical treatment has not worked for them.
- Facet joint injections are sometimes (at least transiently) helpful in selected patients (documented facet syndrome) and is more easily available than radiofrequency ablation. Couldn't the following be added: "except in selected cases, such as well documented facet syndrome..."
- There is still a place for facet injections.

- **Other comments:**
  - Liever te behandelen. Wat met epiduroscopie?
  - Apart from the lack of evidence to support injections, interventionalist therapies shift the patient away from the key message that back pain should be dealt with actively.

Strength of the recommendation 30 on spinal injections: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	The GDG agreed that there was no consistent good quality evidence to recommend the use of spinal injections for the management of non-specific low back pain. There was minimal evidence of benefit from injections, and reason to believe that there was a risk of harm, even if rare. The GDG consequently agreed that it was appropriate to recommend against the use of spinal injections for people with non-specific low back pain.
Quality of evidence	Moderate to very low
Values and preferences	The GDG noted that many sclerosants were not licensed as injection agents for the treatment of low back pain in the UK but were licensed for other indications, however they did not agree that there was evidence to recommend these injections for low back pain.
Costs (resource allocation)	No economic evaluations identified.

Agreement with the strength of the NICE recommendation 35: 3 strong, 3 weak, 0 no opinion, 0 no answer, 12 not completed

- **Comments for a weak recommendation**
  - Too much different treatments covered in one recommendation.

Belgian GDG comments during the GDG meeting on the 12th October 2016

- The GDG acknowledged that several respondents of the Lime survey suggested a possible efficacy of facet joint injections.
- The question is “have we sufficient evidence against the spinal injection”? The NICE GDG members mentioned that there is no literature on adverse events in the NICE systematic review but, based on clinical reports, they suspected a risk of harm justifying this recommendation.
- There is evidence pro the spinal injections but it is poor (see CIB in the table in the PPT). However, the fact that different populations are included in the same analysis weaken probably the results.
- Facet joint syndrome diagnosis is difficult to establish. There is no clear definition.
- The problem is that often facet injections do not exactly reach the facet joint, this is why the technique remains controversial.
- Adding “routinely” can soften the recommendation and take into account the limits of the meta-analysis (heterogeneity of populations, of technical aspects…)
- Is an initial treatment or not? NICE did not specify that.
- There is a review in Spine 2014 by Poetcher et al. with Forest plots on corticoids facet injection vs facet joint radiofrequency denervation (FJRD) which is more favourable for FJRD.

- Also a primary study (Lakemeier 2013) is mentioned by one of the GDG members in which spinal injections were compared to radiofrequency denervation. No clinical differences were found between both techniques (but this primary study was excluded by NICE due to wrong population i.e. patients with facet joint osteoarthritis).
- Thus, it would be useful to review the literature in details on facet joint injection and discussed this topic during a next meeting.
- One can wonder if facet joint syndrome is not a kind of selected cases. However, one GDG member quotes that about 20% of chronic LBP are facet join syndromes (depending of the definition of course). This deserves attention.

⇨ **Conclusion: the recommendation NICE 30 has to be discussed again after a detailed review of the literature on facet infiltration.**

Stakeholders' comments and replies from NICE team on draft of MArch 2016 (edited the 30th November 2016)

- Homerton University Hospital NHS Foundation Trust: There needs to be an auditable review of effectiveness of each invasive spinal procedure after administration. At Homerton, all patients who receive spinal injections or denervation, are offered a post injection review with a senior physiotherapists working within Homerton's Locomotor pain team, within two weeks of the injection. This **review assesses for effectiveness and response**. Where the patient has benefited, rehabilitation, during the window of opportunity afforded by the injections analgesic effect is offered. Where no benefit occurs, other pain management options (such as pain management programs, functional exercise, pain Psychology, and a consultant review) are discussed and support arranged according to the biopsychosocial model with the interdisciplinary team. We believe this should be adopted as best practice nationally. **NICE answered** the GDG agreed that the main area of uncertainty the spinal injection review would address was the effectiveness of various injectates, rather than the route or mode of administration. Furthermore, spinal injections have not been recommended by this guideline (see recommendation 30). The effectiveness of the spinal injections and denervation were assessed in the studies included for these evidence reviews, and the GDG considered this when formulating the respective recommendations. It would be a part of routine practise to assess responsiveness post-administration of any intervention. (p53/111)
- The British pain society notes that The American Society of Anesthesiology has recently stated: "Maintaining access to spinal injection therapies can provide patients with the significant benefits of pain relief, improved function and quality of life, reducing their need for surgery or opioids, which is particularly important in light of the national opioid abuse epidemic." This opinion is supported by a wide number of organizations: American Academy of Pain Medicine, American Pain Society, American Society of Regional Anesthesia and Pain Medicine, American Academy of Physical Medicine and Rehabilitation, American Association of Neurological Surgeons, American College of Radiology, American Society of Neuroradiology, American Society of Spine Radiology, Congress of Neurological Surgeons, North American Neuromodulation Society, North American Spine Society, Society of Interventional Radiology and Spine Intervention Society. Recommendations
  - 1. The British Pain Society considers that the guideline is a helpful document in clarifying the evidence-based management of non-specific back pain and sciatica.
  - 2. The scope of the guidance must be reconsidered and the management of mainly elderly patients with back pain due to specific degenerative conditions should be excluded from this guidance.
  - 3. The guideline correctly highlights the lack of scientific evidence to support many elements of current clinical pain management but the use of the guideline to exclude these treatments in all patients would be unwarranted.

  NICE answered Thank you for highlighting the American guidance which we were aware of. The evidence reviewed did not support the use of spinal injections for low back pain, although we have recommended that epidurals should be considered for people with acute severe sciatica. (p36/111)
- Homerton University Hospital NHS Foundation Trust**:** It should be stressed that repeat injections should not be offered without demonstrating efficacy, Homerton's Locomotor pain service has stopped offering repeat injections unless patients attend for a post injection specialist pain Physiotherapy review and demonstrate benefit (increased function and reduction in pain) over a three month period. **NICE reply:** Spinal injections for low back pain have not been recommended in this guideline. (p70/222)
- Cost-effectiveness model for nerve root ablation in those with suspected facet joint pain and using a pain clinic population. The stated ICER is £13,000 per QALY but the base case assumes no improvement in the control group without injection. This would seem to be the wrong base case since by the time patients are identified, then assessed for suitability, some patients will improve without the injection – so fewer will be eligible for the injection / nerve root ablation. The sensitivity analysis assumes improvement as per the studies included (£16,000 per QALY), so the probability of cost-effectiveness will reduce. Also, there are no harms incorporated in the economic model e.g., radiation exposure, allergic reactions, bleeding etc. Estimates for these risks could have been sought from GDG opinion, in line with most of the clinical

parameters in the model**. NICE reply:** The population represented in the model is made of people who already had usual care and have exhausted all the possibilities in the non-invasive care; the GDG advised that longitudinal studies show that these patients do not improve with time; they could be different from the population in the RCTs where a regression to the mean could be observed. Therefore we do not think we need to change our base case. However we have also accounted for this possibility in a sensitivity analysis which shows that even when the placebo arm effect is used the intervention is cost effective.

- Arthritis Research UK: No evidence was available on the harm of the procedure so this could not be incorporated into the model. However the GDG have considered potential harm from the procedure, including radiation, and thought this was negligible. We have added some considerations in the model write up to explain this. (p77/222)
- Spine Intervention Society: In the introduction to the review section, the authors note that, "The GDG agreed that the main uncertainty …was the effectiveness of various agents, rather than the route or mode of administration." As a result, no consideration is given to the proper diagnosis of the low back condition prior to assessing an intervention for that particular condition. In essence, as previously mentioned, the review lumps all forms of back pain (except lumbar facet pain) in one basket, and assesses their treatments together by considering manuscripts that have not identified a specific etiology of the LBP. Since many different etiologies may account for "non-specific low back pain" obviously there is substantial, unaccounted heterogeneity. There was also heterogeneity in the procedures performed for non- specific etiologies: intra-articular facet injections, peri-capsular injections, peri-facet injections, intra-discal injections, nerve blocks, caudal epidurals, interlaminar epidurals, EMG-guided trigger point injections, spinal ligament injections, spinal ligament injections and non-image guided paraspinal injections. The SIS guidelines adequately describe evidence-based methodologies for stratifying low back pain patients based on etiology. Stratification based on cause then allows a meaningful analysis of various types of treatment. The authors would find that quality evidence based data already exists in this realm. The flaws in this analysis render the authors' conclusions equally flawed. **NICE reply: T**he review does consider the effectiveness of injections for facet joint pain, disc pain (intradiscal injection) and soft tissue/ligament pain. However, the GDG agreed that the key area of uncertainty was the injectate, so the review was stratified by agent and image guidance, however full details of the inclusion criteria of trials were available to the GDG in the evidence tables and they GDG did consider the evidence for injections for a particular structural pathology as part of this review. The review only considered therapeutic injection procedures and not diagnostic injection interventions. Injections of the sacroiliac joint were not included as the sacroiliac joints were considered a 'pelvic ring structure' and were excluded from the scope of the guidance. (p80/222)
- British Institute of Musculoskeletal Medicine: Prolotherapy: We found it very difficult from your tables with breakdown of the studies to work out which study was which without knowing them myself in some detail. However you mention only 3 studies – the small one with only 11 patients (? Matthews) and then the Ongley and Klein studies which you rightly criticise as 'weak'. However you fail to mention the importance of the subgroup analysis in the Klein study which subtracted the hyperalgesic patients from both groups and then reanalysed the data to find a significant result in favour of the prolotherapy group. Most importantly you excluded the Yelland study of 2004 altogether due to 'SR – used as a source of references' which needs explaining. [Yelland MJ, Glasziou PP, BogdukN, Schluter PJ,McKernon M. Prolotherapy injections, saline injections and exercises for chronic low back pain: a randomised trial. Spine 2004; 29(1):9–16.] Considering the growing popularity of this treatment around the world and the relative simplicity I am most surprised that you do not consider it worthy of a recommendation for further research using defined subgroups of NSLBP which are now clearly accepted as existing. **NICE reply:** References are not provided in the GRADE summary tables to focus on the body of the evidence rather than the individual studies. The Klein subgroup analysis has not been included in our review as it did not match the subgroup analysis pre-specified at protocol stage (please see Appendix C.15 for details) The exclusion reason for Yelland 2004A has been corrected in the excluded papers list; it was excluded from this on account of incorrect intervention (Appendix L.15). Participants were randomised to both spinal injections or saline and exercise or normal activity. Some of the participants in the prolotherapy group would also have received exercise, and therefore this did not meet our protocol for inclusion. Regarding research recommendations, the GDG considered that there was a sufficient evidence base for this topic to inform recommendations and prioritised research recommendations in other areas. (p84/222)
- Homerton University Hospital NHS Foundation Trust: The guidelines consider injections in isolation from the rest of the MDT. We feel it is poor practice to deliver any spinal injection without ongoing MDT support (physiotherapy, psychology, consultant anaesthetist). Current clinical practice in Homerton's Locomotor pain service is to offer all patients physiotherapy during the window of opportunity of a facet joint injection, before further injections or progression to denervation, are considered by the MDT. NICE answered that the review protocol includes combinations of treatment with any other intervention within the scope of the guideline, therefore this is considered if evidence were identified, but no such trials were identified relevant to the review. (p85/222)

Belgian GDG comments during the GDG meeting 14/12/2016

- The evidence quoted by NICE was reviewed, some studies suggested by the GDG members were checked and an additional literature search on spinal injections in lumbar facet joints was performed by the KCE team. However, no evidence could be found in favour of therapeutic injections of steroids in lumbar facet joints compared to placebo or other interventions. A single RCT (Lakemeier 2013) indicated that spinal injections obtained a similar pain improvement than radiofrequency denervation of the facet joints.
- Several guidelines mentioned the lack of evidence (on short and long term effectiveness) and recommended against the use of spinal injections.
- However, none of the studies reported harmful effects. Therefore, the GDG members are not convinced by a strong recommendation "against" as formulated in the NICE guideline.
- One of the GDG members mentions that most spinal injections are image-guided and suggests that avoiding unnecessary exposure to radiation is an extra argument to formulate a recommendation against the use of spinal injections.
- A clear recommendation could also counteract the current (over)use of spinal injections in clinical practice.
- The studied population was broad and studies did not separate chronic from acute pain nor clearly identify patients with facet pain.
- If spinal injections would be recommended, the GDG members emphasize the importance of the multidisciplinary approach, in which spinal injections could maybe be part of the multimodal package.
- One of the GDG members mentions the review of Manchikanti which is more in favour of spinal injections for facet joint pain, but the conclusions of this review should be carefully interpreted due to scientifically cheating by the author.
- After discussion on the wording, such as adding "routinely" or "alone" or "only in a multidisciplinary approach", the recommendation against spinal injection was agreed by all present GDG members, with the addition of a footnote on the lack of evidence on the use of spinal injections in facet joint pain syndrome.
- This recommendation focuses on the therapeutic use of spinal injections, and does not encompass the diagnostic purposes (this is discussed in the following recommendation on radiofrequency denervation).

⇨ **The final NICE recommendation 32 has been changed into:**
⇨ Do not offer spinal injections for managing low back pain*.
⇨ *No separate recommendation could be formulated on the potential use of spinal injections for facet joint pain syndrome, due to the low level of evidence on the benefits and harms of these injections.

Additional Belgian GDG comments by e-mail

- **"**As far as I know NICE has taken into account the literature mentioned below, at least they are in search strategy time window. The NICE recommendation is also in line with our local guidelines of 2011. There is in general much better outcome literature on RF facet, than on the facet injections. The findings of the Lakemeier article seems to be rather isolated in the literature and I think overruled by the Spine 2014 article. It would be "nice" to hear from NICE their point of view and evaluation of that issue. Another concern are the technical considerations, while the RF facet is a standardized technique, incl the recommendation for diagnostic blocks to improve the specificity and sensitivity, the facet injections are technical much more uncertain and so more controversial. Another reason for me that we don't have to change the NICE recommendation**."**
- "According to the SR attached. there is a positive effect of radiofrequency denervation (RFD) compared to placebo in different domains and a possible positive effect of RFD compared to injection on pain, not on function or Qol. As I mentioned earlier, the quality of evidence is rather moderate/low. On the other hand I've looked at the paper of Lakemeier. This seems a rather
- The paper of Lakemeier was included in the SR, but also a paper of Duger C. I can't find this last one in pubmed. This paper creates the effect in favor of RF in the forest plot of the SR, but seems to have a lot of risk of bias, reading the results part of the SR. Taking all these things and papers cited by NICE into account (unless there are other good quality papers on this topic) I would rather make a weak positive recommendation on facet joint injections.

NICE final recommendations on spinal injection (November 2016)

32. Do not offer spinal injections for managing low back pain.

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

No comment

KCE 2017 final recommendation on spinal injection (February 2017)

XX. Do not offer spinal injections for managing low back pain*.

*No separate recommendation could be formulated on the potential use of spinal injections for facet joint pain syndrome, due to the low level of evidence on the benefits and harms of these injections.

(Strong recommendation based on moderate to very low quality evidence from RCTs and Cohort studies)

7.16. Radiofrequency denervation for facet joint pain

Radiofrequency denervation for facet joint pain in patients with low back pain ± radicular pain

NICE search question
"What is the clinical and cost-effectiveness of radiofrequency denervation for facet joint pain in the management of non-specific low back pain?"

Introduction based on the draft version of NICE guideline (March 2016)

- The lumbar facet joints are pairs of joints that stabilize and guide motion in the spine. These joints are well innervated by the medial branches of the dorsal rami. The prevalence of facet joint pain in heterogeneous populations using local anaesthetic nerve blockade (medial branch block), where 75–100% pain relief is used as a criterion standard, is thought to be 25–40%.
- In current clinical practice, people with non-specific low back pain may be offered local anaesthetic facet joint nerve blockade to determine the presence or absence of a facet joint pain component. Those who experience significant but short term relief may then be offered a neurodestructive procedure called 'radiofrequency denervation' in an attempt to achieve longer term pain relief.
- Radiofrequency denervation has evolved as a treatment for spinal pain over the last 40 years and is a minimally invasive and percutaneous procedure performed under local anaesthesia or light intravenous sedation. Radiofrequency energy is delivered along an insulated needle in contact with the target nerves. This focussed electrical energy heats and denatures the nerve. This process may allow axons to regenerate with time requiring the repetition of the radiofrequency procedure.
- Radiofrequency denervation is not an appropriate treatment of people who have sciatica without back pain.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with non-specific low back pain
	  • Populations with low back pain only and low back pain with/without sciatica will be pooled for analysis
	  • Patients with sciatica were excluded from this review

Intervention(s)	• Radiofrequency denervation of facet joint medial • Pulsed radiofrequency is excluded
Comparison(s)	• Sham/placebo • Usual care/waiting list • Other treatment (non-invasive and invasive treatments being considered by the guideline) Pulsed radiofrequency is excluded.
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (>30% improvement in pain or function) • Adverse events: morbidity.

	• Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

- Eight randomised controlled trials were included in the review. Following comparisons were found (see Table 44):
  - Radiofrequency denervation versus placebo/sham (in 6 RCTs)
  - Radiofrequency denervation versus medial branch block (in 1 RCT)
- One RCT was included but could not be analysed as no relevant outcomes were reported.
- NEW: Two Cochrane reviews were identified but could not be included due to methodological reasons (mixed populations). The included studies were individually assessed and included if they matched the review protocol.

- **Radiofrequency denervation versus placebo/sham**
  - A clinical benefit favouring radiofrequency denervation was found for **pain**, both at short term and long term (VAS 0-10; 4 RCTs; low to moderate quality, n=96-160). However, a single study which measured pain with the McGill questionnaire reported no clinical difference in pain at both time points (low to very low quality; n=30). Additionally a benefit for radiofrequency denervation in **responders to pain reduction** measured by global perceived effect was demonstrated by 2 studies at both time points although this was not seen for pain reduction measured by VAS at less than 4 months reported by a single study (low quality, n=111).
  - No differences between RF denervation and placebo/sham were found for **function** (ODI 0-100 and RMDQ 0-100; 3-1 RCTs; low to very low quality; n=66-70-40), **healthcare utilisation** (analgesic use; 1 RCT; very low quality; n=31-40) and in two of the reported **adverse events** (change of sensibility and loss of motor function; 1 RCT; very low quality; n=79). No long term data for adverse events were reported.
  - Conflicting evidence from 1 study for **quality of life** at short term showed clinical benefit for radiofrequency denervation for the SF-36 domains of general health and vitality. Radiofrequency denervation was inferior to sham for the domains of physical functioning and no differences between treatments was found for the domains mental health, pain and social functioning (moderate to very low quality, n=81). No long term data for QoL were reported.
  - Harms: Evidence from a single study demonstrated an increase in **adverse events** for radiofrequency denervation in terms of the number of patients with moderate or severe treatment related pain (at short term; low quality, n=78).
  - Not reported outcomes: psychological distress
- **Radiofrequency denervation versus medial branch block**
  - A single study reported a short term and long term clinical benefit in favour of radiofrequency denervation for **pain** (VNS 0-10; very low quality; n=100). No clinical differences were found for **QoL** (EQ-5D 5-15; very low quality; n=100). The outcome QoL was reported in the forest plots but not in evidence statements (text) due to difficulties to interpret the EQ-5D data (analysis in a non-typical format).
  - Not reported outcomes: psychological distress, function, healthcare utilisation, responder criteria, adverse events

Table 44 – Clinical effectiveness of radiofrequency denervation in patients with low back pain

Radiofrequency denervation in patients with non-specific LBP		
Outcomes	**Radiofrequency (RF) denervation versus placebo/sham**	**Radiofrequency (RF) denervation versus medial branch block**
QoL	At short term (<4mo): • **SF-36 0-100:** o **No diff** in mental health, pain, social functioning (1 RCT; low to very low; n=81) o **CIB favouring RF denervation** in general health, vitality (1 RCT; moderate to low; n=81) o **CIB favouring placebo/sham** in physical functioning (1 RCT; low; n=81) At long term (4mo-1y): Not reported	At short term (<4mo): • **EQ-5D 5-15: no diff** (1 RCT; very low; n=100) At long term (4mo-1y): • **EQ-5D 5-15: no diff** (1 RCT; very low; n=100)
Pain	At short term (<4mo): • **VAS 0-10: CIB favouring RF denervation** (4 RCTs; moderate; n=96) • **McGill 0-78: no diff** (1 RCT; low; n=30) At long term (4mo-1y): • **VAS 0-10: CIB favouring RF denervation** (3 RCTs; low; n=160) • **McGill 0-78: no diff** (1 RCT; very low; n=30)	At short term (<4mo): • **VNS 0-10: CIB favouring RF denervation** (1 study; very low; n=100) At long term (4mo-1y): • **VNS 0-10: CIB favouring RF denervation** (1 study; very low; n=100)
Function	At short term (<4mo): • **ODI 0-100 (change and final score): no diff** (3 RCTs; low; n=66) • **RMDQ 0-100 (change and final score): no diff** (1 RCT; very low; n=70) At long term (4mo-1y): • **ODI 0-100 (change and final score): no diff** (1 RCT; very low; n=40)	

Healthcare utilisation	At short term (<4mo): • **Analgesic use (number of tablets/4 days): no diff** (1 RCT; very low; n=31) At long term (2y): • **Analgesic use (global perception of improvement 0-6): no diff** (1 RCT; very low; n=40)	
Responder criteria	At short term (<4mo): • **% of patn with >50% pain reduction-global perceived effect: CIB favouring RF denervation** (1 RCT; very low; n=31) • **% of patn with >50% back pain or pain reduction-global perceived effect: CIB favouring RF denervation** (2 RCTs; moderate; n=111) • **% of patn with >50% back pain reduction VAS 0-10: no diff** (1 RCT; low; n=81) At long term (>4mo): • **% of patn with >50% back pain or pain reduction-global perceived effect: CIB favouring RF denervation** (1 RCT; very low; n=31)	
Adverse events	At short term (<4mo): • **Number of patn with treatment-related pain (moderate or severe): CIB favouring placebo/sham** (1 RCT; low; n=78) • **Number of patn with change of sensibility (irritating or evident dysaesthesia or allodynia): no diff** (1 RCT; very low; n=79) • **Number of patn with loss of motor function (irritating or evident motor loss): no diff** (1 RCT; very low; n=79) At long term (4mo-1y): Not reported	

CIB: clinically important benefit

Economic evidence

- One cost-consequence analysis on the comparison of RF denervation versus placebo/sham (Van Wijk 2005 (NL)) found that radiofrequency denervation was more costly and more effective (£186 more per patient, SF-36 general health and vitality and global perception of reduction in back pain and pain responder criteria) compared to sham for treating low back pain (with or without sciatica). This analysis was assessed as partially applicable with potentially serious limitations.
- One original economic model found that radiofrequency denervation was cost effective compared to usual care (i.e. active management in primary care) for treating low back pain suggestive of facet joint origin that has not resolved despite non-invasive management (ICER £11,178). This analysis was assessed as partially applicable with potentially serious limitations.

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:**
  - Critical outcomes were health-related QoL, pain severity, function, psychological distress
  - Important outcome were responder criteria for pain and function (>30%), adverse events and healthcare utilisation
  - No evidence was found for psychological distress. The GDG felt there was sufficient evidence for all of the outcomes that were considered important for this review.
- **Trade-off between clinical benefits and harms**
  - **Radiofrequency denervation versus placebo/sham:**
    - **Unreliable results of benefits:** The GDG were not able to place much confidence in the results on function (no difference between groups for both ODI and RMDQ) due to different baseline ODI scores between groups and both groups were in the 'minimal disability' range post intervention. The RMDQ scale reported by 1 study was **not reported in a standard way** and had been converted to a 0-100 scale by the authors, with higher scores indicating benefit, rather than the standard 0-24 scale where higher scores indicate decline in function. For quality of life (SF-36), it was noted that there were **large baseline differences** for physical function between the intervention and sham groups, with the intervention groups being 10 points worse at baseline, and that this data showing benefit to the placebo group was not considered reliable. The GDG therefore agreed that the benefits seen in quality of life outweighed the harm, and additionally noted that there also a trend towards benefit in the other domains that were reported, but not enough to be considered clinically significant. The GDG also noted that 1 study selectively reported domains of SF-36; for role physical and role emotional scales, the results were reported in terms of 'number of patients who went up or down by 1 or more classes' rather than mean differences, which is not standard reporting of SF-36 data and therefore were not able to be included in this systematic review. The GDG considered the evidence for responder criteria (≥50% reduction in pain): there was clinical benefit at both short and long term follow up for global perception of reduction in back pain and pain. However there was no difference in the short-term in reported peak pain on VAS. It was noted that this was from the same study, but as the study only reported 'peak pain' the global perception of pain reduction may be more informative.
    - **Harms:** Nevertheless the clinically significant harm for the radiofrequency group in terms of treatment-related pain (adverse events) at the short term, it was noted that there was some treatment-related harm in the sham group as well, so both groups experienced pain that was considered to be related to the procedure. Data were only reported for less than 4 months but the GDG noted that one would not expect any treatment-related pain to occur beyond 4 months. The GDG noted that dysaesthesia or allodynia (adverse events) were important outcomes to the patient, although the event rate in the study was very small, it was higher than expected (based on the GDG's clinical experience). The group agreed that although the effect size for these adverse events was considered clinically important, because of the concerns noted (small study size and only reported at less than 4 months), they **did not have confidence in extrapolating this data to clinical practice**. The GDG also considered that although allodynia may occur, it is likely to only affect a small number of patients. They concluded that as the risk is low and the 5% seen in the evidence is higher than would be expected, the **benefits observed in terms of pain and quality of life outweighed this risk of harm**. The study additionally reported 'loss of motor function' as an adverse

event. The event rate was extremely small (zero events versus 1 event in the radiofrequency group and placebo/sham group respectively). This was considered as clinically important, but again due to the study having a small sample size, short duration of follow up, and low event rate, this risk of harm was also not considered to outweigh the benefits. The GDG considered that although there was limited data from the included studies on adverse events, there are no case reports that the GDG are aware of reporting serious complications (such as paralysis or death) from radiofrequency denervation. Several studies looked at analgesic use following the procedure at less than four months. There was no detail provided regarding number of treatments per day or what the baseline medication intake was. The GDG considered that there was no clinically important difference between groups, but this could not be accurately interpreted from the data reported. Patient perception of their global improvement of analgesic use rated on a 0-6 scale, at greater than 4 months was reported by 1 study. This was noted as a small effect on a scale that was difficult to interpret or determine whether there was benefit or not and **did not consider it informative for decision making**. When discussing adverse events, the GDG noted that studies looking specifically at adverse events show that radiofrequency is associated with only a very low incidence of minor complications.

- **Radiofrequency denervation versus medial branch block:** The GDG noted that the only retrieved study only looked at 2 outcomes relevant to this review; pain and quality of life assessed by EQ-5D. There were no data reported for adverse events. Pain assessed on a VNS was lower in the group receiving radiofrequency denervation at both short and long-term follow-ups, and this reduction was considered clinically important. The quality of life data (EQ-5D) showed no clinical difference between interventions but the GDG noted that the EQ-5D data was incompletely reported, and had not been analysed in the typical format that is appropriate for EQ-5D (i.e. summarised as a scale of 0-1; it was not weighted or in a linear scale). They were therefore unable to interpret the EQ-5D data and so it was **not considered to be useful for decision-making**.

- **Trade-off between net clinical effects and costs**
  - One cost-consequence analysis was identified that compared radiofrequency denervation with sham. This study reported higher cost with radiofrequency denervation (£186 when cost of sham is excluded as not real world treatment option). It was the only study reporting adverse events and health related quality of life. However, unlike the other studies, it does not report function or pain outcomes (with the exception of responder criteria) and therefore it is difficult to determine whether or not this study reflects the wider body of evidence. As QALYs weren't calculated it is not possible to judge if it is cost effective. It was noted that in this study participants did not receive a diagnostic block but rather an intra-articular injection and therefore the selection of eligible patients for radiofrequency denervation may not reflect current practice. Furthermore, the GDG highlighted that the intervention cost outlined in the study (£197) is lower than current practice. Finally, the GDG noted that this procedure would require a follow-up appointment either in person or by telephone. This was not detailed in the study.
  - The unit cost of radiofrequency denervation was estimated to be £1,450 per person who had a positive response to a diagnostic block and went on to receive radiofrequency denervation (NHS reference costs 2013-201435). This cost includes an initial consultant-led outpatient appointment with the pain management service, a diagnostic block (HRG code AB05Z: intermediate pain procedure), radiofrequency denervation (HRG code AB08Z: pain radiofrequency treatments) and a non-consultant-led non-face to face outpatient appointment. Given that radiofrequency denervation reduces pain it is plausible that downstream healthcare utilisation (such as other interventions) might also be reduced however there was very little evidence regarding this.
  - An original economic model was built for this guideline; this was based on pain score reported in the clinical review conducted for this guideline and also on some expert opinion for duration of treatment effects. The model showed that radiofrequency denervation is cost effective in the base case compared to usual care. The pain score at baseline was used for the usual care arm instead of the pain score in the placebo arm of the trials to reflect what would happen in real life. This was varied in a sensitivity analysis which showed that radiofrequency denervation was still cost effective if pain score for usual care was obtained from the placebo arm. The results were sensitive to the duration of the intervention; in the base case it was assumed that the pain relief from radiofrequency denervation would last for 24 months; when this was less than 16 months radiofrequency denervation was not cost effective anymore as the ICER would go above the £20,000 per QALY threshold.

  New version: No imaging before the procedure was considered in the model as the GDG experts advised this would not be required and therefore would be an inefficient use of NHS resources.

  - The GDG considered the various limitations of the model together with the main results and concluded that although radiofrequency denervation is a cost effective intervention in the base case analysis and in various sensitivity analyses, there was **not enough confidence to make a strong ('offer') recommendation** for

this intervention. In addition, as the low back pain population is potentially very large, the GDG expressed **concern about the potential cost impact of a strong recommendation**.

NEW version: The committee agreed the recommendation should include the criteria that should be met before radiofrequency denervation should be considered. It was noted there were several criteria limiting the likelihood of radiofrequency denervation being carried out and therefore, even in the context of the guideline as a whole, they did not expect this recommendation to generate a significant resource impact.

- **Quality of evidence**
  - **Quality of included studies (7 RCTs, ranged from moderate to low quality)**:
    - The GDG **did not place much confidence** in the study comparing radiofrequency denervation with medial branch block. This was because although the study met the inclusion criteria of the review, the methods used did not follow current clinical practice (diagnostic medial branch block was not performed on any of the participants prior to randomisation), but rather, all participants were randomised to radiofrequency denervation or a medial branch block (which would not pre-select those who were most likely to respond to treatment). Additionally, people in both groups were given additional therapy in the form of a rehabilitation programme if they showed a post-intervention response.
    - The GDG highlighted **limitations** that could be drawn from the study by LeClaire et al. (FR denervation versus placebo). It was noted that a letter to the editors was published by the authors acknowledging some of the methodological limitations. In particular the criteria used to select patients, as the study was carried out prior to medial branch blocks being commonly used for diagnostic purposes. This resulted in the study enrolling 94% of back pain patients from a pain clinic. The GDG estimate and are aware of research showing that the proportion of back pain patients whose pain is related to the facet joint is approximately 40-60% in clinical practice, and therefore this study likely includes a large proportion of patients who would not have facet joint pain and would not be expected to benefit from this treatment.
    - The GDG recognised that many of the studies of radiofrequency denervation are compared with placebo/sham rather than usual care or waiting list control, which was the most common comparison with other non-invasive interventions reviewed in the guideline.
    - It was also noted that the study reporting analgesic use ended blinding at 3 months and did not provide a definition of whether the analgesic use measured was prescribed or not. The GDG noted that in the study comparing radiofrequency denervation with a medial branch block, responders 1 week after treatment (in both arms) were entered into a rehabilitation programme which may affect subjective outcomes, but as this was for both arms, this was not considered to be a limitation to the study.
    - The GDG deemed this **sufficient evidence to base a recommendation on** and therefore the search was not extended to cohort studies.
  - **Reported outcomes**:
    - For function (ODI), the GDG noted that post intervention value for the radiofrequency denervation group was very low (and was 10 points lower for physical function than the control group). This meant that the modest improvement seen may be as a consequence of the '**ceiling effect**'. The quality of the evidence was therefore downgraded to reflect this.
    - Some quality of life characteristics were only reported as numbers up and numbers down, which further **reduced the quality of the data**. The same study additionally reported **baseline differences between the groups** for a few of the quality of life domains, and the evidence for this outcome was therefore downgraded as a result.
  - **Economic analysis:** The economic evaluation was assessed as partially applicable with potentially serious limitations.
- **Other considerations**
  - The GDG highlighted that all of the evidence came from **populations with chronic pain (ranging from 2 to 3 years duration or longer)** who had failed to respond to conservative treatment. The mean pain scores in the studies reviewed was >5 and the GDG considered that this would reflect the population for which RF might be appropriate. It was agreed that the recommendation should emphasize that this treatment **should be considered only for that population** and not for all people with low back pain.

- The GDG noted that current clinical practice is to administer a single initial diagnostic medial branch block to identify the population who might respond to radiofrequency denervation, and that the majority of the studies included in this review conformed to this practice. The GDG also agreed that patients who experienced prolonged pain relief from medial branch blocks (i.e. an analgesic effect outlasting the expected duration of local anaesthesia) should be offered **radiofrequency denervation rather than repeated medial branch blocks when seeking further treatment**.
- The GDG agreed that this recommendation would equally apply for **pregnant women** and this should be considered on a case by case basis.
- The GDG were concerned about **the potential for re-referrals** as some nerve regrowth may be expected after the procedure. The GDG were aware of a study finding that of 55 patients, 17 had repeat procedures. It was noted that the subgroup involved would have been patients that had not responded well to any other intervention.
- The health economic model suggests that radiofrequency denervation is **cost effective over usual care** provided the duration of pain relief exceeds 16 months. However, the GDG did not review the evidence for repeat radiofrequency denervation. The GDG were aware of the recent development of a National Spinal Radiofrequency Registry and would encourage clinicians performing this intervention to submit patient outcome information to this database. The GDG agreed that clinicians should be cautious about recommending repeat denervation procedures until longer term effectiveness data becomes available. They agreed that a **research recommendation was required to inform long terms outcomes** from radiofrequency ablation, beyond the timeframe of evidence in this review. In terms of cost and implementability, the GDG noted that it would be helpful for clinicians to be able to identify patients who may be suitable for this intervention. Although no reliable clinical features or physical signs identify 'facet joint pain' accurately, a recent UK based consensus group have published **clinical features suggestive of a facet joint pain component**. The GDG agreed that the features identified by the consensus group might be helpful in identifying those patients who may benefit from a radiofrequency denervation.
  - The features include: Increased pain unilaterally or bilaterally on lumbar para-spinal palpation
  - Increased back pain on 1 or more of the following:
    - extension (more than flexion)
    - rotation
    - extension/side flexion
    - extension/rotation

    AND
    - No radicular symptoms

    AND
    - No sacroiliac joint pain elicited using a provocation test.
- Radiofrequency denervation is a technically demanding procedure and should **only be performed by appropriately trained clinicians**.

Research recommendation

The lumbar facet joints are pairs of joints that stabilize and guide motion in the spine. These joints and periarticular structures are well innervated by the medial branches of the dorsal rami. The prevalence of pain thought to be arising from the facet joints and periarticular structures in heterogeneous populations using local anaesthetic nerve blockade (medial branch block), where 75–100% pain relief is used as a criterion standard, is thought to be 25–40%. (Manchikanti, 200099).

The current guidance recommends that for people with non-specific low back pain who have failed to respond to conservative management, local anaesthetic medial branch nerve blockade to determine the presence or absence of a pain arising from the facet joints and periarticular structures may be offered. Those who experience significant but short term relief may then be offered a neurodestructive procedure called 'radiofrequency denervation' in an attempt to achieve longer term pain relief. Radiofrequency denervation has evolved as a treatment for spinal pain over the last 40 years and is a minimally invasive and percutaneous procedure performed under local anaesthesia or

light intravenous sedation. Radiofrequency energy is delivered along an insulated needle in contact with the target nerves. This focussed electrical energy heats and denatures the nerve. This process may allow axons to regenerate with time requiring the repetition of the radiofrequency procedure.

The duration of pain relief following radiofrequency denervation is uncertain. Data from randomised controlled trials suggests relief is maintained for at least 6-12 months but no study has reported longer term outcomes. Pain relief for more than 2 years would not be an unreasonable clinical expectation. The de novo economic model undertaken for this guideline for radiofrequency denervation suggested that the treatment is likely to be cost effective provided the duration of effect exceeds 16 months. If radiofrequency denervation is repeated, we do not know whether the outcomes and duration of these outcomes are similar to the initial treatment. If repeated radiofrequency denervation is to be offered, we need to be more certain that this intervention is both effective and cost effective.

NICE 2016 recommendations: 2 clinical recommendations and 1 research recommendation (March 2016)

31. Consider referral for assessment for radiofrequency denervation for people with chronic non-specific low back pain with suspected facet joint pain when:
    - non-surgical treatment has not worked for them, and
    - they have moderate or severe levels of back pain (rated as greater than 5 on a visual analogue scale, or equivalent).

32. Only do radiofrequency denervation after a positive response to a diagnostic medial branch block for people with chronic non-specific low back pain with suspected facet joint pain.

Research recommendation

5. What is the clinical and cost effectiveness of radiofrequency denervation for chronic low back pain in the long term?

Belgian GDG considerations mentioned in the Lime survey at the end of June 2016

NICE recommendation 31. Consider referral for assessment for radiofrequency denervation for people with chronic non-specific low back pain with suspected facet joint pain when:

- **non-surgical treatment has not worked for them, and**
- **they have moderate or severe levels of back pain (rated as greater than 5 on a visual analogue scale, or equivalent).**

Agreement with the content of the NICE recommendation 31: 10 Agree, 2 Disagree, 1 no opinion, 0 out of competence, 1 no answer, 4 not completed

- **Comments from those who do not agree:**
  - "Met het vermoeden van facetgewrichtspijn". Diagnostisch probleem, want geen eenvormigheid rond de testen of beeldvorming om symptomatisch facetlijden aan te tonen. Suggestie om het in de aanbeveling dit deel te laten wegvallen.
  - Although this may be outside my competence as a non-anesthesiologist, I find this recommendation ambiguous. First, what is meant with non-surgical treatment? Is this pharmacological treatment, or does this refer to all treatment that are not surgical, such as multidisciplinary treatment, psychological, etc....In addition, a recommendation based on negative criteria is weak. Pain report only does seem to be a strange criterion for radiofrequency denervation
- **Other comments:**
  - I would state "traitement non chirurgical bien conduit" (or in accordance with EBM)
  - Indeed, the technique is 'demanding' and of high importance. This reflect the potentially unrecognized differences between the studies. One of the most important ones is the lesion size. For more explanation, please see the very interesting review: Cohen SP et al, Nat Rev Rheumatol 2013;9,101-16.

Strength of the recommendation 31 on radiofrequency denervation: According to NICE formulation, it is a weak recommendation

GRADE Factors	
Balance between desirable and undesirable effects	The GDG highlighted that all of the evidence came from populations with chronic pain (ranging from 2 to 3 years duration or longer) who had failed to respond to conservative treatment. The mean pain scores in the studies reviewed was >5 and the GDG considered that this would reflect the population for which RF might be appropriate. It was agreed that the recommendation should emphasize that this treatment should be considered only for that population and not for all people with low back pain. The GDG agreed that the benefits seen in QoL and pain outweighed the harm (treatment-related pain, dysaesthesia, allodynia).
Quality of evidence	Moderate to low
Values and preferences	All evidence came from populations with chronic pain, it was agreed that this treatment should only be considered for that population.
Costs (resource allocation)	The GDG concluded that although radiofrequency denervation is a cost-effective intervention, there was not enough confidence to make a strong recommendation. The GDG expressed concern about the potential cost impact of a strong recommendation.

Agreement with the strength of the NICE recommendation 31: 2 strong, 7 weak, 0 no opinion, 1 no answer, 8 not completed

- **Comments for a weak recommendation**
  - Depending of the values of the patients, may be proposed, or not.
  - Because of the rather limited evidence (effect on pain, not really on function), the potential costs and harms (for example the risk of multifidus denervation - could be a research recommendation) I would recommend "weak".
- **Comments for a strong recommendation**
  - There are 7 RCT's - in line with the local guidelines: Evidence based medicine according to clinical diagnoses" van Kleef M, Vanelderen P, Cohen SP, Lataster A, Van Zundert J, Mekhail N. 12. Pain originating from the lumbar facet joints. Pain Pract. 2010;10(5):459-69

NICE recommendation 32. Only do radiofrequency denervation after a positive response to a diagnostic medial branch block for people with chronic non-specific low back pain with suspected facet joint pain.

Agreement with the content of the NICE recommendation 35: 12 Agree, 0 Disagree, 0 no opinion, 1 out of competence, 1 no answer, 4 not completed

- **Comments from those who do not agree: none**
- **Other comments:**
  - As part of a multidisciplinary approach
  - Zelfde opmerking voor "vermoeden van facetpijn". Hoe aan te tonen.
  - Although this is outside my competence, this looks much better to me than the previous recommendation

Strength of the recommendation 32 on radiofrequency denervation: According to NICE formulation, it is a weak recommendation

GRADE Factors	
Balance between desirable and undesirable effects	The GDG agreed that the benefits seen in QoL and pain outweighed the harm (treatment-related pain, dysaesthesia, allodynia).
Quality of evidence	Moderate to low
Values and preferences	The GDG noted that current clinical practice is to administer a single initial diagnostic medial branch block to identify the population who might respond to radiofrequency denervation, and that the majority of the studies included in this review conformed to this practice.
Costs (resource allocation)	The GDG concluded that although radiofrequency denervation is a cost-effective intervention, there was not enough confidence to make a strong recommendation. The GDG expressed concern about the potential cost impact of a strong recommendation.

Agreement with the strength of the NICE recommendation 32: 2 strong, 8 weak, 2 no opinion, 0 no answer, 6 not completed

- **Comments for a weak recommendation**
  - Balance between desirable and undesirable effects.
  - Cost (argument GDG)
- **Comments for a strong recommendation**
  - In line with the local guidelines: Evidence based medicine according to clinical diagnoses"van Kleef M, Vanelderen P, Cohen SP, Lataster A, Van Zundert J, Mekhail N. 12. Pain originating from the lumbar facet joints. Pain Pract. 2010;10(5):459-69
  - Here the recommendation should be strong. One should only consider RF after a positive
  - respons to a medial branch block.

NICE research recommendation 5. What is the clinical and cost effectiveness of radiofrequency denervation for chronic low back pain in the long term?

Agreement with the content of the NICE research recommendation 5:: 11 Agree, 0 Disagree, 2 no opinion, 0 out of competence, 1 no answer, 4 not completed

- **Comments from those who do not agree: none**
- **Other comments:**
  - In french, I would say : "Quels sont le rapport coût-efficacité et l'efficacité clinique à long
  - terme de la dénervation par radiofréquence dans la lombalgie chronique ?"
  - no recommendation but question ?
  - Provided the total burden of disease is taken into consideration and not only the treatments.

Belgian GDG comments during the GDG meeting on the 12th October 2016

- The GDG globally agrees with the NICE recommendation 31.
- The uncertainty regarding the diagnosis is stressed by the GDG members but it is taken into account in the recommendation with the words "suspected facet joint pain". And there is more precision in the next recommendation.
- There is unanimous agreement for the recommendation 32
- The discussion concerns the strength of the recommendation. Is it a weak or a strong recommendation for NICE? It is difficult to decide.
- The Belgian GDG reads this as a strong recommendation and agrees with this strength.
- According to the experts, radiofrequency denervation is a standardized technique, which typically involves 3 to 4 levels at one side.

- **Conclusion: recommendation NICE 2016 31 and 32 unchanged**

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30th November 2016)

- Society for Back Pain Research: We welcome the recommendation for further research for radiofrequency denervation. Based on the findings and discussion suggested Research is as follows:
  - What is the validity and reliability of clinical features of suspected facet joint pain in a population presenting with non-specific low back pain.
  - What is the clinical and cost effectiveness of radiofrequency denervation in people with suspected facet joint pain, who have completed an optimal pathway of care (NICE algorithm) and have a positive response to a medial branch block?
  - What are the adverse effects of facet joint pain?
  - What is the clinical and cost effectiveness of facet radiofrequency denervation versus fusion in people who have completed an optimal pathway of care (NICE algorithm) and have a positive response to a medial branch block?

  Concern related to the identification of facet joint pain as a distinct subgroup,
  - The clinical reliability of clinical features subjected of facet joint pain has not yet been validated. The GDG acknowledge this in the introduction to this section.
  - We support that some pain may come from facet joints, but is it is highly likely that symptoms arise from other lumbar structures.
  - There are 10 facet joints in the lumbar spine. Are the proposed clinical features able to reliably differentiate which level to perform RF denervation at?
  - We note that in the literature review the population studied had low back pain with/without sciatica. This is in conflict with the proposed criteria of clinical features supporting the diagnosis of facet joint pain.

  economic model:
  - It is not clear why the GDG selected this topic over other interventions for economic modelling.
  - Probability data: Nath 2008 was used to inform, but the population in the study had 2 diagnostic blocks. This is not reflected in the Table 27-base costs inputs.
  - Table 25: the proportion of patient requiring repeat radiofrequency denervation is likely to be higher than the 10% quoted. The GDG acknowledge this under the other considerations section.
  - Page 56;line 4. It is wrong to assume that there would be no improvement from baseline pain in the radiofrequency arm. Back pain is variable and improvement is observed without treatment in all populations, including chronic back pain.
  - The duration of effectiveness was GDG opinion (potential bias), but this is not based on evidence and seems to conflict with evidence. We are disappointed that a literature search was not undertaken to inform this point.
  - The mechanism for prolonged pain relief is also questionable: nerve regrowth of 1mm/month would see facet innervation return around 4/12 and certainly well before 16/12.
  - Table 27: The cost of diagnostics (MRI or x-ray) is not included and highly likely to be done in this population prior to receiving an invasive procedure.
  - The conclusion was that there was "not enough evidence to make a firm recommendation".

  concern related to the strength of the recommendation
  - The reported adverse effect (5%) is concerning as this is a treatment aiming to reduce pain, but may be increasing pain for 4/12 for a clinically important number of people. We appreciate that this is only from one paper, but the adverse effects really are unknown,
  - The GDG report that 31% (17 out of 55) have repeat procedures. We recognise that repeat denervation (outwith research) is not being recommended, but 31% requiring repeat injection raises concern about the effectiveness.
  - The quality of evidence is low and from small trials. This is acknowledged by the GDG.

  suggested amended recommendation:

  Do not offer facet joint denervation for people with non-specific low back pain, unless part of a national registry or randomised controlled trial.

  algorithm

- We support that facet joint denervation should not be considered until after the person has had insufficient response to optimal non-invasive care, including combined physical and psychological programme.
- It would be helpful if this point is highlighted in both the short and long guideline documents.

inconsistency in the discussion compared to other interventions

- Page 60: A "trend towards benefit" was not considered to be important in the discussion of any other interventions.
- Page 62: The assumption "plausible that downstream healthcare utilisation (such as other interventions) might also be reduced". This statement is not evidence based and has not been included in other interventions.
- Like acupuncture this intervention is passive and as such likely to create dependence. This point was not included in the discussion

conflict of interest

- As stated previously there is over-representation from pain service clinicians on the GDG. It is of concern that these clinicians attract private income from this procedure.
- It is of significant concern that despite declaring that the interventional pain clinicians participated in the discussion and recommendations. This is in contrast to the pharmacological section where there was declaration and withdrawal.
- Concern regarding cost to the NHS:
- It is well known that back pain persists through life. Many treatments have not been recommended. We predict that this will result in an increased number of patients who have completed the non-invasive pathway and have pain greater than 5/10 who will then be referred for consideration of a facet joint denervation. As demonstrated in the economic model this is a costly procedure with uncertain benefit which is certainly not long term.

NICE reply

Research recommendations can only be drafted on areas that were specifically reviewed within the guideline. Therefore, whilst we acknowledge that there are other elements relating to radiofrequency denervation that may benefit from further research, our research recommendation has focussed on the area of uncertainty identified from the review. The LETR details clinical features which may be helpful in determining which patients may be suitable for this intervention although the GDG accept that reliably identifying patients with facet joint pain is challenging and the evidence to support this identification is conflicting.

We would recommend proceeding to radiofrequency denervation for those who experience 50% relief or greater from medial branch nerve blocks. This suggests that there are patients who might have facet joint pain but an additional contribution of pain from other spinal structures or sources.

The evaluation prior to radiofrequency denervation would include a clinical examination to determine the likely level (and side) of facet joint involvement. The recommendation has been amended to suggest that radiofrequency denervation should be restricted to those patients who have 'localised' pain.

Medial branch nerve blocks are then used to confirm the clinical suspicion and to determine whether or not radiofrequency denervation is then offered.

In the review protocol it was agreed that mixed populations in which it was unclear whether people also had sciatica (not stated) as well as low back pain would be included if identified, but low back pain and sciatica as inclusion criteria for trials would not. This is not in conflict with the proposed criteria.

economic model:

a) We have added some more details to why this was prioritised in Appendix N, section N.1.

b) Although people had more than one block in the study, we only used the data referring to the screening (first) block in our model.

c) The proportion of patients requiring repeat procedure was varied in a sensitivity analysis and this showed that RFD is always cost effective (ICER ranges from £13,658 per QALY when 0% of patients repeat RFD to £16,270 per QALY when 100% of patients repeat RFD).

d) We do assume there is an improvement in pain in the radiofrequency arm.

e) None of the studies included in our systematic review reported the duration of effectiveness. These values were subject to sensitivity analyses which influenced the GDG final recommendations.

f) There are no studies that we are aware of that suggest medial branch nerves, once coagulated, regenerate at this rate. The evidence reviewed by the GDG suggests that relief of pain relief exceeding at least 12 months duration is not an unreasonable expectation (Tekin 12 month outcomes). Observational studies (MacVicar et al 2013) support this view.

g) The GDG advised that a diagnostic test such as MRI or x-ray would not be done before this procedure.

The 4 month time-point at which adverse events are reported is not a reflection of the length at which adverse events occurred for. The GDG are aware that literature in the past few decades has not associated any serious adverse events with radiofrequency ablation. The GDG also agree that 31% repeat procedures does not equate to treatment failure. The adverse event profile of radiofrequency denervation cannot be adequately determined from the trials reviewed by the GDG. The topic experts were unaware of any major adverse events reported in the literature since the advent of this intervention almost 4 decades ago.

When discussing risk, the GDG were aware of a study by Cormick et al (Spine 2004) where a total of 616 radiofrequency lesions, over a period of 5 years yielded a 1.0% overall incidence of minor complications per radiofrequency site. Complications included: 3 cases of localized pain lasting more than 2 weeks (0.5%) and 3 cases of neuritic pain lasting less than 2 weeks (0.5%). This level of risk was consistent with the clinical experience of the topic experts.

algorithm

The recommendation does highlight that radiofrequency denervation should be considered when non-surgical treatment has not worked for them, therefore this will appear in both the short and long guideline documents as well as in the algorithm.

inconsistency

Regarding your comment about inconsistency in the discussion, we apologise for the apparent inconsistency and have removed the statement about trend to benefits and have removed the statement regarding dependence from the acupuncture review.

conflict of interest:

All GDG members' private practice was discussed and declared in appendix B and agreed that this was not a conflict to their involvement in discussions on topics relevant to these areas. All members who have private practice provide the same treatments as in their NHS clinics. All GDG members who had not withdrawn from the discussions were involved in all recommendation making and no member unduly influenced the decision of the committee.

Concern regarding cost to the NHS: this weak recommendation is not considered to have major cost impact issues on the NHS.

The effectiveness of radiofrequency denervation may diminish with time and this is reflected in the difference in outcomes at our defined short and long term time points. That 31% of trial subjects required repeat denervation is not an estimate of effectiveness but duration. The economic review has suggested the intervention is likely to be cost effective provided this duration exceeds 15 months and further evaluation of long term outcomes forms part of our research recommendation.

Therefore we believe the recommendation is appropriate and do not agree it should be changed to the suggested amended recommendation. (p74/222)

- Society of British Neurological Surgeons: Facet Injections - On the specific treatment issues- it is interesting that radio frequency denervation is recommended but facet joint injection is not, whilst facet injection is advised as diagnostic! No advise is given in whom this diagnostic injection should be tried! Clarity is needed in this area. NICE reply: As described in sections 22.6 and 23.6, the GDG decided against recommending facet joint injections due to the inconsistency of the evidence across the review. Furthermore, for the comparison against placebo/sham, benefits in long-term outcomes were seen which didn't appear in short-term measures. This created uncertainty among the GDG regarding the true nature of the benefits seen in the longer-term outcomes. The GDG therefore did not feel they could justify recommending facet joint injections in a NHS setting. Evidence for radiofrequency denervation compared to placebo/sham showed consistent short and long-term benefit for pain and responder criteria outcomes, as well as benefits for some quality of life measures. Along with the low incidence of adverse events, the GDG felt they could form positive recommendations for radiofrequency denervation. The recommendation developed is for a diagnostic medial branch nerve block prior to radiofrequency denervation and not an intraarticular facet joint injection. The LETR details clinical features which may be helpful in determining which patients may be suitable for this intervention although the GDG accept that reliably identifying patients with facet joint pain is challenging and the evidence to support this identification is conflicting. (p79/222)
- Spine Intervention Society: Regarding study inclusion criteria for radiofrequency denervation, the guideline stipulates, "RCTs and SRs will be included in the first instance. If insufficient RCT evidence to form a recommendation is found, non-randomised studies will be included." The critical analysis of all of the quoted studies (with the exception of a more recent one by Civilek) was provided by Bogduk et al. (2009). The Civilek study, which wasn't included in the Bogduk et al. appraisal, has a number of

flaws but most importantly, the technique itself appears to be invalid. Civilek's supplied images seem to indicate that the needle was placed in an anteroposterior (AP) view onto the superior articular process along a portion of the course of the nerve. Because the lateral view was not obtained, the needle tip could therefore lie on the nerve but is as likely to still be on the SAP. At best, this would create a pinpoint lesion of 1-2 mm, resulting in a short-term response. The radiofrequency (RF) technique is too poor to justify further analysis of the study. The controlled trials are sufficient to demonstrate efficacy, but not to optimize the technique. It is imperative to review high quality prospective studies that implement appropriate technique (e.g. Dreyfuss 2000, MacVicar 2013). The best practices document from the British Pain Society in the reference list refers to the SIS Guidelines as the correct methodology for both medial branch blocks and radiofrequency neurotomy. NICE reply: The GDG considered the study and did not see a reason to exclude it. We are not able to include Dreyfuss 2000 or MacVicar 2013 as they are case series studies, which were not included within the review protocol.(p85/222)

- James Cook University Hospital: Economic evaluation. It is not clear why GDG chose to use the expert opinion of the group for an estimate of the duration of the therapy. In a systematic review published in 2010 (1), five RCT's were included in the analysis for radio frequency denervation of facet joints in a placebo model following positive response to medial branch block. They reported evidence favouring denervation in short term outcomes (4 weeks). They report evidence of no improvement in the intermediate term (one to six months) or in the long term (six months). In a single cohort study of repeated denervation treatments, a publication in 2004 (2) indicated average duration of relief of 10.5 months for a first injection, 11.6 months for a second injection, 11.2 months for a third injection and nine months for a fourth injection. Gofeld 2007 (3) in a ten year perspective audit noted 68 percent "success" at 12 months and 30 percent at 24 months. Cohen 2010 (4) reported in their single nerve block paradigm a 42 percent successful outcome at three months (8 of 19). The GDG may wish to review the availability of evidence of duration of treatment effect before relying on consensus opinion. If published evidence is preferred then the treatment would not be cost effective on the new model. NICE reply: A systematic review was also conducted for this guideline and this included the studies identified in the systematic review that you have cited. Both reviews show the average pain score obtained at different time points after radiofrequency denervation. These studies were used in the model; however they did not report on the duration of pain relief. We have edited the model write up to explain that other studies on duration of effectiveness were considered and that more weight was given to the study by MacVicar. The study by Schofferman et al (2004) is a retrospective chart review including only patients for whom the initial procedure was successful but then benefits were subsequently dissipated and at least one additional radiofrequency denervation was performed. This study is selecting people in whom the procedure is less likely to be successful in the long run as all of them had a repeat procedure. The study by Gofeld et al (2007) does not report the meanpain score at baseline and at follow up; also they report the median pain relief duration, while we are interested in the mean. The median would not take into account the outliers (possibly on the higher end) and therefore could reduce the overall duration. The study by Cohen at al (2010) was considered unreliable due to the small sample size (n=19). (p89/222)
- United Kingdom Spinal Societies Board and British Orthopaedic association: It is not clear why GDG chose to use the expert opinion of the group for an estimate of the duration of the therapy. In a systematic review published in 2010 (1), five RCT's were included in the analysis for radio frequency denervation of facet joints in a placebo model following positive response to medial branch block. They reported evidence favouring denervation in short term outcomes (4 weeks). They report evidence of no improvement in the intermediate term (one to six months) or in the long term (six months). In a single cohort study of repeated denervation treatments, a publication in 2004 (2) indicated average duration of relief of 10.5 months for a first injection, 11.6 months for a second injection, 11.2 months for a third injection and nine months for a fourth injection. Gofeld 2007 (3) in a ten year perspective audit noted 68 percent "success" at 12 months and 30 percent at 24 months. Cohen 2010 (4) reported in their single nerve block paradigm a 42 percent successful outcome at three months (8 of 19). The GDG may wish to review the availability of evidence of duration of treatment effect before relying on consensus opinion. If published evidence is preferred then the treatment would not be cost effective on the new model. It has been suggested (da Rocha 2014, 5) that prolonged relief from a medial branch block is evidence that facet joint pain is not the cause of the symptoms and actually prolonged relief would be a contra indication to subsequent denervation. It would be greatly appreciated if the GDG would consider providing guidance on the evidence for an apparent prolonged response to medial branch block being an indication of active facet joint pain, given the duration of the local anaesthetic agents most commonly employed. This is a significant factor as the GDG have recommended a denervation procedure in patients with prolonged response to a local anaesthetic injection but have at present not based this in evidence. The GDG might wish to provide this evidence in the light of different opinions in the literature.
  NICE reply: systematic review was also conducted for this guideline and this included the studies identified in the systematic review that you have cited. Both reviews show the average pain score obtained at different time points after radiofrequency denervation. These studies were used in the model; however they did not report on the duration of pain relief. We have edited the model write up to explain that other studies on duration of effectiveness were considered and that the study by MacVicar was considered the most reliable study. The study by Schofferman et al (2004) is a retrospective chart review including only patients for whom the initial procedure was successful but then benefits were subsequently dissipated and at least one additional radiofrequency denervation was performed. This study is selecting people in whom

the procedure is less likely to be successful in the long run as all of them had a repeat procedure. The study by Gofeld et al. (2007) does not report the mean pain score at baseline and at follow up; also they report the median pain relief duration, while we are interested in the mean. The median would not take into account the outliers (possibly on the higher end) and therefore could reduce the overall duration. The study by Cohen et al. (2010) was considered unreliable due to the small sample size (n=19). Denervation would only be offered to those who experienced relief from medial branch blocks and in whom the pain has subsequently returned. The assumption that prolonged relief from medial branch blocks equates to another mechanism for pain other than pain arising from the facet joints (as proposed by Rocha), whilst an interesting premise, remains theoretical. Studies of repeated medial branch blocks (by Manchikanti et al (2008) for example) suggest that facet joint pain remains the mechanism following prolonged relief. (p89/222)

- Spine Intervention Society: “Only do radiofrequency denervation after a positive response to a diagnostic medial branch block for people with chronic non-specific low back pain with suspected facet joint pain."We are pleased to see support for radiofrequency denervation, but have concerns about a relying on results of a single positive response to a diagnostic lumbar medial branch block. Single medial branch blocks have a credibility of 50% when 100% relief is considered a positive response. (Engel 2016) The combination of the low prevalence of the condition and the known risk of false positive responses to medial branch blocks means that a single block will identify far too many patients who do not have the condition as appropriate for treatment. Giving physicians permission to treat people who have had a response to a single block will result in a large number of failed treatments, and harm the reputation of the procedure. RF should only be recommended when there have been positive responses to two sets of medial branch blocks. The criterion for a positive response to medial branch blocks should be 80-100% relief of the index pain. **NICE reply**: the false positive rate following single blocks is one of the reasons that radiofrequency denervation is only successful for a proportion of patients – this is reflected in the meta-analysis. The majority of the reviewed trials incorporated a 50% relief from a single block paradigm and the results reflect the inclusion of patients who have a false positive response to the test injection. Where studies introduced two blocks or higher expectations of relief following the blocks, no heterogeneity was observed. 50% relief from single medial branch blocks is consistent with current accepted UK practice. (p91/222)
- British Institute of Musculoskeletal Medicine: if you suspect facet joint pain’ when all else has failed then proceed to a diagnostic medial branch block – with no clinical features supposedly helpful every candidate should get this. We know that the prevalence of facet pain in the population of chronic low back pain patients is 15% in the younger adult rising to 40% in the older adult.(Schwarzer1994, Schwarzer 1995). Limiting factors applying to the recommendation: High false positive rate “placebo” of 32-38% Given that facet pain accounts for approx.. 25% all chronic low back pain (15-40%) 1000 patient injections would yield > 600 positive results - of which only 250 would be true positive and 320-380 false positive. You could improve the specificity by doing double diagnostic blocks eg. 1600+ patient injections would yield 250 true positive However your cost /resource calculations seem to have been generously assuming that upwards of 40% of patients (Nath’s study suggests 69%) will give a true positive response. **NICE reply:** The false positive rate following single blocks is one of the reasons that radiofrequency denervation is only successful for a proportion of patients – this is reflected in the meta-analysis. The majority of the reviewed trials incorporated a 50% relief from a single block paradigm and the results reflect the inclusion of patients who have a false positive response to the test injection. Where studies introduced two blocks or higher expectations of relief following the blocks, no heterogeneity was observed. (p92/222)
- Warwick Clinical Trials Unit: Recommendation 31. The available data from clinical trials indicate that radiofrequency denervation has promise as an intervention in selected populations. The GDG have highlighted the weakness in the available clinical evidence and in patient selection. On careful examination of the data presented for effect of radiofrequency ablation on pain presented to the GDG we have identified substantial concerns in the analyses and approach to inclusion of data. Our view is that these might have led to the GDG making a recommendation that is not adequately supported by the available data.(see separate comment on Figure 1117). Others looking at the same data have not considered the evidence supports the use of radiofrequency denervation. We draw the GDG’s attention to a Cochrane review, published after the GDG had drafted their recommendations, concluded. ‘The review authors found no high-quality evidence suggesting that RF denervation provides pain relief for patients with CLBP. Similarly, we identified no convincing evidence to show that this treatment improves function (Maas ET, Ostelo RW, Niemisto L, Jousimaa J, Hurri H, Malmivaara A, van Tulder MW. Radiofrequency denervation for chronic low back pain. Cochrane Database Syst Rev. 2015 Oct 23;10:CD008572. doi: 10.1002/14651858.CD008572.pub2). **NICE reply**: Following stakeholder feedback, errors in the radiofrequency analysis have been corrected, however did not change the results of the overall analysis. It also did not change the results of the economic model and the base case has remained the same as before. The GDG are aware of the Cochrane review, which although found no high-quality evidence, did in fact find moderate evidence for a large effect size in both short and long term outcomes, when pulse frequency is discounted. Regarding the on-going trial you highlight, we are unable to include studies that are not yet published so cannot consider this data. We have responded to your concerns on the economic model in your comments relating to Appendix N and we have explained there that we do not think the base case of the model should be changed. However we have clarified some additional limitations in the Appendix. (p94/222)

- Warwick Clinical Trials Unit: Recommendation 32. We support this recommendation; but does it also need to clarify that there is a pain score of five or more on a 0 – 10 numerical rating scale prior to the intervention? **NICE reply**: We have considered this, but recommendation 31 specifies that referral for assessment for radiofrequency denervation should be considered for with chronic non-specific low back pain with suspected facet joint pain when non-surgical treatment has not worked for them, and they have moderate or severe levels of back pain (rated as greater than 5 on a visual analogue scale, or equivalent). Therefore, all patients relevant to recommendation 32, having radiofrequency denervation after a positive response to a diagnostic medial branch block, will have already had a pain severity score of 5 or more in order to be referred for treatment. (p96/222)
- United Kingdom Spinal Societies Board and British Orthopaedic association: The GDG have proposed clinical features which may be helpful in identifying patient suitable for denervation. This proposal represents the only place in the overall guidance document where clinical advice on identification is proffered, and may be held to represent an area where the treatment of evidence and analysis is distinctly different for one treatment than others in the guidance. The consensus document referred to, was constructed on the Delphi principal and no evidence of the sensitivity or specificity of these clinical findings were available in the original publication. Published investigations of specificity and sensitivity have demonstrated little utility of the features investigated. The GDG may wish to consider providing evidence for the use of this paradigm. **NICE reply**: The LETR details clinical features which may be helpful in determining which patients may be suitable for this intervention although the GDG accept that reliably identifying patients with facet joint pain is challenging and the evidence to support this identification is conflicting. For this reason this full level of detail is not included in the recommendation, which states that it should be considered in people in whom the main source of pain is thought to come from structures supplied by the medial branch nerve.
- Homerton University Hospital NHS Foundation Trust: Anecdotally there seems to be a population of patients who derive good benefit from standard FJI but gain no extra duration of pain relief from the radiofrequency treatment. In these cases time and money will be expended to no extra advantage. **NICE reply:** We did not review any evidence that would support this. As described in sections 22.6 and 23.6, the GDG decided against recommending facet joint injections due to the inconsistency of the evidence across the review. Furthermore, for the comparison against placebo/sham, benefits in long-term outcomes were seen which did not appear in short-term measures. This created uncertainty among the GDG regarding the true nature of the benefits seen in the longer-term outcomes. The GDG therefore did not feel they could justify recommending facet joint injections in a NHS setting. Evidence for radiofrequency denervation compared to placebo/sham showed consistent short and long-term benefit for pain and responder criteria outcomes, as well as benefits for some quality of life measures. Along with the low incidence of adverse events and the evidence from the economic model, the GDG felt they could form positive recommendations for radiofrequency denervation.(p140/222)
- United Chiropractic Association: We are concerned that proceeding to a referral level of this intervention may be premature if an appropriate trial of conservative spinal manipulative therapy has not been undertaken. Considering the clinical effectiveness of spinal manipulation therapy, as indicated and recommended in CG88, surely in addition to other non-surgical interventions, SMT should be considered prior to radiofrequency denervation referral. Of course, if this intervention is found not to be effective in the patient, appropriate referral can be recommended. **NICE reply:** eferral for radiofrequency denervation has been recommended for a specific group of people with chronic non-specific low back pain. With reference to your comment, non-surgical treatment should have not worked for this group of people before such referral is considered. Please see section 23.6 (Recommendations and link to evidence) for details. (p188/222)
- Homerton University Hospital NHS Foundation Trust: Radiofrequency denervation carries greater cost and a stronger placebo effect than facet joint injections. **NICE reply**: As described in sections 22.6 and 23.6, the GDG decided against recommending facet joint injections due to the inconsistency of the evidence across the review. Furthermore, for the comparison against placebo/sham, benefits in long-term outcomes were seen which didn't appear in short-term measures. This created uncertainty among the GDG regarding the true nature of the benefits seen in the longer-term outcomes. The GDG therefore did not feel they could justify recommending facet joint injections in a NHS setting. Evidence for radiofrequency denervation compared to placebo/sham showed consistent short and long-term benefit for pain and responder criteria outcomes, as well as benefits for some quality of life measures. Along with the low incidence of adverse events, the GDG felt they could form positive recommendations for radiofrequency denervation. (p194/222)
- Faculty of Pain Medicine: Facet joint injections are widely performed by various specialists (e.g. Orthopaedic Surgeons, Pain Medicine Specialist, Radiologists) If this procedure is reduced or stopped altogether, there will be some cost savings which can be directed towards MBB and Facet Radiofrequency, (RF) which has a stronger evidence base. However, the FPM has concerns regarding the Medial Branch Blocks (MBB)/Facet joint denervation financial model used in the new guidance is. It appears to be based on a single test MBB followed by denervation lasting 28 months. There is great variability in how long a denervation lasts, and many patients will gain substantial relief for periods considerably less than the over two years benefit suggested. It is possible that the number of repeat denervation procedures will be considerably

higher than modelled, and as this will increase the costs. Criteria for what is a "positive response" or a "prolonged response" need to be clearly defined. It would be helpful if the guidance specified the degree of pain relief that should be achieved following MBB before proceeding to RF. **NICE reply:** Resources may be released by decommissioning interventions no longer recommended. If there are resource implications from implementing these guidelines, the GDG were reassured that the interventions were likely to be cost effective at a willingness to pay the threshold of £20,000 per QALY. The time period of 28 months was horizon for the economic model, and is not the recommended interval for repeat procedures. Whilst the economic review showed that procedures lasting 15 months were likely to be cost effective, the GDG urged caution when considering repeat radiofrequency denervation given the lack of long term outcome data. A prolonged response would be a period of pain relief significantly beyond the expected duration of local anaesthesia and one that would preclude the need for further treatment. In terms of a positive response, the majority of the trials in the review of radiofrequency denervation (Van Kleef, Van Wijck, Tekin) required 50% pain relief or greater from medial branch blocks. The topic experts suggested that >50% relief was the accepted practice in the UK currently.

- Medtronic: We question whether the GDC concerns regarding the potential cost impact for this intervention may have affected their confidence in the cost effectiveness evidence and their decision not make a firm recommendation on this intervention. The GDC have concluded that radiofrequency denervation is a cost effective intervention in the base case analysis and in various sensitivity analyses. We respectfully request that you reconsider this recommendation in line with the "Developing NICE guidelines: the manual (2104) guidance. https://www.nice.org.uk/article/pmg20/chapter/7-Incorporating-economic-evaluation#the-role-of-economics-in-guideline-development "It is particularly important for Committee members to understand that economic analysis is not only about estimating the resource consequences of a guideline recommendation, but is concerned with evaluating costs in relation to benefits (including benefits to quality of life) and harm of alternative courses of action. **NICE reply**: The rationale for not making a strong recommendation is explained in the Recommendation and Link to evidence section which says: "The GDG considered the various limitations of the model together with the main results and concluded that although radiofrequency denervation is a cost effective intervention in the base case analysis and in various sensitivity analyses, there was not enough confidence to make a strong ('offer') recommendation for this intervention. In addition, as the low back pain population is potentially very large, the GDG expressed concern about the potential cost impact of a strong recommendation."Considerations about the cost impact had been made and this is reasonable within the NICE guideline process. (p57/111)
- Warwick Clinical Trials Unit**:** The decision to support the use of radiofrequency ablation is, we think, dependent on the meta-analyses in this figure 1117. We have identified several serious concerns about the validity of these analyses that need addressing before the findings, and the economic model they inform are re-presented to the GDG. Our attention was drawn to this as in the four months analysis the direction of change in the Leclaire study has been entered in the wrong direction. Additionally, the SE for the Van Kleef study is wrong. The relevant confidence interval in Van Kleef is 2.46 (0.72 to 4.20). However, note that this is a 90% CI, and not a 95% CI. The width of this 90% CI is 3.48 points. Since a 90% confidence interval is (assuming normality) calculated as +/- 1.645 x SE (not 1.96 x SE, as for a 95% CI), then the SE is calculated as one-half of this width divided by 1.645, i.e. 1.74/1.645=1.0578 and NOT 1.74/1.96=0.8878 (as stated in the figure). This large underestimate of the SE results in too much weight being given to the Van Kleef study. A further serious problem with interpreting this figure is the data in the four month analysis from the Tekin study are the immediate post-treatment data collected six hours after the intervention. These immediate post-procedure data are meaningless when pooled with data collected several months after the procedure and cannot be safely used to inform a decisions on longer term benefits. We suggest that the six month outcome data are more relevant and that the six our follow up data should be used. There are also further numerical problems with using Tekin in the analyses. We cannot see how it is possible to calculate an exact SE from Tekin. There are no reports of between group difference SE or CIs for change from baseline that we can find to use, and so we seem to be limited to imputation from p-value. For example, in the <4m data, all we can do is impute an SE using the p-value for the between group comparison (in accordance with section 16.1.3.2 of the Cochrane handbook, part of a section we are told was observed by GDG), which we are told by Tekin is <0.001. Given the between-group difference (which must be calculated from Table 2 – we also assume an error here: the difference should be -1.7 rather than -2?), it follows (since the Tukey test refers to a t distribution on 39 degrees of freedom, two-tailed, at 0.001 the test statistic is approx. 3.558, and therefore SE=|-1.7/3.558|=0.4778, or <0.4778 since p<0.001) that all we can glean from the paper is that the SE was less than 0.478; we cannot calculate it exactly. Please could the technical team revisit how they have obtained the 0.3847 estimate of SE for this study? (and how they calculated a difference of -2 if they believe this to be correct?) In the >4m data from Tekin, we can impute an SE using the p-value for the between group comparison, which we are told by Tekin is <0.05. Given the between-group difference in here – the difference should be -1.2 rather than -1.5?), it follows (working omitted - but t on 39 df here is 2.0227) that all we can tell from the paper is that the SE was less than 0.593, but again, we cannot tell exactly what it was. Please could the technical team revisit these analyses to clarify how they have obtained the 0.3847 estimate of SE for this study? (and also how they calculated the difference of 1.5 if they believe this to be correct?) Inspection of the Gallagher paper shows that the data used in this meta-analysis come from, what appears to be, a post-hoc subgroup of those randomised. What has been presented are just from the 30 subjects who had a good response to the diagnostic block. Data from another 11 subjects who had

an equivocal response to diagnostic injections have not been included. In this group the intervention was detrimental with a point estimate for harm of 3.5 at four months and 3.2 for > four months. It is not clear to us why these relevant data have been omitted. We note that the original authors used non-parametric tests suggestion that these data re not normally distributed. We suggest that his may make it unsafe to include these data in a meta-analysis. Other commentators have previously questioned the validity of the studies by Gallagher, Leclaire and Wijk and suggested that they should not be used to inform decision making https://www.britishpainsociety.org/static/uploads/resources/files/members_articles_bupa_nov09.pdf We suggest that this whole analysis needs re-visiting by the technical team

NICE reply: The Leclaire and Van Kleef errors have been corrected however; this did not lead to significant changes in the outcome of the meta-analysis. The post procedure data from the Tekin study was used because, when setting the protocol for the review, the GDG agreed that results reported at any time before or equal to four months (including post procedure) should be pooled. However in the economic model conducted for this guideline, the pre-procedure pain score was used to inform the baseline score (and the usual care arm) while the pain score at one year was used to inform the effectiveness of the procedure as the longest effectiveness data from each study were selected for the modelling purpose. The SE in the Tekin analysis was calculated using the final values and SD reported in the paper, rather than the p-value. The values presented in the review are correct using this method. The GDG considered the Gallagher paper and agreed to only look at patients who had a good response to the diagnostic block. This is because radiofrequency denervation would only be carried out in patients who have had a good response to the diagnostic block. The changes made to the analyses were presented to the GDG for consideration and did not impact the recommendation. (93/111)

NICE changes in the final version of the guideline (November 2016)

- In the final version of the NICE guideline the wording of the recommendation has changed into recommendation 33: “Consider referral for assessment for radiofrequency denervation for people with chronic low back pain with suspected facet joint pain when:
- non-surgical treatment has not worked for them, and
- the main source of pain is thought to come from structures applied by the medial branch nerve and
- they have moderate or severe levels of localised back pain (rated as 5 or more on a visual analogue scale, or equivalent) at the time of referral.”
- The words “non-specific” have been removed, the second bullet has been added, in the third bullet “localised” has been added to back pain and the wording of the rating of the pain levels has slightly been modified without changing the content)

NICE final recommendations on spinal injection (November 2016)

33. Consider referral for assessment for radiofrequency denervation for people with chronic low back pain when:
- non-surgical treatment has not worked for them and
- the main source of pain is thought to come from structures supplied by the medial branch nerve and
- they have moderate or severe levels of localised back pain (rated as 5 or more on a visual analogue scale, or equivalent) at the time of referral.

34. Only perform radiofrequency denervation in people with chronic low back pain after a positive response to a diagnostic medial branch block.

35. Do not offer imaging for people with low back pain with specific facet join pain as a prerequisite for radiofrequency denervation.

Research recommendations 5. What is the clinical and cost effectiveness of radiofrequency denervation for chronic low back pain in the long term?

Belgian GDG comments during the meeting on the 14th December 2016

- The GDG globally agrees with the new formulation of the NICE recommendation.
- The wording “non-surgical treatment” in the second bullet is considered as not clear enough. It should imply that the patient has received appropriate multimodal management of his/her pain complaints. An explanation appears to be needed. A reference to the pathway would also be foreseen.

⇨ **The final NICE recommendation 33 is accepted without major change.**
⇨ **“Consider referral for assessment for radiofrequency denervation for people with chronic low back pain with suspected facet joint pain when:**
⇨ **non-surgical management* has not worked for them, and**

⇨ **the main source of pain is thought to come from structures applied by the medial branch nerve and**
⇨ **they have moderate or severe levels of localised back pain (rated as 5 or more on a visual analogue scale, or equivalent) at the time of referral."**
⇨ ***By non-surgical treatment, the GDG means multimodal evidence-based treatment**

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

No comment

KCE 2017 final recommendation on radiofrequency denervation for fact joint pain

19. Consider assessment for radiofrequency denervation for people with chronic low back pain with suspected facet joint pain when:

• non-surgical evidence-based multimodal management has not worked for them, and

• the main source of pain is thought to come from structures applied by the medial branch nerve and

• they have moderate or severe levels of localised back pain (rated as 5 or more on a on a numeric rating scale (NRS 0-10)) at the time of referral.

Imaging for people with low back pain with specific facet joint pain is NOT a prerequisite for radiofrequency denervation.
(weak recommendation based on moderate to low evidence from RCTs)

20. Only do radiofrequency denervation in people with chronic low back pain after a positive response to a diagnostic medial branch block.
(consensus-based expert opinion)

Research recommendations 5. What is the clinical and cost effectiveness of radiofrequency denervation in the long term for chronic low back pain with suspected facet joint pain?

7.17. Epidural injections for radicular pain

Epidural injections in patients with radicular pain

NICE search question
"What is the clinical and cost-effectiveness of epidural injections in the management of people with sciatica?"

Introduction based on the draft version of NICE guideline (March 2016)

- The epidural space lies within the spinal canal, outside the dura mater, and contains the spinal nerve roots, fat, connective tissue and blood vessels. An epidural injection is an injection of a therapeutic substance into this canal. Administration may involve a caudal injection at the base of the spine, in the midline between the vertebral laminae (interlaminar epidural) or laterally, through the intervertebral foramen (transforaminal epidural, nerve root injection, dorsal root ganglion injection). The most commonly used epidural injectate for the management of sciatica is corticosteroid, with or without local anaesthetic. The immunosuppressant and anti-inflammatory effects of corticosteroids provide a theoretical basis and rationale for epidural injection. However, some studies suggest that local anaesthetic epidural injection alone may also be therapeutic. Recent studies have also examined the role of anti-TNF (Tumour Necrosis Factor) agents into the epidural space on the premise of a TNF-α mediated inflammatory mechanism.
- Although performed widely since the 1950s, the administration of steroids into the epidural space remains unlicensed. HES data from 2010–2011 estimates that nearly 79 000 epidural and nerve root injections were performed in England.[20]
- Currently there are areas of uncertainty beyond the effectiveness of epidural injections to be considered, including the ideal route of administration, the use of imaging to improve accuracy, the timing of injection and the safety profile.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with sciatica
	  • Primarily (≥70%) disc prolapse (likely to be confirmed by imaging), other spinal pathologies may or may not also be present.
	  • Primarily (≥70%) not disc prolapse (confirmed by imaging).
	  • Mixed population / unclear spinal pathology (no clinical diagnosis);
	  1. Trial participants required to have pathology confirmed by imaging but could have either disc prolapse or other spinal pathology for inclusion.
	  2. Pathology not confirmed (may or may not have had imaging).

Intervention(s)	• Steroid (including steroid and saline) • Local anaesthetic • Anti-tumour necrosis factor (TNF) • Combination: local anaesthetic and steroid
Comparison(s)	• Sham (needle alone) / placebo / saline • Usual care • Each other (including head to head comparisons between strata) • Other treatment (non-invasive and invasive treatments being considered by the guideline for sciatica)
Outcomes	**Critical**

	• Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (>30% improvement in pain or function) • Adverse events: morbidity; mortality. • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

- Twenty randomised controlled trials were included in the review. Following comparisons were found:
  - *Image-guide epidurals*
    - *Sciatica primarily caused by (≥70%) disc prolapse*
      - *Anaesthetic versus sham/placebo (1 RCT)*
      - *Anti-TNF (mean of 3 doses) versus sham/placebo (2 RCTs)*
      - *Anti-TNF + anaesthetic versus anaesthetic (1 RCT)*
      - *Steroid + anaesthetic versus placebo/sham (2 RCTs)*
      - *Steroid + anaesthetic versus anaesthetic (4+1+1 RCTs)*
      - *Steroid + anaesthetic versus anti-TNF + anaesthetic (1 RCT)*
      - *Steroid + anaesthetic epidural versus combination of non-invasive interventions (1 RCT)*
    - *Sciatica primarily caused by non-disc lesion*
      - *Steroid + anaesthetic versus anaesthetic (3 RCTs)*
    - *Sciatica primarily caused by mixed population/unclear spinal pathologies*
      - *Steroid + anaesthetic versus anaesthetic (4 RCTs)*
  - *Non image-guided epidurals*
    - *sciatica primarily caused by (≥70%) disc prolapse*
      - *Steroid epidural versus placebo (2 RCTs)*
      - *Steroid + anaesthetic epidural versus combination of non-invasive interventions (1 RCT)*
      - *Steroid + anaesthetic epidural versus pharmacological treatment (NSAIDs) (1 RCT)*
      - *Steroid + anaesthetic epidural versus pharmacological treatment (combination) (1 RCT)*
      - *Steroid + anaesthetic epidural versus anaesthetic (1 RCT)*
      - *Steroid + anaesthetic epidural versus anaesthetic epidural (2 RCTs)*
    - *Sciatica primarily caused by non-disc lesion*
    - *Sciatica primarily caused by mixed population/unclear spinal pathologies*
      - *Steroid epidural versus placebo (1 RCT)*
      - *Steroid epidural versus usual care (1 RCT)*
      - *Steroid epidural versus anaesthetic epidural (1 RCT)*
      - *Steroid + anaesthetic epidural versus placebo (1 RCT)*

- *Steroid + anaesthetic epidural versus anaesthetic epidural (1 RCT)*

- No RCTs were found for the comparison 'steroids versus sham', a search for non-randomised studies revealed no relevant cohort studies.

Image-guided epidurals

- **Sciatica primarily caused by (≥70%) disc prolapse (see Table 45)**
  - Anaesthetic versus sham/placebo (saline):
    - A single study (fluoroscopy guided injections of 0.75ml of 0.5% bupivacaine) reported a short term clinical benefit in leg **pain** (VAS 0-10; low quality; n=64) in favour of sham/placebo, however no difference was found in the proportion of patients reporting a more than 50% reduction in pain (**responder criteria**; low quality; n=64). No long term data were reported.
    - Not reported outcomes: QoL, function, psychological distress, adverse events, healthcare utilisation
  - Anti-TNF (mean of 3 doses) versus sham/placebo (saline)
    - A single RCT (contrast flow/fluoroscopy guided injections of 0.5-2.5mg or 12.5mg etanercept) reported a clinical benefit in leg **pain** (mean daily worst pain 0-10; very low quality; n=37) at short term in favour of anti-TNF. Another study reported the **adverse events** but found none in both groups (low quality; n=24) at both time points.
    - Not reported outcomes: QoL, function, psychological distress, responder criteria, healthcare utilisation
  - Anti-TNF + anaesthetic versus anaesthetic
    - A single study (fluoroscopy guided injections of 4mg etanercept + 0.5% bupivacaine versus 0.5% bupivacaine + saline) found no difference in short term **pain** (VAS 0-10; low quality; n= 56) and **function** (ODI 0-100; moderate quality; n=56), nor in **healthcare utilisation** (surgery and >20% opioid use or cessation non-opioids; low quality; n=56-23) or in **responder criteria** (>50% reduction in pain at short and long term; low quality; n=56).
    - Not reported outcomes: QoL, psychological distress, adverse events
  - Steroid + anaesthetic versus placebo/sham
    - A clinical benefit of the combination of steroids and anaesthetics (fluoroscopy guided injections of 1.75ml triamcinolone 40ml/l + 0.75ml of 0.5% bupivacaine) compared to placebo (saline) was found for (leg) **pain** (VAS 0-10; 1 RCT; moderate quality; n=65) and for **responder criteria** (number of patients reporting >5°% pain reduction; high quality; n=65)). However, no difference in **function** (ODI 0-100; low-moderate quality; n=160) was found at both time points.
    - Not reported outcomes: QoL, psychological distress, adverse events, healthcare utilisation
  - Steroid + anaesthetic versus anaesthetic
    - Within this comparison, 3 different approaches of epidural injections were found: transforaminal, caudal and interlaminar approach.
      Studies on the transforaminal approach (4 RCTs; fluoroscopy-guided injections of methylprednisolone/triamcinolone/betamethasone + bupivacaine/lidocaine) revealed no differences in **pain** (VAS 0-10; 3-1 RCTs; moderate-high quality; n=233-120), **function** (ODI 0-100; 2-1 RCTs; low-moderate quality; n=178-120) and **healthcare utilisation** (opioid intake; 1 RCT; moderate quality; n=120) at both time points. Two outcomes of **responder criteria** (number of patients reporting a >50% pain reduction at short term; 3 RCTs; very low quality; n=233 and number of patients who underwent surgery at long term; 1 RCT; low quality; n=55) showed a clinical benefit in favour of the combination of steroids and anaesthetics. Other outcomes of responder criteria (function improvement; 1 RCT; low-moderate quality; n=120) revealed no differences.
      A study on the caudal approach (1 RCT; fluoroscopy-guided injections of 6mg betamethasone or 40mg methylprednisolone + 0.5% lidocaine) showed no difference in **pain** (VAS 0-10; low quality; n=353-120), **function** (ODI 0-100; low-moderate quality; n=120), **healthcare utilisation** (opioid intake; moderate quality; n=120) and **responder criteria** (>50% improvement in pain or function; moderate-low quality; n=120) at both time points.
      One study reported on the interlaminar approach (1 RCT; fluoroscopy-guided injections of 80mg methylprednisolone + 0.5% lidocaine) and found a clinical benefit in **responder criteria** (>50% pain reduction; very low quality; n=69) in favour of the combination of steroids and anaesthetics, both at

short and long term. No differences in long-term **healthcare utilisation** (additional injections; very low quality; n=69) and in **adverse events** (complications; very low quality; n=69) were found.
- Not reported outcomes: QoL, psychological distress

- Steroid + anaesthetic versus anti-TNF + anaesthetic
  - A single RCT (fluoroscopy-guided injections of 60mg methylprednisolone + 0.5% bupivacaine) reported a short term clinical benefit in **pain** (VAS 0-10; moderate quality; n=54) and **function** (ODI 0-100; moderate quality; n=54) in favour of the combination of steroids and anaesthetics. However, no differences were found for **responder criteria** (>50% pain reduction; low quality; n=54) and **healthcare utilisation** (surgery; low quality; n=54 and medication reduction; moderate quality; n=54-23).
  - Not reported outcomes: QoL, psychological distress, adverse events
- Steroid + anaesthetic epidural versus combination of non-invasive interventions (pharmacological (Tizanidine, Diclofenac, amitriptyline), manual therapy (traction), physiotherapy (TENS, short wave diathermy) and biomechanical exercises (Back extension exercises))
  - A single RCT (injections of saline + 2% xylocaine + 2ml triamcinolone acetate) reported a long-term clinical benefit in **QoL** (numerical pain intensity of HRQoL; moderate quality; n=100), **pain** (VAS 1-10; moderate quality; n=100), **function** (ODI 1-100; moderate quality; n=100), **responder criteria** (complete pain relief; high quality; n=102) in favour of the combination of steroids and anaesthetics. No difference was found for **psychological distress** (BDI 0-63; moderate quality; n=100). No short term data were reported.
  - Not reported outcomes: adverse events, healthcare utilisation

Table 45 – Clinical effectiveness of image-guided epidural injections with steroid + anesthetic in patients with low back pain and sciatica

Epidural injections (steroid + anesthetic) in patients with LBP and sciatica				
Outcomes	**Steroid + anaesthetic versus placebo/sham**	**Steroid + anaesthetic versus anaesthetic**	**Steroid + anaesthetic versus anti-TNF + anaesthetic**	**Steroid + anaesthetic epidural versus combination of non-invasive interventions**
QoL				At short term (<4mo): Not reported At long term (4mo-1y): • **Numerical pain intensity: CIB favouring steroid** (1 RCT; moderate; n=100)
Pain	At short term (<4mo): • **Leg pain VAS 0-10 (final scores): CIB favouring steroid** (1 RCT; moderate; n=65)	At short term (<4mo): • **Transforaminal approach VAS 0-10: no diff** (3 RCTs; moderate; n=233) • **Caudal approach VAS 0-10: no diff** (1 RCT; low; n=353)	At short term (<4mo): • **VAS 0-10: CIB favouring steroid** (1 RCT; moderate; n=54)	At short term (<4mo): Not reported

	At long term (4mo-1y): No reported	At long term (4mo-1y): • **Transforaminal approach VAS 0-10: no diff** (1 RCT; high; n=120) • **Caudal approach VAS 0-10: no diff** (1 RCT; low; n=120)	At long term (4mo-1y): No reported	At long term (4mo-1y): • **VAS 1-10: CIB favouring steroid** (1 RCT; moderate; n=100)
Function	At short term (<4mo): • **ODI 0-100: no diff** (1 RCT; low; n=160) At long term (4mo-1y): • **ODI 0-100: no diff** (1 RCT; moderate; n=160)	At short term (<4mo): • **Transforaminal approach ODI 0-100: no diff** (2 RCTs; low; n=178) • **Caudal approach ODI 0-100: no diff** (1 RCT; low; n=120) At long term (4mo-1y): • **Transforaminal approach ODI 0-100: no diff** (1 RCT; moderate; n=120) • **Caudal approach ODI 0-100: no diff** (1 RCT; moderate; n=120)	At short term (<4mo): • **ODI 0-100 (final scores): CIB favouring steroid** (1 RCT; moderate; n=54) At long term (4mo-1y): No reported	At short term (<4mo): Not reported At long term (4mo-1y): • **ODI 1-100: CIB favouring steroid** (1 RCT; moderate; n=100)
Psychological distress				At short term (<4mo): Not reported At long term (4mo-1y): • **BDI 0-63: no diff** (1 RCT; moderate; n=100)
Healthcare utilisation		At short term (<4mo): • **Transforaminal approach** o **Opioid intake: no diff** (1 RCT; moderate; n=120) • **caudal approach** o **Opioid intake: no diff** (1 RCT; moderate; n=120)	At short term (<4mo): • **surgery: no diff** (1 RCT; low; n=54) • **medication reduction: no diff** (1 RCT; moderate; n=54)	

		At long term (4mo-1y): • **Transforaminal approach** o **Opioid intake: no diff** (1 RCT; moderate; n=120) o **surgery: CIB in favour of steroid** (1 RCT; low; n=55) • **caudal approach** o **Opioid intake: no diff** (1 RCT; moderate; n=120) • **Interlaminar (parasaggital) approach** o **Additional injections: no diff** (1 RCT; very low; n=69)	At long term (4mo-1y): • **medication reduction: no diff** (1 RCT; moderate; n=23)	
Responder criteria	At short term (<4mo): • **% of patn with >50% pain reduction: CIB favouring steroid** (1 RCT; high; n=65) At long term (>4mo):	At short term (<4mo): • **Transforaminal approach** o **>50% pain reduction: CIB favouring steroid** (3 RCTs; very low; n=233) o **>50% function reduction: no diff** (1 RCT; low; n=120) • **caudal approach** o **>50% pain reduction: no diff** (1 RCT; low; n=120) o **>50% function reduction: no diff** (1 RCT; moderate; n=120) • **interlaminar (parasaggital) approach >50% pain reduction: CIB favouring steroid** (1 RCT; very low; n=69) At long term (4mo-1y):	At short term (<4mo): • **% of patn with >50% pain reduction: no diff** (1 RCT; low; n=54) At long term (>4mo):	At short term (<4mo): Not reported

	Not reported	• **Transforaminal approach** o **>50% pain reduction: no diff** (2 RCTs; moderate; n=178) o **>50% function reduction: no diff** (1 RCT; moderate; n=120) • **caudal approach** o **>50% pain reduction: no diff** (1 RCT; low; n=120) o **>50% function reduction: no diff** (1 RCT; moderate; n=120) • **interlaminar (parasaggital) approach >50% pain reduction: CIB favouring steroid** (1 RCT; very low; n=69)	• **% of patn with >50% pain reduction: no diff** (1 RCT; low; n=54)	At long term (4mo-1y): • **Complete pain relief: CIB favouring steroid** (1 RCT; high; n=102)
Adverse events		At short term (<4mo): Not reported At long term (4mo-1y): • **interlaminar (parasaggital) approach complications: no diff** (1 RCT; very low; n=69)		

CIB: clinically important benefit

Outcomes not reported: psychological distress

- **Sciatica primarily caused by non-disc lesion**
  - Steroid + anaesthetic versus anaesthetic
    - Three studies compared steroids and anaesthetics (fluoroscopy-guided injections of triamcinolone/bethamethasone/methylprednisolone + lidocaine) to anaesthetics alone and found no clinical differences for all reported outcomes: **QoL** (EQ-5D 0-1; at short term; 1 RCT; low quality; n=386), **pain** (VAS 0-10; both time points; 3-2 RCTs; low-moderate quality; n=606-202), **function** (RMDQ 0-24; short term; 1 RCT; very low quality; n=386 and ODI 0-100; both time points; 1 RCT; moderate quality; n=100), **responder criteria** for pain (>30% reduction; short term; 1 RCT; low quality; n=386 and >50% reduction; both time points; 1 RCT; very low quality; n=100) and for function (>30% reduction; short term; 1 RCT; very low quality; n=386 and >50% reduction; both time points; 1 RCT; low-very low quality; n=100), **healthcare utilisation** (opioid intake; both time points; 1 RCT; moderate-low quality; n=100) and serious **adverse events** (both time points; 2-1 RCTs; very low-moderate quality; n=500-100).
    - Not reported outcomes: psychological distress

- **Unclear spinal pathologies**
  - Steroid + anaesthetic versus anaesthetic
    - Four studies compared steroids and anaesthetics (fluoroscopy-guided injections of methylprednisolone/betamethasone + bupivacaine/lidocaine) to anaesthetics in a mixed population and found no clinical differences for all reported outcomes: **pain** (VAS 0-10; short term; 2 RCTs; very low quality; n=205 and PPI 0-5; short term; 1 RCT; very low quality; n=69), **function** (ODI 0-100; short term; 2 RCTs; very low quality; n=263), **healthcare utilisation** (surgery; both time points; 2-1 RCTs; very low quality; n=127-129 and medication reduction; both time points; 1 RCT; moderate quality; n= 58-24) and **adverse events** (both time points; 1 RCT; low quality; n=129-124). In 3 of the 4 studies, the transforaminal approach was applied. In the fourth study the approach was not specified.
    - Not reported outcomes: QoL, psychological distress, responder criteria
- In conclusion, comparing the effectiveness of image-guided epidural injections with steroids and anaesthetics to anaesthetics in the three included populations (sciatica caused by disc prolapse, sciatica caused by non-disc lesion and mixed population) revealed some clinical benefits (in responder criteria for >50% pain reduction and a reduced number of patients who underwent surgery) in the population with disc prolapse, although the effects are small, reported in a small number of studies with moderate to very low quality.

Table 46 – Clinical effectiveness of image-guided epidural injections with steroids + anesthetic according to the cause of sciatica

Epidural injections (steroids + anaesthetic) compared to anaesthetic in patients with LBP and sciatica (in different populations)			
Outcomes	**Sciatica primarily caused by (≥70%) disc prolapse**	**Sciatica primarily caused by non-disc lesion**	**Sciatica primarily caused by mixed population/unclear spinal pathologies**
QoL		At short term (<4mo): • **EQ-5D 0-1: no diff** (1 RCT; low; n=368) At long term (4mo-1y): Not reported	
Pain	At short term (<4mo): • **Transforaminal approach VAS 0-10: no diff** (3 RCTs; moderate; n=233) • **Caudal approach VAS 0-10: no diff** (1 RCT; low; n=353) At long term (4mo-1y): • **Transforaminal approach VAS 0-10: no diff** (1 RCT; high; n=120) • **Caudal approach VAS 0-10: no diff**	At short term (<4mo): • **VAS 0-10: no diff** (3 RCTs; low; n=606) At long term (4mo-1y): • **VAS 0-10: no diff** (2 RCTs; moderate; n=202)	At short term (<4mo): • **VAS 0-10: no diff** (2 RCTs; very low; n=205) • **PPI 0-5: no diff** (1 RCT; very low; n=69) At long term (4mo-1y): Not reported

	(1 RCT; low; n=120)		
Function	At short term (<4mo): • **Transforaminal approach ODI 0-100: no diff** (2 RCTs; low; n=178) • **Caudal approach ODI 0-100: no diff** (1 RCT; low; n=120) At long term (4mo-1y): • **Transforaminal approach ODI 0-100: no diff** (1 RCT; moderate; n=120) • **Caudal approach ODI 0-100: no diff** (1 RCT; moderate; n=120)	At short term (<4mo): • **RMDQ 0-24: no diff** (1 RCT; very low; n=386) • **ODI 0-100: no diff** (1 RCT; moderate; n=100) At long term (4mo-1y): • **ODI 0-100: no diff** (1 RCT; moderate; n=100)	At short term (<4mo): • **ODI 1-100: CIB favouring steroid** (2 RCTs; very low; n=263) At long term (4mo-1y): Not reported
Healthcare utilisation	At short term (<4mo): • **Transforaminal approach** o **Opioid intake: no diff** (1 RCT; moderate; n=120) • **caudal approach** o **Opioid intake: no diff** (1 RCT; moderate; n=120) At long term (4mo-1y): • **Transforaminal approach** o **Opioid intake: no diff** (1 RCT; moderate; n=120) o **surgery: CIB in favour of steroid** (1 RCT; low; n=55) • **caudal approach** o **Opioid intake: no diff** (1 RCT; moderate; n=120) • **Interlaminar (parasaggital) approach** o **Additional injections: no diff** (1 RCT; very low; n=69)	At short term (<4mo): • **Opioid intake: no diff** (1 RCT; moderate; n=100) At long term (4mo-1y): • **Opioid intake: no diff** (1 RCT; low; n=100)	At short term (<4mo): • **surgery: no diff** (2 RCTs; very low; n=127) • **opioid intake: no diff** (1 RCT; moderate; n=58) At long term (4mo-1y): • **surgery: no diff** (1 RCT; very low; n=129) • **opioid intake: no diff** (1 RCT; moderate; n=24)
Responder criteria	At short term (<4mo): • **Transforaminal approach**	At short term (<4mo):	

	o **>50% pain reduction: CIB favouring steroid** (3 RCTs; very low; n=233) o **>50% function reduction: no diff** (1 RCT; low; n=120) • **caudal approach** o **>50% pain reduction: no diff** (1 RCT; low; n=120) o **>50% function reduction: no diff** (1 RCT; moderate; n=120) • **interlaminar (parasaggital) approach >50% pain reduction: CIB favouring steroid** (1 RCT; very low; n=69) <u>At long term (4mo-1y):</u> • **Transforaminal approach** o **>50% pain reduction: no diff** (2 RCTs; moderate; n=178) o **>50% function reduction: no diff** (1 RCT; moderate; n=120) • **caudal approach** o **>50% pain reduction: no diff** (1 RCT; low; n=120) o **>50% function reduction: no diff** (1 RCT; moderate; n=120) • **interlaminar (parasaggital) approach >50% pain reduction: CIB favouring steroid** (1 RCT; very low; n=69)	• **% of patn with >30% pain reduction: no diff** (1 RCT; low; n=386) • **% of patn with >50% pain reduction: no diff** (1 RCT; very low; n=100) • **% of patn with >30% function improvement: no diff** (1 RCT; very low; n=386) • **% of patn with >50% function improvement: no diff** (1 RCT; low; n=100) <u>At long term (>4mo):</u> • **% of patn with >50% pain reduction: no diff** (1 RCT; very low; n=100) • **% of patn with >50% function improvement: no diff** (1 RCT; very low; n=100)	
Adverse events	<u>At short term (<4mo):</u> Not reported <u>At long term (4mo-1y):</u>	<u>At short term (<4mo):</u> • **serious AE: no diff** (2 RCTs; very low; n=500) <u>At long term (4mo-1y):</u> • **serious AE: no diff**	<u>At short term (<4mo):</u> • **AE: no diff** (1 RCT; low; n=129) <u>At long term (4mo-1y):</u> • **AE: no diff**

	• **interlaminar (parasaggital) approach complications: no diff** (1 RCT; very low; n=69)	(1 RCT; moderate; n=100)	(1 RCT; low; n=124)

CIB: clinically important benefit

Non-image guided epidurals

- **Sciatica primarily caused by (≥70%) disc prolapse**
  - Steroid epidural versus placebo
    - Two RCTS reported no short term clinical difference between steroids epidural (injections of methyl prednisolone) and placebo for **pain** (VAS 1-10; 2 RCTs; moderate quality; n=174 and McGill 1-5; 1 RCT; high quality; n=156 and McGill 0-50; 1 RCT; high quality; n=156), **function** (0DI/RMDQ 0-100; 2 RCTs; low quality; n=221) and (minor) **adverse events** (2 RCTs; low quality; n=232). No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, healthcare utilisation, responder criteria
  - Steroid + anaesthetic epidural versus combination of non-invasive interventions (self-management + static and dynamic exercises) (see Table 47)
    - A single study (injections of methyl prednisolone + bupivacaine) reported only one outcome: no clinical difference for **pain** (VAS 1-10; short term; moderate quality; n=139) was found.
    - Not reported outcomes: QoL, function, responder criteria, psychological distress, healthcare utilisation, adverse events.
  - Steroid + anaesthetic epidural versus pharmacological treatment (NSAIDs)
    - A single study (injections of methyl prednisolone + prilocaine) reported no clinical differences in **pain** (VAS 1-10; low quality; n=64), **function** (ODI 1-100; low quality; n=64) and **healthcare utilisation** (paracetamol use; low quality; n=64). No long term data were reported.
    - Not reported outcomes: QoL, psychological distress, responder criteria, and adverse events.
  - Steroid + anaesthetic epidural versus pharmacological treatment (combination of NSAIDs + opioids+ muscle relaxants)
    - A single study (injections of methyl prednisolone + xylocaine) reported no clinical differences in **pain** (VAS 1-10; at both time points; very low-low quality; n=50) and long term (minor) **adverse events** (low quality; n=50).
    - Not reported outcomes: QoL, function, psychological distress, responder criteria, and adverse events.
  - Steroid + anaesthetic epidural versus anaesthetic
    - No critical outcomes were reported for this comparison. A single RCT (injections of carbocaine + hydrocortisone) reported no clinical differences in **responder criteria** (>75% pain reduction at both time points; very low quality; n= 30) and in **healthcare utilisation** (number of patients who underwent surgery; at long term; very low quality; n=30).
    - Not reported outcomes: QoL, pain, function, adverse events, healthcare utilisation
  - Steroid + anaesthetic epidural versus anaesthetic epidural
    - One RCT compared different modalities of steroids and anaesthetics and found following results (no long term data were reported):
      - Methyl prednisolone vs bupivacaine: a clinical benefit in short term **pain** (VAS 1-10; moderate quality; n=105) and **healthcare utilisation** (use of physiotherapy; low quality; n=81).
      - Triamcinolone + Bupivacaine vs anaesthetic: a clinical benefit in short term **pain** (VAS 1-10; moderate quality; n=107) and **healthcare utilisation** (use of physiotherapy; low quality; n=84).
      - Dexamethasone + Bupivacaine vs anaesthetic: no differences in short term **pain** (VAS 1-10; moderate quality; n=105) and **healthcare utilisation** (use of physiotherapy; low quality; n=82).
    - Another RCT (injections of carbocaine + hydrocortisone) found no differences in **healthcare utilisation** (number of patients who underwent surgery; very low quality; n=33) and in responder criteria (>75% pain reduction: at both time points; very low quality; n=33).

- Not reported outcomes: QoL, function, adverse events, psychological distress

Table 47 – Clinical effectiveness of non-image guided epidural injections with steroid + anesthetic in patients with low back pain and sciatica

Non-image guided epidural injections (steroid + anesthetic) in patients with LBP and sciatica					
Outcomes	**Steroid + anaesthetic versus combination of non-invasive interventions**	**Steroid + anaesthetic versus NSAIDs**	**Steroid + anaesthetic versus combined pharmacological intervention**	**Steroid + anaesthetic versus anaesthetic**	**Steroid + anaesthetic versus anaesthetic epidural**
Pain	At short term (<4mo): • **VAS 1-10: no diff** (1 RCT; moderate; n=65) At long term (4mo-1y): No reported	At short term (<4mo): • **VAS 1-10: no diff** (1 RCT; low; n=64) At long term (4mo-1y): Not reported	At short term (<4mo): • **VAS 1-10: no diff** (1 RCT; very low; n=50) At long term (4mo-1y): • **VAS 1-10: no diff** (1 RCT; low; n=50)		At short term (<4mo): • **Methyl prednisolone vs bupivacaine VAS 1-10: CIB favouring steroids** (1 RCT; moderate; n=105) • **Triamcinolone + Bupivacaine vs anaesthetic VAS 1-10: CIB favouring steroids** (1 RCT; moderate; n=107) • **Dexamethasone + Bupivacaine vs anaesthetic VAS 1-10: no diff** (1 RCT; moderate; n=105) At long term (4mo-1y): Not reported
Function		At short term (<4mo): • **ODI 1-100: no diff** (1 RCT; low; n=64) At long term (4mo-1y): Not reported			
Healthcare utilisation		At short term (<4mo): • **Paracetamol use: no diff**		At short term (<4mo): Not reported	At short term (<4mo): • **Methyl prednisolone vs bupivacaine use of**

		(1 RCT; low; n=64) At long term (4mo-1y): Not reported		At long term (4mo-1y): • **surgery: no diff** (1 RCT; very low; n=30)	**physiotherapy: CIB favouring steroids** (1 RCT; low; n=81) • **Triamcinolone + Bupivacaine vs anaesthetic use of physiotherapy: CIB favouring steroids** (1 RCT; low; n=84) • **Dexamethasone + Bupivacaine vs anaesthetic use of physiotherapy: no diff** (1 RCT; low; n=82) At long term (4mo-1y): • **surgery: no diff** (1 RCT; very low; n=33)
Responder criteria				At short term (<4mo): • **>75% pain reduction: no diff** (1 RCT; very low; n=30) At long term (4mo-1y): • **>75% pain reduction: no diff** (1 RCT; very low; n=30)	At short term (<4mo): • **>75% pain reduction: no diff** (1 RCT; very low; n=33) At long term (4mo-1y): • **>75% pain reduction: no diff** (1 RCT; very low; n=33)
Adverse events			At short term (<4mo): Not reported At long term (4mo-1y): • **Minor AEs: no diff** (1 RCT; low; n=50)		

CIB: clinically important benefit

- **Sciatica primarily caused by non-disc lesion**
  - No evidence reported

- **Sciatica primarily caused by mixed population/unclear spinal pathologies**
  - Steroid epidural versus placebo (see Table 48)
    - A single study reported only one outcome: no long term difference in **healthcare utilisation** (discontinuation of analgesics; very low quality; n=51) was found between steroids epidurals (methyl prednisolone) and placebo. No short term data were reported.
    - Not reported outcomes: QoL, pain, function, responder criteria, adverse events, psychological distress
  - Steroid epidural versus usual care
    - A single study (injections of triamcinolone) reported a short term clinical benefit in leg **pain** (NRS 1-10; low quality; n=63) and **function** (RMDQ 0-24; low quality; n=63) in favour of steroids. However, no difference was anymore seen at long term. Other measures of pain severity showed no differences compared to usual care (back pain, pain during day/night, overall pain; low quality; n=63), at both time points. Regarding **QoL**, some conflicting results were found: at short, the majority of the subdomains of SF-36 0-100 showed a clinical benefit in favour of steroids, however a harmful affect was seen for subdomain vitality and no difference for emotional well-being. At long term, no differences were found for 3 subdomains (mental composite, vitality and pain) and a harmful effect for emotional well-being (low-moderate; n=50).
    - Not reported outcomes: responder criteria, psychological distress, adverse events
  - Steroid epidural versus anaesthetic epidural
    - The single RCT (injections of depromedrone) reported only one outcome: no difference was found in patients who underwent back surgery (**healthcare utilisation**) at short term. No long term data were reported.
    - Not reported outcomes: QoL, pain, function, psychological distress, adverse events, responder criteria

  ---

  - Steroid + anaesthetic epidural versus placebo
    - A single RCT (injections of triamcinolone acetonide + bupivacaine) reported no differences compared to placebo for (leg or back) **pain** (VAS 1-10; at both time points; moderate quality; n=228), **function** (ODI 1-100; at both time points; moderate-low quality; n=228), **psychological distress** (HAD 0-21 anxiety and depression; at both time points; low-moderate quality; n=228), **healthcare utilisation** (mean analgesic use/week, referred for surgery, further physiotherapy, referral to pain management services, further epidurals; moderate-low quality; n=228), **responder criteria** (>75% leg or back pain reduction; at short term; low quality; n=228) and (minor) **adverse events** (low quality; n=228).
    - Not reported outcomes: QoL
  - Steroid + anaesthetic epidural versus anaesthetic epidural
    - A single RCT (injections of methyl prednisolone + lignocaine) reported only one outcome: no difference was found in **healthcare utilisation** (reduced drug intake; very low quality; n=29 and back surgery; very low quality; n=30) compared to anaesthetic epidural.
    - Not reported outcomes: QoL, pain, function, psychological distress, adverse events, responder criteria

- A subanalysis, comparing the efficacy of steroids epidural versus placebo in the different populations, was hampered by the lack of reported outcomes. In the mixed population only healthcare utilisation was reported and this outcome was not reported in the 2 RCTs on patients with disc prolapse.

Table 48 – Clinical effectiveness of non-image guided epidural injections with steroids in mixed population/unclear spinal pathologies

Non-image guided epidural injections (steroid) in mixed population/unclear spinal pathologies			
Outcomes	**Steroid epidural versus placebo**	**Steroid epidural versus usual care**	**Steroid epidural versus anaesthetic epidural**
QoL		At short term (<4mo): • **SF-36 0-100: CIB favouring steroids except for vitality (harm) and emotional well-being (no diff)** (1 RCT; low-moderate; n=50) At long term (4mo-1y): • **SF-36 0-100: CIB favouring steroids except for emotional well-being (harm) and mental composite, vitality, pain (no diff)** (1 RCT; low-moderate; n=50)	
Pain		At short term (<4mo): • **Leg pain NRS 1-10: CIB favouring steroids** (1 RCT; low; n=63) • **Back pain NRS 1-10: no diff** (1 RCT; low; n=63) • **Pain during day NRS 1-10: no diff** (1 RCT; low; n=63) • **Pain during night NRS 1-10: no diff** (1 RCT; low; n=63) • **overall pain NRS 1-10: no diff** (1 RCT; low; n=63) At long term (4mo-1y): • **Leg pain NRS 1-10: no diff** (1 RCT; low; n=63) • **Back pain NRS 1-10: no diff** (1 RCT; low; n=63) • **Pain during day NRS 1-10: no diff** (1 RCT; low; n=63) • **Pain during night NRS 1-10: no diff** (1 RCT; low; n=63)	

		• **overall pain NRS 1-10: no diff** (1 RCT; low; n=63)	
Function		At short term (<4mo): • **RMDQ 0-24: CIB favouring steroids** (1 RCT; low; n=63) At long term (4mo-1y): • **RMDQ 0-24: no diff** (1 RCT; low; n=63)	
Healthcare utilisation	At short term (<4mo): Not reported At long term (4mo-1y): • **Discontinuation of analgesics: no diff** (1 RCT; very low; n=51)		At short term (<4mo): • **Back surgery: no diff** (1 RCT; very low; n=35) At long term (4mo-1y): Not reported

CIB: clinically important benefit

Outcomes not reported: psychological distress, adverse events, responder criteria

Economic evidence

Two economic evaluations were identified**:**

- One cost-utility analysis on the comparison of **non-image guided epidural injections of steroids + local anaesthetics versus placebo** (Price 2005 (UK)) found that the epidural injections of steroids was not cost effective compared to placebo for adults with low back pain and sciatica (ICER: £44,701 per QALY gained). This analysis was assessed as partially applicable with potentially serious limitations.
- One cost-effectiveness analysis on the comparison of **non-image guided steroids epidural versus usual care** (Spijker-Huiges 2014 (NL)) found that steroids are more costly and more effective than placebo in adults with sciatica (ICER: £60 per 1 point improvement in NRS back pain score). This analysis was assessed as partially applicable with potentially serious limitations.
- The study by Spijker-Huiges 2015 was not combined with the previous one as the costs were reported only from a societal perspective and the QALYs calculated did not match with the results of the previous study and the individual SF36 scores reported for each intervention, ie while the individual SF36 scores show an improvement in the group receiving epidural, the QALY estimates were in favour of the control group.

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:**
  - Critical outcomes were health-related QoL, pain severity, function, psychological distress
  - Important outcome were responder criteria for pain and function (>30%), adverse events and healthcare utilisation
  - For image-guide epidurals, evidence was reported for all of the critical outcomes, but there were limited data for quality of life. For non-image guided epidurals there was no evidence for quality of life.

- **Trade-off between clinical benefits and harms**
  - The GDG agreed that there was sufficient RCT evidence for all comparisons except for image-guided epidurals versus placebo/sham. However, there was no relevant cohort data found to address this.
  - **Steroids:** The GDG agreed that the evidence for the effectiveness of epidurals was conflicting. They noted that sciatic symptoms usually improve over the course of a few months in the majority of people without treatment. The placebo-controlled trials did show some evidence of an effect for epidurals, particularly for the combination of steroid plus anaesthetic. The overall evidence suggested the important component was the steroid, but there was no evidence of benefit of steroid alone or anaesthetic alone when compared to placebo/sham for any critical outcome. As a responder analysis suggested a 35% increase in the probability that people obtain substantial pain relief following epidural injections (steroid plus anaesthetic) compared to placebo, it was agreed that **epidural injection of local anaesthetic and steroid should be considered as a treatment option**. Most of the RCT evidence in the review came from **people with acute and moderately severe sciatica**, and the GDG considered that this would be the population most likely to benefit from epidural injection.
  - **Anti-TNF:** The group discussed the evidence for anti-TNF. There was no evidence found for non-image guided anti-TNF, but there was evidence for image-guided anti-TNF epidurals. Despite the evidence showing a positive effect of image-guided anti-TNF epidurals on pain and function, the GDG noted that the evidence was limited as it came from three studies which could not be pooled together because different comparisons were used.
  - **Harms:** The group discussed the risks associated with the different routes of administration of an epidural. The opinion of the group was that serious complications are very rare. The most common adverse event was a temporary increase in pain which the GDG considered could be outweighed by the potential benefits. The group discussed that there is some guidance in the UK suggesting epidurals should be given under image-guidance based on safety grounds, although there was limited evidence for a difference in effectiveness of image guided compared to non-image guided epidural injections from this review. It was therefore agreed that a **recommendation for future research** should be drafted to ascertain the evidence base for safety and effectiveness for image guided and non- image guided epidural injections.
  - **Population in the studies**:
    - **Sciatica:** The studies were conducted in small populations who had at least **moderately severe** sciatica and did not have further treatment options available to them (other than surgery). The evidence reviewed by the GDG suggests that epidural injection of local anaesthetic and steroid may reduce the number of people who would require surgical intervention. This evidence was reinforced by evidence from 2 trials that were included in the spinal decompression review that compared decompression to epidurals showing that 50% of people who had an epidural did not go on to have surgery. The group therefore agreed that in acute, severe sciatica where patients would otherwise be offered surgery, an epidural injection of local anaesthetic and steroid should be considered.
    - **Spinal stenosis:** The group discussed the evidence that had been conducted in sciatica patients with central spinal canal stenosis. The populations studied comprised people with neurogenic claudication primarily. There was insufficient evidence that epidural injections of local anaesthetic and steroid were effective in this group of people and it was noted that current opinion also reflects this. The group therefore agreed to make a **recommendation against using epidurals** in people with claudicant leg symptoms caused by central spinal canal stenosis.
  - **Image guided vs non-image guided**: The GDG discussed that the purpose of this review had been to determine efficacy of different injectates, rather than comparing image guided to non-image guided injections. However, the stratification of the review by those delivered under image guided to those that weren't did not demonstrate a clear indication of improved efficacy of image guided epidurals over non-image guided. They therefore agreed that a research recommendation was warranted in this area**.**
  - **Overall**, the GDG considered that epidural injection, whether administered under image guidance or without, is a relatively safe and routinely used procedure, and had some evidence demonstrated by placebo-controlled trials for effectiveness in pain relief for epidurals of local anaesthetic and steroid. There was insufficient/lack of evidence for effectiveness to support epidural injections using anti-TNF.

- **Trade-off between net clinical effects and costs**
  - A cost-utility analysis was identified comparing the non-image guided epidural with placebo and reported **increased costs and improved health** (increased QALYs) with epidurals, with an incremental cost-effectiveness ratio of £44,701 per QALY gained. In sensitivity analysis where the costs were adjusted assuming only 1 epidural injection was administered and the impact on QALYs was assumed to be unchanged, the ICER went down to £25,746. The group noted that as the recommendation for epidurals was for the acute sciatica population (most likely to be defined as having symptoms for <3 months), then multiple injections would not usually be performed within this short period of time.
  - The GDG discussed the likely higher effectiveness observed with placebo as opposed to no treatment and concluded that if epidural was compared to no treatment or usual care it would probably be associated with a higher QALY gain, and therefore it would be more cost effective. In the same study no cost was attached to the placebo arm while in reality patients could incur the cost of other treatments such as medications and the cost of their side effects.
  - The GDG noted that the studies from which the cost effectiveness data was derived did not have a diagnosis of sciatica confirmed by imaging. The GDG felt that clinical diagnosis alone may overestimate the numbers of patients with true sciatica and lower their confidence in the results.
  - There was evidence suggesting that **epidural injection may reduce the number of people with severe sciatica requiring surgical intervention**; this would generate some cost savings. For these reasons, the GDG decided not to make a strong recommendation on epidural injections but they concluded that they may be cost effective for some patients and therefore it should be considered.
- **Quality of evidence**
  - **Overall quality:** 20 RCTs, ranged from moderate to low quality due to risk of bias caused by selection or performance bias, small sample sizes and imprecision
  - **Anti-TNF:** There was evidence to show an effect of anti-TNF (image-guided), however this was only from single studies, which mostly had small sample sizes. Some of the studies had incomplete reporting of outcome data (for example, no standard deviations were reported for some outcomes and 1 study only had data for 1 participant in the comparison arm). This also meant that the evidence was rated as being at **high risk of bias** and so overall the group **did not have confidence in the findings**.
  - **Steroids:** The GDG had more confidence in the evidence for epidurals in sciatica patients with spinal stenosis (steroid was given as an adjunct) because the main study contributing to the meta-analysis was conducted in 400 participants. The group were less confident in the results of the other contributing study, since it was smaller and although it was also conducted in spinal stenosis patients, it differed considerably to the other studies in the review. The population consisted of chronic sciatica patients with over 100 months of pain, and patients could be given as many epidural injections as they needed (the average given was 4). The GDG felt that this did not reflect clinical practice.
  - **Economic analysis:** The economic evaluations were assessed as partially applicable with potentially serious limitations.
- **Other considerations**
  - The group discussed the effectiveness of giving multiple / subsequent epidural injections. The group noted that as the recommendation for epidurals was for the acute sciatica population (most likely to be defined as having symptoms for <3 months), then **multiple injections would not usually be performed** within this short period of time.
  - The GDG agreed that this recommendation would equally apply for **pregnant women** and should be considered alongside BNF guidance.
  - The GDG were aware of existing NICE interventional procedure guidance for Therapeutic endoscopic division of epidural adhesions (IPG333) recommending special arrangements for clinical governance, consent, audit and research. This procedure was therefore excluded from this review and if its use is considered for people with sciatica, existing guidance should be followed.

Research recommendation

Epidural injection of therapeutic substances that include corticosteroids is commonly offered to people with sciatica. Epidural injection might improve symptoms, reduce disability and speed up return to normal activities. Several different procedures have been developed for epidural delivery of corticosteroids. Some practitioners inject substances through

the caudal opening to the spinal canal in the sacrum (caudal epidural), whereas others direct the injection through the foraminal space at the presumed level of nerve root irritation (transforaminal epidural). There is a rationale that transforaminal epidurals might be most effective, by ensuring delivery of corticosteroids directly to the region in which the nerve root might be compromised. However, transforaminal epidural injection requires imaging, usually within a specialist setting, potentially limiting treatment access and increasing costs. Caudal epidural injection might be undertaken without imaging, or with ultrasound guidance in a non-specialist setting, but, it has been argued, the drug might not reach the affected nerve root and therefore this approach might not be as effective as would be transforaminal injection. Empirical evidence that 1 approach is clearly superior to the other is currently lacking. Access to the two procedures varies between healthcare providers, and people who do not respond to caudal corticosteroid injection might subsequently receive image guided epidural injection. People with sciatica might therefore currently experience unnecessary symptoms at unnecessary cost to the NHS than would be the case if the most cost effective modes of delivering epidural corticosteroid injections were used.

NICE draft recommendations on imaging (March 2016): 2 clinical recommendations and 1 research recommendation

33. Consider epidural injections of local anaesthetic and steroid in people with acute sciatica.

34. Do not use epidural injections for neurogenic claudication in people who have central spinal canal stenosis.

NICE 2016 Research recommendation

6. What is the clinical and cost effectiveness of image guided compared to non- image guided epidural injections for people with acute sciatica?

Belgian GDG considerations mentioned in the Lime survey in October 2016

<u>NICE draft recommendation 33. Consider epidural injections of local anaesthetic and steroid in people with acute sciatica.</u>

- **Agreement with the content of the NICE recommendation 33: 9 Agree, 2 Disagree, 0 no opinion, 2 out of competence, 1 no answer, 4 not completed**
- **Comments from those who do not agree:**
  - This recommendation is obviously OK ! However, didn't we decide to make recommendations for LBP and radicular pain only ? If mentioned here, at least should the following be precised: (1) after which duration the injection has to be considered (2) do not consider it for positional radicular pain (not permanent sciatica)
  - to be added: "Consider image-guided epidural..." "... as an option if too much pain in spite of accurate painkillers"
- **Other comments:**
  - Please replace "lokale narcotica' with lokale anesthetica
  - I would suggest to change the recommendation as follows: Consider transforaminal epidural injections of local anaesthetic and steroid in people with radicular pain.

Strength of the recommendation 33 on epidural injections: According to NICE formulation, it is a weak recommendation

GRADE Factors	
Balance between desirable and undesirable effects	The GDG considered that epidural injection, whether administered under image guidance or without, is a relatively safe and routinely used procedure, and had some evidence demonstrated by placebo-controlled trials for effectiveness in pain relief for epidurals of local anaesthetic and steroid. There was insufficient/lack of evidence for effectiveness to support epidural injections using anti-TNF. The evidence reviewed by the GDG suggests that epidural injection of local anaesthetic and steroid may reduce the number of people who would require surgical intervention. This evidence was reinforced by evidence from 2 trials that were included in the spinal decompression review that compared decompression to epidurals showing that 50% of people who had an epidural did not go on to have surgery. The group therefore agreed that in acute, severe sciatica

	where patients would otherwise be offered surgery, an epidural injection of local anaesthetic and steroid should be considered.
Quality of evidence	Moderate to low
Values and preferences	The group discussed the effectiveness of giving multiple/subsequent epidural injections. The group noted that as the recommendation for epidurals was for the acute sciatica population (most likely to be defined as having symptoms for <3 months), then multiple injections would not usually be performed within this short period of time.
Costs (resource allocation)	There was evidence suggesting that epidural injection may reduce the number of people with severe sciatica requiring surgical intervention; this would generate some cost savings. For these reasons, the GDG decided not to make a strong recommendation on epidural injections but they concluded that they may be cost effective for some patients and therefore it should be considered.

Agreement with the strength of the NICE recommendation 33: 4 strong, 3 weak, 0 no opinion, 2 no answer, 9 not completed

- **Comments for a weak recommendation**
  - Limited evidence, rather low quality
  - We prefer subacute over acute. Preference of transforaminal route of administration of epidural corticosteroids. Following publications: Cohen SP, Epidural steroids: a comprehensive, evidence-based review. Reg Anesth Pain Med. 2013;38(3):175-200. Bhatia A, Transforaminal Epidural Steroid Injections for Treating Lumbosacral Radicular Pain from Herniated Intervertebral Discs: A Systematic Review and Meta-Analysis. Anesth Analg. 2016;122(3):857-70. Van Boxem K, Lumbosacral radicular pain. Pain Pract. 2010;10(4):339-58.
- **Comment for a strong recommendation**
  - Balance between desirable and undesirable effects. Cost

NICE draft recommendation 34. Do not use epidural injections for neurogenic claudication in people who have central spinal canal stenosis.

- **Agreement with the content of the NICE recommendation 34: 4 Agree, 6 Disagree, 1 no opinion, 2 out of competence, 1 no answer, 4 not completed**
- **Comments from those who do not agree:**
  - I suggest to use epidural injection (max 3) as a last therapeutic choice before surgery. if this step doesn't work enough or long enough (at least 6 months) than surgery would be advised
  - Recommandation is based on mixed populations categorized as with "central spinal stenosis" in which there are several subgroups, including some with mixed pathologies (spinal and/or foraminal stenoses, severe or moderate, unilateral or bilateral, static or dynamic symptoms). Then, a global/systematic/strong recommandation cannot be drawn from these data.
  - In older people that are not suitable for surgery, epidurals are the only treatment option and sometimes efficient.
  - Zelfde argument als hierboven: epidurale injecties bij de indicatie claudicatio kan chirurgie uitstellen en som vermijden.
  - May help in diagnostics in difficult pain patterns in elderly. " do not use .... for the management of..."
  - This is for the moment the only indication for reimbursment in Belgium, based on scientific publications
- **Other comments:**
  - Injection would be a non sense...

Strength of the recommendation 34 on epidural injections: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	The group discussed the evidence that had been conducted in sciatica patients with central spinal canal stenosis. The populations studied comprised people with neurogenic claudication primarily. There was insufficient evidence that epidural injections of local anaesthetic and steroid were effective in this group of people and it was noted that current opinion also reflects this. The group therefore agreed to make a recommendation against using epidurals in people with claudicant leg symptoms caused by central spinal canal stenosis.
Quality of evidence	Moderate to low
Values and preferences	
Costs (resource allocation)	

Agreement with the strength of the NICE recommendation 34: 1 strong, 3 weak, 0 no opinion, 0 no answer, 14 not completed

- **Comments for a weak recommendation**
  - I think you can consider it in selected cases trying to avoid surgery or when surgery is contraindicated.
- **No comment for a strong recommendation**

NICE draft research recommendation 6. What is the clinical and cost effectiveness of image guided compared to non- image guided epidural injections for people with acute sciatica?

- **Agreement with the NICE research recommendation 6: 9 Agree, 1 Disagree, 3 no opinion, 0 out of competence, 1 no answer, 4 not completed**
- **Comments from those who do not agree:**
  - For radicular pain only the transforaminal approach is indicated in Belgium (image guided).
- **No other comments:**

Belgian GDG comments during the GDG meeting on the 12 October 2016

NICE recommendation 33: Consider epidural injections of local anaesthetic and steroid in people with acute sciatica

- One GDG member stresses that subacute (2 à 3 weeks) would be better than acute (3 days) because in Belgium, patients have directly access to specialist, even within 3 days after the onset of pain.
- There is a change in the Belgian nomenclature. From the 1st November 2016, only the transforaminal injection will be reimbursed.
- The transforaminal injection is standardized in Belgium as image-guided.

⇨ **The NICE research recommendation 33 is accepted with following change:**
⇨ "Consider epidural injections* of local anaesthetic and steroid in people with subacute (2-3 weeks) radicular pain?" *In Belgian, since the 1st November 2016, only the transforaminal injection is reimbursed.

NICE recommendation 34: Do not use epidural injections for neurogenic claudication in people who have central spinal canal stenosis.

- The GDG acknowledged that a majority of the respondents to the Lime survey disagreed with this recommendation.
- During the meeting the discussion focuses on:
  - The utility of epidural injections before surgery
  - The fact that it is the single option in older people that are not suitable for surgery.

- The terms "central spinal stenosis" in which there are several subgroups, including some with mixed pathologies (spinal and/or foraminal stenoses, severe or moderate, unilateral or bilateral, static or dynamic symptoms). Then, a global/systematic/strong recommendation cannot be drawn from these data and “central” is not correct.
- The inclusion of neurogenic claudication within the scope that it is not clear for everybody.
- The need to add “routinely”.

⇨ **The NICE recommendation 34 deserves to be discussed again during a next meeting after a detailed review of the literature**

NICE research recommendation 6

- Because of the change in the Belgian nomenclature which allows a reimbursement only for transforaminal injection, this research recommendation is not useful. Transforaminal injection is indeed always image guided.
- This research recommendation will be not included in the Belgian guideline

Stakeholders’ comments and replies from NICE team on draft of March 2016 (edited the 30th November 2016)

Quality of evidence

- Society for Back Pain Research:

  RECOMMENDATION: The evidence presented does not look strong enough for the recommendation “consider”/ Low quality, weak, meets MID in the short term. / Cost of MRI not included. CLARITY: Does this recommendation apply to therapeutic nerve root blocks? Guidance on the use of repeat injections would be helpful.

  CONFLICT OF INTEREST: Several of the GDG receive a private income from epidural. It appears that these individuals did not withdraw from the discussion/recommendation. This is in contrast to the pharmacological process.

  NICE reply: Following stakeholder feedback, the GDG discussed the recommendation and the evidence. The GDG are aware that the evidence is conflicting, however considered that epidural injection is a relatively safe and routinely used procedure, and that some evidence demonstrated by placebo-controlled trials for effectiveness in pain relief. They agreed that this should only be considered for people with acute, severe sciatica, and that for this specific subset of people there was sufficient evidence to maintain the recommendation for epidurals. This recommendation does apply to therapeutic nerve root block, which is synonymous with transforaminal epidural. The GDG considered the effectiveness of giving multiple / subsequent epidural injections but noted that as the recommendation for epidurals was for the acute sciatica population (most likely to be defined as having symptoms for <3 months), then multiple injections would not usually be performed within this short period of time. This is stated in the ‘other considerations’ section of the evidence and link to recommendations table of this chapter.All GDG members’ private practice was discussed and declared in appendix B and agreed that this was not a conflict to their involvement in discussions on topics relevant to these areas. All members who have private practice provide the same treatments as in their NHS clinics. All GDG members who had not withdrawn from the discussions were involved in all recommendation making and no member unduly influenced the decision of the committee. (p74-75/222)
- Arthritis Research UK: The evidence for epidural injection of local anaesthetic is of low quality and shows very small effects, yet the GDG recommend they should be considered. There are some effects for those with >70% disc prolapse in sciatica of less than 4 months, but the evidence (1 to 2 studies of low quality and small effect sizes) is not sufficient to warrant consideration of epidural injections outside of a randomised controlled trial. **NICE reply**: The GDG acknowledged that evidence for epidurals of local anaesthetic alone did not show much benefit. However they noted that clinical benefit was observed against placebo/sham when the local anaesthetic was combined with steroid. The GDG agreed this should only be considered in people with acute severe sciatica, and there was sufficient evidence to warrant a ‘consider’ recommendation for epidurals with steroid and local anaesthetic for this subset of people. (p77/222)
- Warwick Clinical Trials Unit: We have failed to identify how the evidence presented relates to this recommendation. The GDG agreed that the evidence for epidurals was conflicting. They seem to be basing this recommendation on the observation that these might reduce incidence of surgery in people being considered for surgery. This observation may be relevant in a context where surgery is being considered but is not relevant in other circumstances. So far as direct evidence of effectiveness is concerned the most informative part of the data extraction are Figures 1136 and 1137 in appendix K 17. Here the meta-analysis shows a short term effect on pain of steroid plus anaesthetic vs anaesthetic alone is 0.52 (95% CI -1.04 to -0.00) for a transforaminal approach and -0.70 (95% CI -1.33 to 0.07) for a caudal approach when image guided respectively. For long term outcomes these are 0.20 (-0.37 to 0.77) and -0.60 (-1.24, 0.04). For non-image guided compared to placebo Figure 1193 is the

most informative. Here the short term effect on pain is -0.19 (95% CI -1.09 to 0.71). In Figures 1205 and 1206 the result for the one included study comparing non image guided steroid + anaesthetic compared to anaesthetic alone where the diagnosis was unclear; here effect sizes for short and term leg and back pain were -0.31 (95% CI -1.21 to 0.61), - 0.10 (95% -0.93 to 0.73), -0.50 ((-1.36 to 0.36), and -2.0 (-8.12 to 4.12). In none of these analyses is the effect statistically significant. The GDG's decision has also been informed by the within trial cost effectiveness analysis in the study reported by Price et al (the clinical paper is Arden et al). We invite the GDG members to read this report for themselves as they may find it informative. An importance weakness of this study is that it relied upon a clinical diagnosis of sciatica rather than there being confirmed radiological evidence of nerve root compression. Although, radiological confirmation may be less important when considering epidural injection than if surgery is being considered. The headline cost per QALY figures are that cost to purchasers were £354,171 per QALY under the trial protocol and £167,145 per QALY if only one injection was given. An alternative approach to assessing costs to provider came to costs per QALY of £44,701 and £25,745 respectively. The GDG have used the lowest of these figures arguing that only single injections will be needed for the majority of people receiving epidural steroids who will have acute sciatica. This trial included around a third of participants with acute sciatica. Although the trial was seriously underpowered for sub-group analyses, comparisons have been made between response to treatment of those with acute and chronic sciatica. If anything the evidence here appears to support the hypothesis that people with chronic sciatica will gain more benefit from epidural steroids. Overall the intervention was ineffective; any trend for an enhanced effect in the chronic group will reduce even further the possibility of effectiveness in the acute group. We think the GDG are seriously misinterpreting the data here and that there can be no cost-effectiveness argument for supporting the use of epidural steroids. We do not think the decision to recommend epidural injections for people with acute sciatica is based on robust clinical and cost-effectiveness data. **NICE reply**: The GDG acknowledged that evidence for epidurals is conflicting. However, they noted that clinical benefit was observed against placebo/sham when the local anaesthetic was combined with steroid in people with acute sciatica. The GDG felt there was sufficient evidence to warrant a 'consider' recommendation for epidurals with steroid and local anaesthetic for this subset of people taking into consideration the limited treatment options available for sciatica. Unlike the epidural review, it was not possible to distinguish a subset of people in whom acupuncture showed benefit. Additionally, with the consistently conflicting evidence and the many treatment options available for low back pain, the GDG agreed not to recommend acupuncture in a NHS setting. (p102/222)

- **Spine Intervention Society:** Inadequate Subgroup Analysis: Stratification of studies according to their technical approach and quality of evidence has not been done. Different types of treatments (e.g. caudal, interlaminar, and transforaminal epidural steroid injections) have been lumped into a category despite the fact that their technical approach may influence outcomes as supported in literature. **NICE reply:** The GDG discussed what subgroup analysis and stratification should be undertaken for each review when setting the review protocols. These are detailed in Appendix C. All reviews were stratified by low back pain/sciatica/mixed low back pain and sciatica as agreed appropriate, and further subgrouping was agreed as relevant. For epidurals and spinal injections, the GDG agreed that this review would focus on the effectiveness of what was injected with stratification by diagnosis, primarily (≥70%) disc prolapse/primarily (≥70%) not disc prolapse/mixed population/unclear spinal pathology (no clinical diagnosis); or pathology not confirmed (may or may not have had imaging). There was further stratification according to whether the injection was image guided or not. Pre-specified subgroup analysis was route of injection: caudal, interlaminar, or transforaminal, however, as stated in the methods section of the guideline, this was only undertaken where heterogeneity was observed. (P79/111)

Population

- Spine Intervention Society: If patients have central canal stenosis with neurogenic claudication, and ESIs are being considered for treatment of neurogenic claudication for the established diagnosis, the recommendation does not pertain to non-specific LBP. **NICE reply**: The epidural review is for the sciatica population only. (p101/222)
- Faculty of Sport and Exercise Medicine: Why are epidural injections not recommended in those with central canal stenosis and neurogenic claudication? What about those not suitable for surgery? **NICE reply:** The evidence review demonstrated that epidural injections were not effective in terms of function, responder criteria, quality of life or pain in those with central canal stenosis and neurogenic claudication. The GDG agreed therefore that there should be a recommendation to advise against their use in this population.The recommendation also applies to those patients who are unsuitable for surgical intervention as the evidence demonstrates that epidural injections are unlikely to be of benefit. (p2/222)
- Spine Intervention Society: When one reviews the evidence on neurogenic claudication and central stenosis, 2 papers are excluded for risk of bias. It is unclear if the analysis includes 2 or 3 papers. These papers are not cited, disallowing an independent review of the results. The authors thus deprive patients with stenosis, a condition known to be poorly responsive to conservative care, of any alternative but surgery (surgery for stenosis was not assessed in the guidelines).**NICE reply**: The inclusion and exclusion of all studies in this guideline are based on their meeting the criteria of the evidence reviews (appendix C). Studies are not excluded based on their risk of bias. All included studies for the epidural injections review are detailed in section 24.3 of the full guideline. The number of studies and study names (first author and year

of publication) included for each outcome are specified in the clinical evidence summary tables (section 24.3.4 and 24.3.5) and in the forest plots (appendix K.17) respectively, and are fully cited within the reference list of the guideline. The GDG agreed that neurogenic claudication is a clinical diagnosis; the symptoms may not always include leg pain. Patients often present with neurological symptoms rather than pain (e.g. my legs feel heavier and heavier when I walk). Pain can often be in the back and buttocks rather than the legs. The cause is usually central spinal canal stenosis. If the search found studies describing 'neurogenic claudication' as the inclusion and we weren't able to discern whether this meant leg pain or weakness/back and buttock pain then they had to be excluded. For this group with the broad term 'neurogenic claudication' , there is little evidence to suggest that epidural injections are helpful and our view, based more on consensus than anything, was that they were unlikely to be of benefit. (p101/222)

- Faculty of Pain Medicine: **Spinal Stenosis**: A concern is for people with spinal stenosis who seem left with very few options. This is of major concern as this is an elderly group of patients, who tolerate analgesia poorly, who are often not fit for surgery and for whom an intervention may be the only option. What are the alternatives in a population unable to tolerate NSAIDs, opioids and anti-neuropathics and not fit for surgery? The group discussed the evidence that had been conducted in sciatica patients with central spinal canal stenosis. The populations studied comprised people with neurogenic claudication primarily. There was insufficient evidence that epidural injections of local anaesthetic and steroid were effective in this group of people and it was noted that current opinion also reflects this. The group therefore agreed to make a recommendation against using epidurals in people with claudicant leg symptoms caused by central spinal canal stenosis."The other paragraph says:"The GDG had more confidence in the evidence for epidurals in sciatica patients with spinal stenosis (steroid was given as an adjunct) because the main study contributing to the meta-analysis was conducted in 400 participants. The group were less confident in the results of the other contributing study, since it was smaller and although it was also conducted in spinal stenosis patients, it differed considerably to the other studies in the review. The population consisted of chronic sciatica patients with over 100 months of pain, and patients could be given as many epidural injections as they needed (the average given was 4). The GDG felt that this did not reflect clinical practice" So their conclusions are contradictory. **NICE reply**: However the evidence reviewed demonstrated that epidurals are unlikely to be of significant benefit in spinal stenosis with neurogenic claudication and this would apply equally to those suitable or unsuitable for surgery. Other non-pharmacological treatments recommended in the guideline may be considered.(p163/222)
- University Hospitals Birmingham NHS Foundation Trust: The guideline has stated that a caudal epidural can be used for disc bulge but not canal stenosis. Further clarification to aid implementation is called for. **NICE reply**: The recommendation is for epidurals to be considered in acute sciatica which may be caused by disc prolapse but also by degenerative stenosis. The recommendation for spinal stenosis refers to the symptoms of neurogenic claudication. (p216/222)

Acute sciatica

- Faculty of Pain Medicine**:** Define acute, first episode and/ or acute exacerbation? Guidance appears to be referring to pain for less than 3 months. However evidence is drawn from heterogeneous group of acute and chronic radicular pains. Repeat epidurals for chronic radicular pain is a significant part of clinical practice. Is this to end? What are the alternatives? SCS for radicular pain as an alternative to surgery? There is also no mention of nucleoplasty or pulsed radiofrequency**. NICE reply:** Acute has been defined within the guideline as less than 3 months duration. This has been added to the glossary for clarity. Although the evidence reviewed was for mixed populations of acute and chronic pain, and in some cases this was not clear, most of the RCT evidence in the review came from people with acute and moderately severe sciatica, and the GDG considered that this would be the population most likely to benefit from epidural injections. This is stated in the 'recommendation and link to evidence' section of this chapter. The recommendation is not specific to the first episode of pain however as this recommended for people who have had pain for < 3 months, the GDG considered it unlikely that repeat injections for the same episode would be offered within this timeframe. The trials reviewed did not suggest that increasing age was associated with a poorer response to radiofrequency denervation. The meta analysed trials varied in terms of inclusion criteria (22-55 yeas, 18-65 years, 36-79 years, 20-60 years , >17 years) and as such, no assumption can be made regards the contribution of age to treatment success or failure. (p40/111)

Route of administration

- Spine Intervention Society: Stratification of studies according to their technical approach and quality of evidence was not adequately addressed. (p100/222) Caudal, interlaminar, and transforaminal epidural steroid injections were all lumped in a same category despite the fact that their technical approach may influence outcomes as supported in literature. **NICE reply**: The GDG agreed that the route of administration was important to consider if heterogeneity was observed, therefore this was considered as a subgroup analysis in the presence of heterogeneity and has been carried out accordingly. For the comparison of steroid and anaesthetic versus anaesthetic (>70% prolapse), such subgroup analysis mostly explained the heterogeneity between meta-analysed studies for pain at longer term follow-up and responder criteria for pain at both long and short term and the results have therefore been presented as per the pre-defined subgroup analysis. There was no difference between interventions in

subgroups for pain. However clinical benefit of steroid plus anaesthetic for responder criteria (pain) was observed when intrelaminar (parasagittal) approach was used, and not other route of delivery. Subgroup analysis for route of administration did not explain heterogeneity for pain and responder criteria for function in the short term. For the comparison of steroid and anaesthetic versus anaesthetic (mixed population / unclear spinal pathologies), the route of administration did not explain the heterogeneity for pain between the meta-analysed studies. Where heterogeneity was not explained by the subgroup analysis, pooled results are presented with random effects, as described in the methods

- United Kingdom Spinal Societies Board and British Orthopaedic association: It has been recommended that epidural injections of local anaesthetic and steroid in people with acute sciatica be considered. In the preamble it is made clear that all routes of administration are included and specifically nerve root block. However, it is possible that commissioners and others reading the brief version of the guidance will not appreciate this and fail to commission appropriately. This is perhaps made more likely as nerve root block and epidural have separate OPCS codes and, therefore, appear separately in SUS and HES data. The CRG are requested to consider a form of words clarifying the scope of their recommendation. **NICE reply:** We were unable to demonstrate, given the available evidence, that image guided epidurals, or that one route of epidural administration was superior to another. A research recommendation was written to address this uncertainty, but we are unable to be more specific in the recommendation. Your comment will be considered by NICE where relevant support activity is being planned. (p105 /222)
- Guy's and St. Thomas NHS Foundation Trust: We support the timely use of injections in patients with sciatica. Locally we have found that pathways that capitilise on extended therapist roles in this management pathway, can provide efficient access. In practice caudal epidurals are easier to administer than tranforaminal epidurals and patients report a good response and so may be more cost effective than more targeted transforaminals. Currently both are offered at a secondary care level They can be organised by therapists based on clinical assessment including imaging review. We recommend this pathway. Caudal epidurals are offered in our organisation to stenotic patients with claudicant leg pain after the risk/ benefit analysis of all management options including surgery has taken place. Changing this management option may be difficult. (p216/222)

MRI

- Arthritis Research UK:.Patients also need an MRI scan before the epidural so the cost of these MRI scans should be included in the economic model**. NICE reply**: Regarding the cost of the MRI scan, the study also included radiology costs so these costs should be covered by the analysis. (p77/222).

Cost

- Arthritis Research UK: The cost-effectiveness for epidural injections for sciatica was based on Prof Nigel Arden's study which demonstrated that epidural steroid injection (ESI) led to a transient benefit in ODQ and pain relief, compared with placebo at 3 weeks (p =0.017, number needed to treat = 11.4). There was no benefit over placebo between weeks 6 and 52. There were no significant differences in any other indices, including objective tests of function, return to work or need for surgery at any time-points. Prof Nigel Arden's study used a range of assumptions and concluded between £26,000 to >£300,000 cost per QALY. ESIs thus failed the QALY threshold recommended by the National Institute for Health and Clinical Excellence (NICE). The GDG has selected the lowest of these estimates to use for the modelling – this was from a sensitivity analysis which included assumptions that could not be confirmed from their own data. This ICER is above the NICE lower threshold (£20,000/QALY) and no probabilistic sensitivity analysis was undertaken, so we do not know the probability of cost-effectiveness at the £20,000 and £30,000/QALY thresholds. Interventions are generally only recommended above £20,000/QALY (and below £30,000) if there is a reasonable level of certainty about the result and the results are robust. We really cannot say this is the case here. Although ESIs appear relatively safe, it was found that they confer only transient benefit in symptoms and self-reported function in a small group of patients with sciatica at substantial costs. Patients also need an MRI scan before the epidural so the cost of these MRI scans should be included in the economic model. A research recommendation is proposed and a change in the clinical recommendation from "Consider epidural injections of local anaesthetic and steroid in people with acute sciatica" to "Do not offer epidural injections of local anaesthetic and steroid in people with acute sciatica unless as part of a randomised controlled trial", in a similar way to some of the other interventions that are also research recommendations. Our group perceive that the NHS is under considerable pressure currently relating to the use of pharmacology, injections and surgery so it is essential that there is clarity and consistency in the GDG's recommendations. **NICE reply**: In the linking evidence to recommendation section we have explained why we gave more weight to the lower ICER estimate from the study (as the GDG advised only one injection is usually administered for the acute sciatica population) and the rationale for concluding that epidural injections could be cost effective. We would also like to note that this is not a strong recommendation as we recommend considering offering this intervention as opposed to routinely offering it. (p77/222).

Research recommendation;

- Warwick Clinical Trials Unit: We do not agree that this is a relevant research question. We are not convinced that the evidence supports the effectiveness of either of these interventions. There is an important research question on the effectiveness and cost effectiveness of epidural steroids for people with acute sciatica and radiological evidence of disc prolapse. The cost effectiveness analysis of any such study would need to include the costs of imaging to identify those who may be eligible. **NICE reply**: Thank you for your comment. This research recommendation was based on the existing guidance in the UK suggesting epidurals should be given under image-guidance based on safety grounds. However the epidurals review did not show much difference in the clinical effectiveness between image-guided and non-image guided epidurals. Bearing in mind the additional costs to the NHS for imaging when delivering image-guided epidurals, the GDG agreed that a recommendation for future research should be drafted. (p104/222)
- Spine Intervention Society: There is a rationale that transforaminal epidurals might be most effective, by ensuring delivery of corticosteroids directly to the region in which the nerve root might be compromised. However, transforaminal epidural injection requires imaging, usually within a specialist setting, potentially limiting treatment access and increasing costs. Caudal epidural injection might be undertaken without imaging, or with ultrasound guidance in a non-specialist setting, but, it has been argued, the drug might not reach the affected nerve root and therefore this approach might not be as effective as would be transforaminal injection. Empirical evidence that 1 approach is clearly superior to the other is currently lacking. Access to the two procedures varies between healthcare providers, and people who do not respond to caudal corticosteroid injection might subsequently receive image guided epidural injection. People with sciatica might therefore currently experience unnecessary symptoms at unnecessary cost to the NHS than would be the case if the most cost effective modes of delivering epidural corticosteroid injections were used. The techniques utilized in the administration of epidural steroids are also critical. No randomized studies examined the use of image guidance as a variable. This has, however, been well examined in non-randomized studies demonstrating that up to 74% of "epidural" steroid injections performed without image guidance either deposit medication external to the epidural space or do not reach the targeted pathology within the ventral epidural space. (1-4) Data from explanatory trials of non-image guided injections yields a number needed to treat (NNT) greater than 90. In contrast, a high quality explanatory trial of image-guided transforaminal injection of steroids yields a NNT of 3. (10) It is the position of the Spine Intervention Society that image guidance is absolutely essential for the safe and efficacious performance of epidural procedures, based on a large body of non-RCT evidence. **NICE reply**: The GDG recognise that there is some existing guidance in the UK suggesting epidurals should be given under image-guidance based on safety grounds. However the epidurals review did not show much difference in the clinical effectiveness between image-guided and non-image guided epidurals. Bearing in mind the additional costs to the NHS for imaging when delivering image-guided epidurals, the GDG agreed that a recommendation for future research should be drafted. (p105/222)

NICE final version of recommendation (November 2016): no major change

36. Consider epidural injections of local anaesthetic and steroid in people with acute and severe sciatica

37. Do not use epidural injections for neurogenic claudication in people who have central spinal canal stenosis

R3. What is the clinical and cost effectiveness of image guided compared to non-image guided epidural injections for people with acute sciatica?

Belgian GDG comments during the GDG meeting the 14th December 2016

NICE recommendation 33. Consider epidural injections of local anaesthetic and steroid in people with acute sciatica

- In the final version of the NICE guideline this recommendation has been changed into: Recommendation 36 "*Consider epidural injections of local anaesthetic and steroid in people with acute and severe sciatica".*
  "Severe" has been added.
- In the previous GDG meeting, the GDG members agreed on following formulation: *"Consider epidural injections of local anaesthetic and steroid in people with subacute (2-3 weeks) radicular pain".* And a footnote has also been added: "*In Belgium, since the 1st November 2016, only the transforaminal injection is reimbursed*".
- The transforaminal injection is standardized in Belgium as image-guided.
- NICE considered pain <3 months as "acute low back pain". But the first week after pain onset is not concerned by this recommendation. To be accurate, the following modification is suggested: adding of (sub) in front of "acute" and "at least" in front of 2-3 weeks.

- A definition of "severe" should be specified. A search of this definition in the NICE guideline (in appendix P) should be performed.

⇨ **The final NICE recommendation 36 is accepted with following change:**
⇨ ***"Consider epidural injections* of local anaesthetic and steroid in people with (sub)acute (at least 2-3 weeks) radicular pain?"***
⇨ ****In Belgium, since the 1st November 2016, only the image-guided transforaminal injections are reimbursed.***

NICE recommendation 34: Do not use epidural injections for neurogenic claudication in people who have central spinal canal stenosis.

- In the final version of the NICE guideline this recommendation has not been changed (recommendation 37).
- NICE based this recommendation on studies mainly comparing steroids + anaesthetic versus anaesthetic in patients with stenosis. But the similar comparison in patients with disc prolapse provided the same results and did not preclude a potential efficacy of the injections. NICE mentioned this recommendation is mostly based on a consensus.
- The term central stenosis is questioned, and also neurogenic claudication because it is a clinical diagnosis.
- This recommendation concerns chronic pain and thus is different from the recommendation 36.
- The terms "neurogenic claudication" is useless and confusing (in disc prolapse there is also neurogenic claudication). It should be removed.
- In patients with neurogenic claudication, surgery is the first option. However, in chronic, elderly patients who are not suitable for surgery, epidural injections could be an option.
- Some suggestions are proposed such as "only if surgery is not an option", "to avoid surgery" or "if surgery is contraindicated" but without consensus.
- **The GDG members conclude that this recommendation is too strong given the lack of evidence and prefers not to formulate a recommendation on this topic. A footnote should be added to the first recommendation on epidural injections.**

⇨ **The final NICE recommendation 37 will be modified as follows and added as footnote to the first recommendation:**
⇨ **"In patients with chronic radicular pain due to a stenotic condition, no clear recommendation on epidural injections can be formulated given the lack of evidence".**

NICE research recommendation 6: What is the clinical and cost effectiveness of image guided compared to non-image guided epidural injections for people with acute sciatica?

- Because of the change in the Belgian nomenclature which allows a reimbursement only for transforaminal injection, this research recommendation is not useful. Transforaminal injection is indeed always image guided.

⇨ **The final NICE research recommendation 3 is removed for the Belgian guideline**

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

- The number of possible injections for the same patient was discussed and it was decided to add in the text that since November 2016, the reimbursement is limited to 3 injections/year**.**
- A proposition for adding less than 3-6 months in the recommendation was formulated but after the meeting: subacute = before 3 month, it was suggested by e-mail that adding 3-6 month is not useful and maybe confusing.

KCE 2017 final recommendations on epidural injections (February 2017)

21. Consider epidural injections of local anaesthetic and steroid* in people with (sub)acute (at least 2-3 weeks) and severe** radicular pain

*Since the 1st of November 2016, only image-guided radicular and transforaminal injections are reimbursed in Belgium.

**Severe radicular pain should be defined on an individual basis with the patient but a score rated as 5 or more on a numeric rating scale (NRS 0-10) could be considered as a reasonable yardstick.
(weak recommendation based on high to very low quality evidence from RCTs)

7.18. Surgery and prognostic factors

Surgery and prognostic factors in patients with low back pain ± radicular pain

NICE search questions

1. **Does history of previous fusion surgery, smoking status, BMI or psychological distress[f] predict response to surgery in people with non-specific low back pain (with/without sciatica) or low back pain without sciatica who have failed to respond to appropriate conservative therapy?**
2. **Does image concordant pathology or presence of radicular symptoms predict response to surgery in people with suspected sciatica?**

Introduction based on the draft version of NICE guideline (March 2016)

- Surgery for low back pain and sciatica is most commonly carried out when more conservative treatments have failed. As with most major invasive procedures, surgery to manage back pain and sciatica carries with it an inherent risk of serious harm.
- For surgery in people with low back pain, a number of prognostic factors are thought to be linked to better or worse response to surgery. These include a history of previous spinal fusion surgery, smoking status, BMI and psychological distress. The likelihood of successful surgery may be important therefore to help inform the clinical decision to refer a person for surgery. In people with suspected sciatica however, the prognostic factors for response to surgery are thought to be distinct and may be more affected by the presence of radicular symptoms and presence of pathology on imaging.

PICO used by NICE (March 2016)

Population	RQ1 • People aged 16 or above with low back pain with or without sciatica or low back pain without sciatica who have failed to respond to appropriate conservative therapy. RQ2 • People aged 16 or above with sciatica who have failed to respond to appropriate conservative therapy.
Prognostic variables	RQ 1 • History of previous fusion surgery • Smoking • BMI>30 • Psychological distress RQ2

[f] Psychological distress is largely defined as a state of emotional suffering characterized by symptoms of depression (e.g., lost interest; sadness; hopelessness) and anxiety (e.g., restlessness; feeling tense) (Mirowsky and Ross 2002) (in Internet). This concept is not defined by NICE 2016.

	• Image concordant pathology (diagnosis supported by imaging to see if compression is present or not) • Radicular symptoms (pain that extends to leg vs pain in back/button only)
Confounding factors	• Duration of symptoms
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) • Adverse events 1. Mortality 2. Morbidity 3. Re-operation rate **Important** • Surgery conversion rate
Study design	• Prospective and retrospective cohorts (with multivariate analysis adjusted for key confounders) • Randomised trials (with multivariate analysis adjusted for key confounders) • Systematic reviews of the above

Literature quoted by NICE 2016 guideline

- For low back pain, four studies (cohort studies) were included in the review but only the results of 2 studies were reported due to very high risk of bias. For sciatica, two studies (cohort studies) were included in the review.
- No relevant economic evaluations were identified.

1. **"Does history of previous fusion surgery, smoking status, BMI or psychological distress predict response to surgery in people with non-specific low back pain (with/without sciatica) or low back pain without sciatica who have failed to respond to appropriate conservative therapy?"**

- **Smoking**

Low quality evidence from a single cohort study (Pearson 2012, spinal stenosis with or without sciatica) with a multivariable analysis, showed smoking status was a prognostic factor after adjusting for duration of symptoms in predicting improvement in function (ODI 0-100) after surgery (standard open decompressive laminectomy compared to non-operative treatment of usual care), **favouring not smoking**, in people with non-specific low back pain (n=634).

- **BMI > 30**

Very low quality evidence from a single cohort study (Ostelo 2005, LBP with or without sciatica) with multivariable analysis gave some indication that a **BMI greater than 30 may be a prognostic** factor in predicting **poorer response to surgery** (surgery not defined) in terms of improving function (RMDQ 0-24) in people with non-specific low back pain (n=105) after adjusting for duration of complaints before surgery. This was highly imprecise with an adjusted odds ratio of 0.79 [0.21, 2.97].

- **Psychological distress**

Low-very low quality evidence from a single cohort study (Ostelo 2005, LBP with or without sciatica) with multivariable analysis, suggested that psychological distress was a prognostic factor in predicting response to surgery in terms of improving back pain after adjusting for duration of complaints before surgery (surgery not defined), with **lower levels of distress predicting better outcome**, in people with non-specific low back pain or sciatica (n=105).

- **History of previous fusion surgery**

No relevant evidence was identified.

2. Does image concordant pathology or presence of radicular symptoms predict response to surgery in people with suspected sciatica?

- **Radicular symptoms**

Very low quality evidence from a single cohort study (Ostelo 2005, LBP with or without sciatica) with multivariable analysis suggested presence of radicular symptoms was a prognostic factor for predicting the response to surgery (surgery not defined) (leg pain, VAS 0-100) at less than or equal to 4 months after adjusting for duration of symptoms (n=105) (Odds ratio of 0.24 [0.10, 0.58]).

Low-very low quality evidence from 4 cohort studies with multivariable analyses, suggested presence of radicular symptoms was a prognostic factor in predicting response to surgery (function ODI 0-100 at 4y; leg pain VAS <10 at 12 months; function ODI>10 at 1y; 50% improvement in pain on VAS 0-100 in 1y; 30% and 50% improvement in function on ODI 0-100 in 1y) at greater than 4 months in people with sciatica (n=1782) after adjusting for duration of symptoms, duration of complaints before surgery and duration of pain. This evidence indicated that **greater radicular symptoms / higher leg pain scores indicated better response to surgery**.

- **Image-concordant pathology**

No relevant evidence was identified.

NICE GDG considerations

- **Relative values of different outcomes:**
  - Critical outcomes were health-related QoL, pain severity, function, psychological distress and adverse events (mortality, morbidity and re-operation rate)
  - Important outcome was surgery conversion rate
  - For Q1 and Q2 only evidence for the outcomes of pain and function were available. There was no evidence for any of the other outcomes.
- **Trade-off between clinical benefits and harms**
  - **Overall**, there was a paucity of evidence to effectively explore the effect of prognostic factors on the outcomes of people with low back pain or sciatica following surgery. It was acknowledged by the GDG that in the low quality, evidence identified in this review, there was a trend towards worse outcomes in the groups of people who had prognostic factors identified-for example; smoking and high BMI.
  - **Low back pain population:** There was evidence that non-smokers had a greater improvement in function following surgery compared to smokers. Other evidence reported negative effects on pain and function outcomes following surgery in people with a higher BMI or with psychological distress. The strength of this evidence was weak however and the GDG agreed that this carried significant uncertainty. There was scant evidence supporting better surgical outcome in people who did not have a prognostic factor identified (for example, there were no trials investigating the surgical outcomes of patients post smoking cessation).
  - **Sciatica population:** The evidence suggested better outcomes for patients with predominant leg pain following surgery for sciatica. The GDG noted that the evidence for leg pain prior to surgery was in a population undergoing surgery for sciatica and therefore would be expected to have a more favourable outcome from surgery. The GDG considered that the influence of predominant leg pain on the treatment effect seen at 4 years could be as a result of the long follow up time adopted in this study given that sciatica has a generally favourable prognosis over the long term.
  - **Summary:** The type of surgery carried out was different in each study and not defined in the case of 2 trials. Therefore, differences in surgical outcome could possibly be due to the surgical technique adopted rather than the prognostic factor, despite the adjustments for confounders in the multivariate analyses. Unfortunately, it was not possible to statistically explore this difference due to lack of data. The GDG agreed that there was insufficient evidence to suggest that

smoking and obesity reliably impacted the prognosis for patients undergoing surgical treatment. It was however acknowledged that weight loss and smoking cessation have public health benefits and therefore should be encouraged. (See the NICE guideline for obesity and smoking cessation for more information). It was noted that these prognostic factors may increase the risk of surgery, but do not appear to affect the outcome, and the benefits of surgery in some may outweigh the risks. It was agreed that the prognostic factors identified should not preclude a surgical opinion where the benefits of surgery might outweigh the potential risks.

- **Trade-off between net clinical effects and costs**
  - **No economic evaluations** were identified from the published literature. The GDG noted however that this recommendation was unlikely to impact sciatica surgery referrals as people are not currently being denied referral for surgical opinion on the basis of their BMI, smoking status or psychological distress, however the recommendation has been made specific to sciatica because the evidence reviewed elsewhere in this guideline has led to surgery **only being recommended for sciatica** rather than non-specific low back pain.
- **Quality of evidence**
  - Evidence from 5 prospective cohort and 1 retrospective cohort studies, quality ranged from low to very low, mainly downgraded for high risk of bias due to selection bias and attrition bias.
  - For the prognostic factors of BMI, psychological distress and radicular symptoms, data came from a single, relatively small (N=105) trial, and the evidence was graded as very low quality with serious imprecision. Evidence was only available at short follow up time of 3 months for the majority of outcomes. The GDG noted that it may have been beneficial if the categories of obesity had been stratified further in the study rather than just the 2 cut-offs that were considered (i.e. <25 and >30) as this might reveal further differences in prognosis. A referent of BMI <25 was used in the study and data for the BMI=25-30 group reported separately compared to this referent (in addition the BMI>30 group of interest).
  - The evidence for the prognostic factors of smoking and radicular symptoms was of overall very low quality due to selection bias demonstrated by unclear confounding of all the key confounders that could influence outcomes in the MVA and an >10% group differential attrition bias related to outcomes with no appropriate imputation in the studies.
- **Other considerations**
  - The GDG discussed the ethical issues around shared decision making regarding spinal surgery and using information based on limited prognostic factors to decide treatment for patients. They agreed that using the limited evidence to deny treatment to certain people would be unethical.
  - The GDG noted that the recommendation was based upon the prognostic factors identified in the protocol and there may be other factors, for example, age and the presence of co-morbidities.

NICE 2016 recommendations: 1 clinical recommendation

35. Do not allow a person's BMI, smoking status or psychological distress to influence the decision to refer them for a surgical opinion for sciatica.

Translated to Dutch

35. Houd geen rekening met iemands BMI, het wel of niet roken of psychische spanningen bij de beslissing om door te verwijzen voor een chirurgische opinie over ischias.

Translated to French

35. Votre décision de solliciter un avis chirurgical pour une personne souffrant de sciatique ne doit pas être influencée par l'IMC, le tabagisme ou la détresse psychologique du patient.

Belgian GDG considerations mentioned in the Lime survey in October 2016

Agreement with the content of the NICE recommendation 35: 5 Agree, 6 Disagree, 1 no opinion, 1 out of competence, 1 no answer, 4 not completed

- **Comments from those who do not agree:**
  - I do not think that because NICE reported only a single cohort study (Ostelo 2005) about psy factors and surgery outcomes one should state that psychological distress should not influence the decision to refer. Considering the important and recognized influence of psychosocial outcomes, one should take them into account and not consider surgery as in other patients. Please have a look at the articles: Alodaibi 2013 and Mannion 2006 (2 SRs), Slosar et al.: "In addition to the diagnostic workup to identify the pain generators, the surgeon should carefully consider any psychological risk factors that may be active in a surgical candidate"
  - Of course that psychological distress will influence my decision to refer for a surgical opinion! But of course, this will be only one factor between others.
  - It should not be the primary focus in the decision for surgery, but, taking into account the limited evidence concerning BMI, smoking and psychological distress on outcome, if these risk factors are present, the patient should at least be aware of the risk of worse outcome.
  - In spite of the poor evidence, we know that there are people with psychosocial risk factors that have worse outcomes of surgery. Given the poor evidence, such recommendation should simply not be made and it should be at the discretion of the care provider to judge.
  - This recommendation is valid if and only if the surgeon takes these risk factors into account before making a decision. As formulated, it could suggest that these factors are not important to assess.
  - Als het voor ischias geformuleerd wordt zoals het er nu staat in de aanbeveling ben ik akkoord. Ik denk dat we voor lage rugpijn afzonderlijk moeten vragen en dan zou ik stellen niet akkoord te zijn
- **Other comments:**
  - Distress = stoornis, nood, onevenwicht moeilijk te vertalen
  - It should be clear that "surgical opinion for sciatica" is not the same as "surgery for sciatica". I think that for any invasive treatment risk factors need to be assessed.
  - Ask for a surgical opinion is free. Making the indication and performing the surgery is another question

Strength of the recommendation 35 on prognostic factors and surgery: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	There was a paucity of evidence to effectively explore the effect of prognostic factors on the outcomes of people with low back pain or sciatica following surgery. It was acknowledged by the GDG that in the low quality, evidence identified in this review, there was a trend towards worse outcomes in the groups of people who had prognostic factors identified- for example; smoking and high BMI. The GDG agreed that there was insufficient evidence to suggest that smoking and obesity reliably impacted the prognosis for patients undergoing surgical treatment. It was however acknowledged that weight loss and smoking cessation have public health benefits and therefore should be encouraged. It was agreed that the prognostic factors identified should not preclude a surgical opinion where the benefits of surgery might outweigh the potential risks.
Quality of evidence	Low to very low
Values and preferences	They agreed that using the limited evidence to deny treatment to certain people would be unethical. The GDG noted that the recommendation was based upon the prognostic factors identified in the protocol and there may be other factors, for example, age and the presence of co-morbidities.
Costs (resource allocation)	No relevant economic evaluations identified.

Agreement with the strength of the NICE recommendation 35: 2 strong, 2 weak, 0 no opinion, 1 no answer, 13 not completed

- **No comments for a weak or a strong recommendation**

NICE final version of recommendation (30 November 2016): no change
38. Do not allow a person's BMI, smoking status or psychological distress to influence the decision to refer them for a surgical opinion for sciatica.

NICE additional considerations answering stakeholders comments

- The review is not specific to the decision to operate, but it is acknowledged (evidence and link to recommendations) that the decision to operate should be a process of shared decision making of the benefits and risks, and that BMI, smoking or psychological distress should not be used to deny people surgery for LBP or sciatica.(p45/111)
- The population covered by this guidance excludes those patients with progressive neurological sensory or motor deficit. Whilst not all patients with progressive neurological deficit require emergency referral, they do require a course of management outside the scope and remit of this guideline.(p46/111)

Belgian GDG comments during the GDG meeting 14/12/2016

- In the Lime survey, a lot of comments were given on this recommendation, mainly due to the confusing formulation of this recommendation. For some respondents it was not clear if these prognostic factors influence the decision of the surgeon to perform surgery or if these factors only could influence the decision to refer the patient to the surgeon.
- In the stakeholders' comments on the NICE draft for public consultation was also mentioned:
  - The decision to operate should be a process of shared decision making of the benefits and risks
  - BMI, smoking or psychological distress should not be used to deny people from surgery for LBP or sciatica
- In Belgium, there is no gatekeeper, every patient can go directly to surgeon, without a mandatory referral.
- Due to the possible confusing interpretation of the recommendation and this lack of added-value, the GDG members agreed to remove this recommendations from the guideline.
- **Conclusion: the NICE recommendation will be removed from the Belgian guideline.**

KCE 2017 final recommendation on surgery and prognostic factors (Februay 2017)
No recommendation.

7.19. Disc replacement

Disc replacement in patients with low back pain ± radicular pain

NICE search question
"What is the clinical and cost-effectiveness of disc replacement surgery in people with non-specific low back pain?"

Introduction based on the draft version of NICE guideline (March 2016)

- Disc replacement, or spine arthroplasty, is an operation carried out to treat spinal pain. The indications and rationale are similar to those of spinal fusion. The procedure involves replacing invertebral units with artificial discs that can act as a functional prosthetic replacement. The pain relief stems from removal of the painful disc. Single discs can be replaced, or alternatively, several levels can be replaced during the same surgery.
- Some clinicians consider that the advantage of disc arthroplasty over spinal fusion is that it preserves movement, which may have some benefits. Other clinicians have the view that the movement confers no significant clinical advantage. The specific selection procedures mean that only a small number of people are suitable for surgery, and the surgical approach inevitably carries with it risks of serious harm. Since it was first introduced, the frequency of use of this procedure appears to have fallen.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with non-specific low back pain • Populations with low back pain only and low back pain with/without sciatica will be pooled for analysis
Intervention(s)	• Disc replacement surgery
Comparison(s)	• Usual care • Other treatment (interventions listed in our guideline review protocols)
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (>30% improvement in pain or function) • Adverse events: morbidity; mortality. • Revision rate • Failure rate • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit) Outcomes to be recorded at: o Short term (≤4 months) (8 weeks to 4 months) o Long-term: - > 4 months (4 months to 1 year) for all outcomes

	- 0-2 years for critical outcomes - 0-10 years for failure rates and revision rates

Literature quoted by NICE 2016 guideline (March 2016)

- Five randomised controlled trials and 2 cohort studies were included in the review. Two comparisons were found:
  - Disc replacement versus spinal fusion in patients with LBP with or without sciatica (in 2 RCTs)
  - Disc replacement versus 3-elements MBR (multidisciplinary biopsychosocial rehabilitation programme) in patients with LBP without sciatica (in 1 RCT)
- In the 2 cohort studies and in 1 RCT no relevant outcomes were reported. In another RCT the evidence was reported in a format that could not be analysed in this report.
- **Disc replacement versus spinal fusion in patients with LBP with or without sciatica**
  - **Total disc replacement versus anterior lumbar interbody fusion** (Gornet 2011): A clinical benefit for the **QoL** SF-36 physical component summary score was found at short term (<4 mo) and at long term (at 1y and at 2y) in favour of disc replacement but not for the SF-36 mental component summary score (both at short term and at long term) (SF-36 0-100; 1 RCT; low to very low quality; n=577). No clinical differences between disc replacement and spinal fusion were found for **pain** (back and leg pain, NRS 0-10; 1 RCT; low to very low quality; n=577) and for **function** (ODI 0-100; 1 RCT; very low quality; n=577) both at short term and long term. The number of patients who reported **adverse events** was higher in the disc replacement group (only reported at short term, 1 RCT; low to very low quality; n=577) but no differences were found in number of **reoperations** (at 2 y; low to very low quality; n=577).
  - **Total disc replacement versus posterior lumbar interbody fusion** (Berg 2009): A clinical benefit for **QoL** was shown at 1y in favour of disc replacement but not anymore at 2y (EQ-5D 0-1; 1 RCT; low to very low quality; n=152). Similar to the anterior approach, no clinical difference was found for **function** (ODI 0-100; 1 RCT; very low quality; n=152) and **pain** (back and leg pain; VAS 0-10; 1 RCT; low to very low quality; n= 152). No clinical difference was found for the **reoperation** outcome, only a lower number of device-related reoperations were found at 5y in the disc replacement group (1 RCT; very low quality; n=152). No short term data were reported.
  - Not reported outcomes: psychological distress, responder criteria, healthcare utilisation
- **Disc replacement versus 3-elements MBR (multidisciplinary biopsychosocial rehabilitation programme with cognitive, physical and education components) in patients with LBP without sciatica**
  - A single study (Hellum 2011) reported a clinically important benefit of disc replacement for **QoL** (EQ-5D 0-1 and SF-36 0-100 physical component; low to very low quality; n=172) in the long term (at 1y and at 2y) but not for the SF-36 0-100 mental component (low quality; n=172). Also a benefit of disc replacement was shown for back **pain** severity in the long term (at 1y and at 2y) (VAS 0-10; low to very low quality; n=172). There was no clinical difference for **function** in the short or longer term (ODI 0-100; low to very low quality; n=172). No short term data were reported for QoL and pain.
  - Not reported outcomes: psychological distress, responder criteria, adverse events, revision rate, failure rate, healthcare utilisation

Economic evidence

- Two economic evaluations were identified: one on total disc replacement versus fusion (Fritzell 2011) and one on total disc replacement versus multidisciplinary rehabilitation (Johnsen 2014):
  - One cost-utility analysis found that total disc replacement was dominant (less costly and more effective) compared to spinal fusion in people with low back pain with or without sciatica. This study was partially applicable with potentially serious limitations.
  - One cost-utility analysis found that total disc replacement was cost-effective compared to multidisciplinary rehabilitation (ICER: £9,544 per QALY gained). This study was partially applicable with potentially serious limitations.
- Limitations of the economic evaluations:
  - The real extent of uncertainty around the conclusion could not be assessed as the probabilistic sensitivity analyses were conducted using societal costs
  - The 2 comparators are not currently recommended in this guideline as they are not considered cost effective, therefore disc replacement might have been compared to cost-ineffective interventions and that could explain why it is cost effective.

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:**
  - Critical outcomes were health-related QoL, pain severity, function, psychological distress
  - Important outcome were responder criteria (for pain and function), adverse events, revision rate, failure rate and healthcare utilisation
  - No evidence was found for psychological distress, responder criteria, failure rate or healthcare utilisation.
- **Trade-off between clinical benefits and harms**
  - **Disc replacement versus spinal fusion for LBP with/without sciatica:** The GDG noted that **evidence for the comparison was limited**, with outcomes analysed from 2 RCTs only. Although the majority of outcomes demonstrated no clinical difference between disc replacement and spinal fusion, some clinical benefit for disc replacement was observed in terms of quality of life. The GDG were concerned that the benefits observed came mainly from a study comparing disc replacement to anterior lumbar interbody fusion, a procedure that is not commonly performed due to perceived lack of effectiveness. The GDG had serious concerns about the **high number of severe adverse events** associated with disc replacement in comparison to spinal fusion. When compared to posterior lumbar interbody fusion, disc replacement demonstrated a clinical benefit in the number of device related reoperations. However, the GDG emphasised the **complexity of revision disc replacement procedures** in patients, resulting in surgeons applying a much higher threshold for carrying out reoperations. For 1 of the intervention trials, insufficient data were reported for pain and function to be meta-analysed and therefore conclusions could not be drawn with any degree of certainty although the GDG noted that the magnitude of the between group differences appeared small.
  - **Disc replacement versus 3-elements MBR for LBP without sciatica:** The GDG observed that the comparison between disc replacement and 3-elements MBR could be **inappropriate**, as people with low back pain would often take part in a MBR programme before undergoing surgery. The GDG noted that evidence for this comparison came from a **single RCT**. Although there was some benefit observed in the outcomes reported, the GDG expressed concerns over the **serious adverse events** related with disc replacement, in particular 1 lower leg amputation and four cases of considerable blood loss (greater than 1500 ml) out of 80 participants. It was noted that this is a high occurrence of adverse events in studies not powered to detect harm. GDG opinion was that this rate was reflective of the risk observed in practice.
  - **Summary:** Despite seeing some signs of benefit from disc replacement compared to other interventions, the GDG felt the **risk of harms associated with disc replacement outweighed the potential benefits**. The GDG were aware of the lack of long term follow-up data for disc replacement surgery. The GDG expressed their concerns about this, particularly as disc replacement is often performed in younger age-groups in consideration of its claimed motion preservation benefits. However, it was highlighted that there is currently **limited evidence of disc replacement benefits regarding motion and adjacent level degeneration compared to other surgical procedures**, and the reported risks of disc replacement would often prevail over the benefits. As a result, **the GDG agreed it was appropriate to recommend against the use of disc replacement** in people with non-specific low back pain with/without sciatica.
- **Trade-off between net clinical effects and costs**
  - Two cost-utility analyses were identified for disc replacement, both concluding that total disc replacement is cost effective in the base case.
  - The unit cost for spinal fusion surgery was estimated to be £7,337 per patient. This cost is based on the weighted average for complications and co-morbidities of the following HRG codes: Extradural Spine Major 2 with CC Score 5+ (HC01A); Extradural Spine Major 2 with CC Score 2-4 (HC01B); Extradural Spine Major 2 with CC Score 0-1 (HC01C); Extradural Spine Major 1 with CC Score 5+ (HC02D); Extradural Spine Major 1 with CC Score 2-4 (HC02E); Extradural Spine Major 1 with CC Score 0-1 (HC02F). The cost of total disc replacement surgery was also discussed by the GDG. This surgical procedure is included in the same HRG codes as spinal fusion and therefore the 2 surgeries do not differ in unit cost.
  - The GDG noted that the comparators in the 2 studies may have affected the overall conclusions as they may not be cost effective interventions themselves. Therefore, disc replacement could have been shown to be cost effective in the studies only because it was **compared to cost ineffective interventions**.
  - In the 2 economic studies a probabilistic analysis was reported only using the **societal perspective**, which is excluded in our guideline, therefore no evidence on uncertainty around the mean ICER was available from them. However in the study comparing disc replacement with multidisciplinary rehabilitation, when SF6D was used as a quality of life measure instead of EQ5D, the ICER was around £29,000 and the intervention was not cost effective anymore.

- **The GDG were concerned about the safety of the procedure and therefore, taking into account the overall body of clinical effectiveness evidence, the uncertainty around the cost effectiveness studies, and the concerns around safety, they decided to recommend against this procedure.**

- **Quality of evidence**
  - Evidence from 3 RCTS, quality ranged from low to very low, mainly downgraded for high risk of bias due to incomplete blinding, high drop-out rates and baseline differences between the groups for several characteristics (including baseline values of critical outcomes).
  - The GDG expressed particular concern over the **high number of patients that dropped out** of the disc replacement group during the trial comparing 3-element MBR versus disc replacement (30% versus 17%). As the trial featured ITT analysis with last value carried forward (assuming patients had no improvement after dropout), this raised a concern about data interpretation. The imprecise nature of the outcomes included in this review further contributed to decreasing the GRADE quality rating.
  - The GDG raised concerns about the **comparators** in the included studies as they were either procedures without proven efficacy, or in the case of MBR, would be expected to be offered earlier in the pathway as an option prior to surgery.
  - The **economic evidenc**e was assessed as partially applicable with **potentially serious limitations**.
- **Other considerations**
  - The GDG were aware of NICE Interventional procedures guidance for prosthetic intervertebral disc replacement in the lumbar spine, IP306 which recommend normal arrangements for clinical governance, consent and audit for this procedure. However, evidence reviewed by this GDG suggests that the effectiveness of these procedures does not outweigh the risks and therefore the GDG agreed that it is appropriate to recommend against the use of disc replacement techniques for this population.

NICE 2016 first version of recommendation: 1 clinical recommendation (March 2016)
36. Do not offer disc replacement in people with non-specific low back pain.

KCE additional information

In 2015, the KCE report 254 on cervical and lumbar total disc replacements (https://kce.fgov.be/sites/default/files/page_documents/KCE_254_Total_disc_replacements_Report_0.pdf) mentioned following recommendations:

- "From a clinical point of view, the lumbar total disc replacement and the lumbar fusion are roughly just as safe and effective in the short and medium term, while there is a lack of long-term data. Consequently, we recommend to reimburse the surgical procedure for lumbar total disc replacement at the same tariff as the surgical procedure for lumbar fusion, but under different nomenclature codes. There are currently not enough arguments to recommend a reimbursement of the lumbar prosthesis without strict conditions. Current and future RCTs should extend their follow-up period (at least 10 years) to study the long-term effectiveness and safety of this procedure.
- In accordance with the law of 2002 relative to the patients' rights, the patient should be clearly informed of the respective advantages and disadvantages as well as the cost of each surgical alternatives.
- Current and future RCTs should extend their follow-up period (at least 10 years) to study the long-term effectiveness and safety of each procedures**."**

In 2009, in the KCE reports 116C Interspinous implants and pedicle screws for dynamic stabilization of lumbar spine: Rapid assessment (https://kce.fgov.be/sites/default/files/page_documents/d20091027346.pdf), it was mentioned:

- "Given the poor quality of evidence on long-term clinical advantages; given the fact that numerous RCTs are ongoing for different lumbar non fusion dynamic stabilization devices, and given the lack of economic data, we do not recommend to include interspinous devices and pedicle screw based devices in the limitative list of reimbursed implants (currently ongoing by the NIHDI)."

KCE GDG considerations mentioned in the Lime survey in October 2016

Agreement with the content of the NICE recommendation 36: 9 Agree, 2 Disagree, 1 no opinion, 1 out of competence, 1 no answer, 4 not completed

- **Comments from those who do not agree:**
  - Cf discussion on fusion. Prosthesis is not inferior to fusion. Cf FDA studies.
  - De literatuur heeft aangetoond dat, rekening houdend met restricties, deze ingreep klinisch efficiënt is. Ik sluit me aan bij het advies betreffende KCE en terugbetaling van 2015.
- **Other comments:**

I agree... but think that in some very specific cases (so it might not be "non-specific low back pain") it might be relevant although I know that we lack long-term data.

Strength of the recommendation 36 on disc replacement: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	The GDG noted that evidence for the comparison of disc replacement versus fusion was limited, with outcomes analysed from 2 RCTs only. The GDG observed that the comparison between disc replacement and 3-elements MBR could be inappropriate, as people with low back pain would often take part in a MBR programme before undergoing surgery. Despite seeing some signs of benefit from disc replacement compared to other interventions, the GDG felt the risk of harms associated with disc replacement outweighed the potential benefits. It was highlighted that there is currently limited evidence of disc replacement benefits regarding motion and adjacent level degeneration compared to other surgical procedures, and the reported risks of disc replacement would often prevail over the benefits. As a result, the GDG agreed it was appropriate to recommend against the use of disc replacement in people with non-specific low back pain with/without sciatica.
Quality of evidence	Low to very low
Values and preferences	The GDG were aware of NICE Interventional procedures guidance for prosthetic intervertebral disc replacement in the lumbar spine, IP306 which recommend normal arrangements for clinical governance, consent and audit for this procedure. However, evidence reviewed by this GDG suggests that the effectiveness of these procedures does not outweigh the risks and therefore the GDG agreed that it is appropriate to recommend against the use of disc replacement techniques for this population.
Costs (resource allocation)	The GDG were concerned about the safety of the procedure and therefore, taking into account the overall body of clinical effectiveness evidence, the uncertainty around the cost effectiveness studies, and the concerns around safety, they decided to recommend against this procedure.

Agreement with the strength of the NICE draft recommendation 36: 7 strong, 2 weak, 0 no opinion, 0 no answer, 9 not completed

- **No comments for a weak recommendation**
- **Comments for a strong recommendation**
  - limited evidence and risk of harms
  - low evidence, high risks

NICE final version of recommendation (30 November 2016): no major change

39. Do not offer disc replacement in people with low back pain.

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30th November 2016)

Existing guidances

- Johnson and Johnson: The recommendations made by the GDG are contradictory to recommendations made by IPAC on spinal fusion and disc replacement surgery. For example, lateral interbody fusion in the lumbar spine (IPG321) and transaxial interbody lumbosacral fusion (IPG387) both have special arrangements for use recommendations, not research only. In addition, IP guidance on non-rigid stabilization techniques for the treatment of low back pain (IPG366) makes normal arrangements for use i.e. the procedure is safe and efficacious. With regards to intervertebral disc replacement in the lumbar spine (IPG306), this has normal arrangements for use. Yes, this difference is "noted" within the GDG considerations but with no indication of how this discrepancy will be resolved by NICE. Which recommendations should patients and commissioners use to inform their decision making? How will this discrepancy be resolved by NICE to avoid any misunderstanding or confusion amongst stakeholders? **NICE reply**: The GDG were aware of the **existing IP guidance** and have been in communication with the IPG team to highlight the differences within the evidence reviews. Both IPG321 and IPG387 recommend special arrangements for the procedures covered and therefore are not considered to conflict with the recommendation that fusion should only take place in the context of an RCT. Although as you state IPG366 (disc replacement) and IPG306 (non-rigid stabilization techniques) do recommend normal arrangements, the evidence reviewed in this guideline does not demonstrate sufficient evidence of effectiveness for spinal fusion or disc replacement that would enable a recommendation in a clinical guideline for their use. Given the finding from this guideline that neither spinal fusion nor disc replacement are clinically effective for low back pain, these treatments should not be offered (unless in the case of an RCT for spinal fusion as stated in the recommendation).(p66/222)
- United Kingdom Spinal Societies Board and British Orthopaedic association: Moreover, It is acknowledged that spinal surgery is a major intervention and will carry a significantly greater risk of patient harm than conservative management. These data were considered in the original NICE guidance IP 306. It is suggested that the GDG may wish to re-consider their presentation and evaluation of the risk of complications. No specific reply from NICE (p113/222)

Limited evidence

- Society for Back Pain Research: Given the limited evidence it would be appropriate to refer to the spine registries. **NICE reply**: There was **limited evidence** of clinical benefit of disc replacement over spinal fusion (from two trials and limited to quality of life and number of reoperations outcomes) and over multidisciplinary biopsychocial rehabilitation (MBR) programmes (a single RCT) The evidence included in the review ranged from low to very low. The GDG was also not convinced of the appropriateness of the comparison of disc replacement versus MBR, as the latter would commonly be offered earlier than surgery in clinical practice The GDG felt that the risk of harms associated with disc replacement outweighed the potential benefits noted in the evidence. (p76/222)
- United Kingdom Spinal Societies Board and British Orthopaedic association. The GDG note that the GRADE quality rating of the evidence was low to very low. However, for the SH, it is inherent in the design of trial between surgical and non-surgical care that there can be no blinding of the patient or of the investigator. This risk of bias cannot be eliminated as the undertaking of sham surgery under general anaesthesia is outside the ethical compass. **NICE reply**: The protocol for this, and all intervention reviews in the guideline included both RCTs and observational studies where RCT evidence was lacking. In this review 2 cohort studies were included. GRADE quality rating informs the overall confidence in the evidence due to factors including risk of bias, and therefore ratings for outcomes where blinding is more problematic are still downgraded. It is noted that double blinded trials are less common in surgery, however this is also true of other interventions included in the guideline and the approach to evidence quality appraisal and consideration is consistent as stated in the methods, section 4.3.2. (p115/222)

Adverse events

- **United Kingdo**m Spinal Societies Board and British Orthopaedic association**:** First paragraph, the GDG note that anterior lumbar interbody fusion is not commonly performed "due to a perceived lack of effectiveness". This statement appears supported only by the collected expert opinion, which may have been coloured by a trial against fusion with BAK cages which were subsequently demonstrated to have unsatisfactory results. An unmatched cohort series of 150 anterior fusions and 150 postero-lateral fusions indicated superiority of anterior fusion over instrumented postero-lateral fusion in function and return to work (9). The GRADE quality rating in surgical trials is usually low because of the inevitable risk of bias owing to the lack of blinding. The GDG may wish to consider the value of lower quality evidence in surgical studies to inform the expressed opinion. The GDG expressed concern over the risk of patient harm from surgical intervention and quote figures from one study with 80 participants in the disc replacement arm, noting

that it was not powered to detect harm. This imprecision must be in both directions however, the risk of an excess of serious complications by chance in a small group is higher. Many of the studies referred to by the GDG were included in the systemic review by Wei in 2013 (10). This systemic review examined the reported complications in five randomised controlled trials comprising of 1081 total disc replacement operations. The complication rate reported was 5.8 percent and in the 500 fusion patients of the same trials**,** the complication rate was 10.8 percent. In this review the re-operation rate was 5.2 percent for total disc replacement and six percent for spinal fusion. It is acknowledged that spinal surgery is a major intervention and will carry a significantly greater risk of patient harm than conservative management. These data were considered in the original NICE guidance IP 306. It is suggested that the GDG may wish to re-consider their presentation and evaluation of the risk of complications. **NICE reply:** The GDG was concerned about the use of **BAK cages** to achieve anterior lumbar interbody fusion in the control group of the Gornet 2011 trial. The GDG was aware that anterior procedures in the lumbar spine for back pain are not commonly performed in the UK setting, and that the BAK cages technique shows a low fusion rate and would not be considered appropriate for a stand-alone anterior fusion in clinical practice. For this reason, as most of the evidence in favour of disc replacement in the review came from the Gornet 2011 trial, the GDG wished to stress that such evidence should be **regarded with caution**. This has now been clarified in section 26.6 (Recommendations and link to evidence). The comparison of different spinal fusion routes was outside the scope of the guideline.(p112/222)

Monitoring in registry

- United Kingdom Spinal Societies Board and British Orthopaedic association*:* Given the paucity of evidence and the inevitably low GRADE evaluation of randomised surgical trials there is strong case for reviewing evidence from other sources. There has been an increase over time of the use of **spinal surgical registries** in a number of specialities including spinal surgery. The GDG are invited to consider whether in the absence of the possibility of high quality studies on the GRADE quality rating, data from spinal registries should be included in the evidence base. Evidence from the Swedish Spine Registry which covers 42 of 45 Spine Centres in Sweden showed in 2012 that total disc replacement provides better outcomes in most modalities than spinal fusion. The data in the registry is sufficiently detailed to permit evaluation of the influence of pre-operative functional scores. They also note that the RCT as a technique for comparison with other fusion techniques might be possible. Not stated in this report is the consideration that to achieve a satisfactory GRADE quality rating, the comparator in such a trial would have to be stand alone anterior fusion otherwise blinding would be impossible with one operation done from the front and the other from the back. The 2014 report of the Swedish Spinal Registry evaluates the results of surgery for degenerative disc disease at one year, two years and five years. These surgeries are fusions of various types and disc replacement (16 percent). Considering the evidence review undertaken by the GDG, outcomes of total disc replacement may be considered not inferior to those of spinal fusion and so these results have validity. The change in EQ5D score from pre-operative to one year follow up was 0.32. The improvement at two years was 0.3 and at 5 years 0.29. Thus surgical procedures resulted in approximately a third of a Qualy in improvement per year for five years. Pain on the VAS scale reduced from 6.2 pre operatively to 2.7 at one year, 2.9 at two years and 3.3 at five years. ODI results are available for two years only, with a reduction from 44 pre operatively to 23 at one year and 24 at two years. Registries have the additional advantage of representing surgery in the real world, with normal health care provision and normal surgical teams. **NICE reply**: The GDG were aware of the availability of spine registries, however when setting the protocol that studies design would be restricted to RCTs in the first instance, and then observational studies if there were limited evidence available, to ensure the best available evidence was used to inform the review question. Observational data was used within the review, but no published analysis of registry data was identified to inform the review, and evidence was available from the included studies. Furthermore, the GDG highlighted that many spine registries are filled on a voluntary basis, and therefore are at very high risk of selection bias. (p115/222)
- United Kingdom Spinal Societies Board and British Orthopaedic association: The audit and **governance all surgical procedures** are of great importance, especially with regard to patient satisfaction, patient outcomes and complications. All specialised spinal surgery is now mandated to be entered on the British Spine Registry. In this regard, what has been termed “special arrangements for clinical governance, consent and audit for this procedure” might be expressed as entry into the British Spine Registry, which would also permit research. The GDG may wish to consider whether improved safeguards, audit and governance might be sufficient reason to modify the recommendation in this manner and allow patient choice. The GDG is unable to comment about how changes in audit and governance may affect the outcomes of surgery. NICE replied on patient choice (p118/222)

Black disc believers

- Society of British Neurological Surgeons**:** The guideline has reversed the decision made in 2009 when this procedure was approved for clinical use with NORMAL arrangements for governance. The decision not to recommend this operation in the current guideline is based on further evidence (which is not of high quality) and the adverse events reported weighed against the benefits. We recommend the procedure to be recommended with SPECIAL governance arrangements. Surgeons may decide to still offer this operation on the basis that a ‘Black disc’ is the likely source of the LBP (see further comments below). The problem with the NICE guidelines are such that the disc replacement

for black disc believers will disregard the guidelines on the basis that they believe (rightly or wrongly) that the pain generator is the disc itself. No specific reply from NICE. (p110/222)

Imaging role

- Medtronic: SH asked to consider that **appropriate imaging** is required to attribute a diagnosis of specific versus non-specific low back pain in the context of disc replacement. **NICE reply**: However, according to the GDG, the importance of assessing an individual's signs and symptoms when considering the appropriate form of imaging has been highlighted in section 7.1, lines 24-26 on page 116 (Full guideline- Assessment and non-invasive). Furthermore, section 7.6, 'Other consideration' box states that 'the presence of symptoms or signs suggestive of possible serious underlying pathology (red flags), including a past history of cancer or trauma may warrant early imaging'. However guidance on assessment of such underlying pathology is beyond the scope of this guideline.(p111/222)

Population

- Society of British Neurological Surgeons: Disc replacement - people will interpret NSLBP is a way that fits with their practice and this term needs clarity. To make a point, I would like to ask- in a 42 year old patient with severe back pain for 2-3 years preventing him to function fully, what is the diagnosis? After failure of conservative treatment should an MRI be done? Should he be asked to "live with this" at this stage? If MRI shows disc degeneration at L4/5 with adjacent modic changes, no facet joint tenderness or failed facet injection, would it be appropriate to consider surgery? **NICE reply:** The evidence reviewed does not support a recommendation for disc replacement. Therefore for people in whom other treatments have failed to adequately remove their symptoms, this evidence suggests further treatment, including surgery, is unlikely to be of benefit.(110/222)

Disagreement with NICE recommendation

- Society of British Neurological Surgeons: Disc replacement and Spinal Fusion - Surgery for back pain has always been a controversial subject. GDG has acknowledged that disc replacement is at least similar to fusion in results. In 27.5.1.32 GDG has acknowledged that fusion may be less effective than disc replacement! GDG should come up with some criteria in which fusion or disc replacement may be considered. A statement to say that this surgery is not totally recommended is possibly not correct. Consideration should be given (after failure of conservative treatment) to level of disc involved, facet joint pathology, modic changes, discogram, SPECT CT etc to guide the decision. **NICE reply:** We agree there is consistency across the disc replacement review and the spinal fusion review for benefits of the former type of surgery over the latter in terms of quality of life outcomes. However after consideration of the evidence reviewed in both chapters, the GDG agreed that disc replacement should not be offered to the population described in the guideline due to risk of harm and lack of cost-effectiveness. Similarly, while acknowledging that other causes of low back beyond the scope of this guideline might be appropriately treated with spinal fusion, people with non-specific low back pain should not be offered spinal fusion, unless as part of a randomised controlled trial.

Patient choice

- United Kingdom Spinal Societies Board and British Orthopaedic association: It is clear that any form of spinal surgery for axial lumbar spine pain is a much larger intervention with significant risk of complications. As such it is appropriate that total disc replacement should be considered only after an inadequate response to an appropriate NBR (CPPP). All health care delivery is **patient centred** and is undertaken in partnership with the patient themselves. It is perhaps inappropriate that the choice of an effective treatment should be denied to patients without their involvement. The uptake of a surgical option after full and open discussion of potential benefits and potential risks is a decision which should be made by patients. It is requested that the GDG consider whether patient choice should take a higher priority. Other considerations and governance might be sufficient reason to modify the recommendation and allow patient choice. **NICE reply**: Patient choice is integral to all NICE guidelines and should apply across all recommendations. This is stated in section 4.5.4 and inside the cover page, highlighting that: "The decision to adopt any of the recommendations cited here must be made by practitioners in light of individual patient circumstances, the wishes of the patient, clinical expertise and resources". However, having reviewed the evidence for disc replacement the GDG agreed that the risks of harms associated with the surgical procedure outweighed the potential benefits and the GDG decided it was appropriate to recommend against the use of disc replacement for non-specific low back pain.(p117/222)

Surgeon experience

- United Kingdom Spinal Societies Board and British Orthopaedic association: It is plain that the risk of complications is potentially correlated with the **experience of the surgeon** and of the multi-disciplinary team. Lumbar total disc replacement is a specialised procedure, directly commissioned by NHS England. The potential for complications might be addressed by performing such surgery only under the auspices of a specialised surgical centre. NICE replied on patient choice. (p117/222)

Economic evidence

- United Kingdom Spinal Societies Board and British Orthopaedic association: Two studies were considered for the **economic evaluation**. One study (Johnsen 2014) demonstrated cost effectiveness against multi-disciplinary rehabilitation. The evidence extract describes this as a three element MBR programme. In paragraph two, the GDG then note that comparator interventions might not be cost effective themselves. However, in the evaluation of multi-disciplinary bio-psychosocial rehabilitation in another part of the guidance, the 3 element MBR is noted to be a cost effective intervention. There appears to be a contradiction here. The inconsistency of the terminology for the multidisciplinary rehabilitation in Johnsen 2014 has been amended and is now consistent across the review. We have amended the LETR in response to your comment.
- There does not appear to be a rationale for preferring the analysis using the FS6D over the EQ5D. When choosing outcomes EQ-5D scores are to be preferred over SF-6D according to the NICE Reference Case and therefore the analysis using EQ5D data was used in the base-case analysis. The SF-6D was reported as a one-way sensitivity analysis and was therefore presented to the GDG as an additional consideration of uncertainty. Changes have been made to the LETR to clarify this.

NICE changes in the final version of the guideline (November 2016)

In the Clinical evidence chapter

One Cochrane review was identified but was not included as the stratification of the people with low back pain, low back pain with/without sciatica and sciatica was unclear. The studies included in the Cochrane review were individually assessed and included if they matched the protocol.

In Trade-off between clinical benefits and harms, two sentences were added:

The GDG were concerned that the benefits observed came mainly from a study comparing disc replacement to anterior lumbar interbody fusion (BAK cages technique). The GDG was aware that anterior procedures in the lumbar spine for back pain are not commonly performed in the UK setting, and that the BAK cages technique shows a low fusion rate and would not be considered appropriate for a stand-alone anterior fusion in clinical practice.

In the summary, one sentence was added at the beginning "The GDG noted that there were some signs of benefit from disc replacement compared to other interventions, but this evidence was very limited and not consistent across outcomes" ; at the end the last sentence "As a result, the GDG agreed it was appropriate to recommend against the use of disc replacement in people with non-specific low back pain with/without sciatica" was replaced by "As a result, the GDG agreed that the limited evidence of effectiveness alongside the above concerns meant it was appropriate to recommend against the use of disc replacement in people with low back pain with/without sciatica."

In other considerations, one sentence was added:

"The GDG agreed there may be specific causes of low back pain for which disc replacement might be an appropriate treatment which are beyond the scope of this guideline**.**

NICE final recommendations on spinal fusion(November 2016)
39. Do not offer disc replacement in people with low back pain.

Belgian GDG comments during the GDG meeting on the 14th December 2016

NICE recommendation 39: Do not offer disc replacement in people with non-specific low back pain.

- In the final version of the NICE guideline this recommendation has slightly been changed: "*Do not offer disc replacement in people with low back pain".*
  "Non-specific" has been removed.
- The KCE report in 2015 emphasised the lack of difference in efficacy and safety between disc replacement and fusion. There was a recommendation to reimburse spinal disc replacement in line with the current reimbursement for spinal fusion.
- A while ago reimbursement for lumbar disc prosthesis was achieved (but not for cervical disc prosthesis), then it was considered as a long standing entitlement and this is difficult to turn back.
- However, the GDG members agree that the NICE recommendation should not be modified due to the limited evidence and the potential risk of harms.

⇨ **The NICE recommendation 39 has been accepted without any change.**
⇨ ***"Do not offer disc replacement in people with low back pain".***

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

- No comments

KCE 2017 final recommendations on disc replacement (February 2017)
XX. Do not offer disc replacement in people with low back pain.

7.20. Spinal fusion

Spinal fusion in patients with low back pain ± radicular pain

NICE search question

"What is the clinical and cost-effectiveness of spinal fusion/arthrodesis in people with non-specific low back pain?"

Introduction based on the draft version of NICE guideline (March 2016)

- Spinal fusion is an operation performed to achieve solid bone union between spinal vertebrae to prevent movement. This involves using the patient's own bone or artificial bone substitutes. The procedure of spinal fusion is commonly carried out as a component part of many types of spinal operation, such as operations to correct deformity, remove tumours and treat spinal fractures. Sometimes a fusion is done as part of an operation to decompress the spinal neurological structures; this is known as a decompression.
- In clinical practice, spinal fusion is sometimes used to treat severe and constant low back pain that has not resolved despite the use of other more conservative treatments. Screws, rods or other implants may be used as an internal splint to stabilise the spine while the fusion is occurring.
- There are different surgical approaches to the spine: from the back, the front or the side. The outcomes from the different approaches are similar. However, the risks of harm vary according to the approach and specific methods used. The risk of harm should be considered in terms of the probability of benefit and the alternative treatments that are known to have a treatment effect.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with sciatica
Intervention(s)	• Spinal fusion/arthrodesis
Comparison(s)	• Usual care; waiting list • No surgery • Different type of surgery (e.g. anterior approach fusion versus disc replacement) • Other treatment (interventions listed in our guideline review protocols)
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Adverse events: post-operative complications (e.g. infection); increased risk of requiring surgery at adjacent segments; mortality. • Revision rate • Failure rate • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit)

Literature quoted by NICE 2016 guideline (March 2016)

- Nine randomised controlled trials and 1 cohort studies were included in the review. As there was only 1 RCT for the comparison of spinal fusion versus usual care, the search was extended to cohort studies for this comparison as well as spinal fusion versus no surgery for which there were no randomised trials. One cohort study was identified that met the inclusion criteria for fusion versus usual care and was included in the review. One Cochrane review was identified but was not included as the stratification of the people with low back pain, low back pain with/without sciatica and sciatica was unclear, however the study included were individually assessed and included in this review if they matched the review protocol. One non-randomised study was identified comparing spinal fusion with spinal decompression. Four RCTs were found the comparison with other non- invasive treatments and 2 RCTs for the comparison with different types of surgery. The results of two RCTs are pooled with previous reported results of the same trial.
- **Spinal fusion versus usual care in patients with LBP with or without sciatica**
  - **Randomised trial** (Fritzell 2001): A single study reported a clinical long term (at 2y) benefit of spinal fusion for **pain** (VAS 0-10; Mean diff: -1.51 [95%CI -2.09, -0.93], very low quality; n=264) and for **function** measured by the General Function Score 0-100 and the Million Visual Analogue Score 0-100 (low to very low quality; n=264). However, function measured by the ODI 0-100 demonstrated no clinical difference (very low quality; n=264). A greater number of **adverse events** (complications) and **reoperations** were seen at 2y in the spinal fusion group (OR 5.00 [95%CI 2.45, 10.19] and OR 4.12 [95%CI 1.30, 13.10]) (low quality; n=283). No short term data were reported.
  - **Cohort study** (Smith 2014 – instrumented lumbar fusion versus UC (physical therapy, epidural injections and medication)): No clinical differences were found at 1y for **QoL** (SF-12 0-100; PCS and mCS; very low quality; n=96), **pain** (NRS 0-10; very low quality; n=96) and **function** (ODI 0-100; very low quality; n=96). No short term data were reported.
  - Not reported outcomes: psychological distress, healthcare utilisation
- **Spinal fusion versus other treatments in patients with LBP without sciatica**
  - Spinal fusion versus 3-elements MBR programme (exercise, education, cognitive behaviour therapy): Evidence from 3 RCTs showed no clinical difference for **pain** (at 1y; VAS 0-10; 2 RCTs; very low quality; n=118), **function** (at 1y; ODI 0-100 and General Function Score 0-100; 2 RCTs; low-very low quality; n=118; and at 2y; ODI 0-100; 1 RCT; low quality; n=349), and the majority of the **QoL** domains (except for general health perception and pain) (SF-36 0-100; 1 RCT; low quality; n=246). In addition, there was no difference for **healthcare utilisation** (unplanned hospital admissions for spinal surgery; GP consultations, practice nurse consultations, GP home visits; practice nurse home visits) (1 RCT; low to very low quality; n=349).
  - Spinal fusion versus mixed modality exercise: A single RCT comparing spinal fusion with mixed modality exercise (aerobic + biomechanical exercise) demonstrated a clinical benefit in **pain** (VAS 0-10, Mean diff. at 1y -2.83 [95%CI -5.68, 0.02] and Mean diff at 2y -3.06 [95%CI -6.08, -0.04]; very low quality; n=41) and **function** (ODI 0-100 at 1y -26.06 [95%CI -47.47, -4.65] & at 2y -26.59 [95%CI -44.82, -8.36] ;and JOAS 0-3 at 1y 0.96 [95%CI 0.36, 1.56] & at 2y 1.16 [95%CI 0.40, 1.92]; very low quality; n=41) in favour of spinal fusion. No short term data were reported.
  - Not reported outcomes: psychological distress, responder criteria, adverse events, revision rate, failure rate
- **Spinal fusion versus different types of surgery (disc replacement) in patients with LBP with or without sciatica**
  - Two RCTs reported no clinical difference in **pain** (VAS 0-10; very low quality; n=577-729) and in **function** (ODI 0-100; low quality; n=577-729) at short term (3 months) and long term (1y and 2y). In terms of **QoL** (measured by EQ-5D 0-1 (at 1y; 1 RCT; very low quality; n=152) and SF-36 0-100 physical component score (at 3mo, 1y and 2y; 1 RCT; low to very low quality; n=577)), spinal fusion was shown to be less effective than disc replacement. No clinical difference in QoL was found for the measurement with EQ-5D 0-1 (low quality; n=152) at 2y and the SF-36 0-100 mental component score (at 3mo, 1y and 2y; low quality; n=577). Statistically no clinical differences were found for **adverse events** (mortality, complications) (2 RCTs; low to very low quality; n=577-729) and number of **re-operations** (very low quality; n=152). However, some conflicting tendencies were noticed: whereas a tendency towards a clinical benefit for fusion was noticed for less complications at 5y (1 RCT; very low quality; n=152), the same study reported more occurrences of surgery at adjacent level at 2y in the spinal fusion group (very low quality; n=152).
  - Not reported outcomes: pain, psychological distress, responder criteria, failure rate

Economic evidence

- Two economic evaluations were identified: one on spinal fusion versus total disc replacement (Fritzell 2011) and one on spinal fusion versus 3-elements MBR programme (Rivero-Arias 2005):
  - One cost-utility analysis found that spinal fusion was dominated (more costly and less effective) compared to total disc replacement in people with low back pain with or without sciatica. This study was partially applicable with potentially serious limitations.
  - One cost-utility analysis found that spinal fusion was not cost-effective compared to a 3-elements MBR programme for treating LBP with or without sciatica (ICER: £48,515 per QALY gained). This study was partially applicable with potentially serious limitations.
- No economic evaluations were identified comparing spinal fusion to no surgery or usual care.

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:**
  - Critical outcomes were health-related QoL, pain severity, function, psychological distress
  - Important outcome were adverse events, revision rate, failure rate and healthcare utilisation
  - No evidence was found for psychological distress and failure rate. The GDG felt there was sufficient evidence for all of the outcomes that were considered important for this review.
- **Trade-off between clinical benefits and harms**
  - **Spinal fusion versus usual care for LBP with/without sciatica:** Low and very low quality randomised evidence from a single large trial suggested a clinical benefit in favour of spinal fusion in terms of pain in the longer term follow up (4 months - 1 year), however there was uncertainty in this effect. The GDG discussed that the difference in pain scores at the end of 2 years between the surgical and non-surgical group was not very pronounced. However, this study reported a marked decrease in pain severity in the first 6 months after surgery in graphical form. The GDG considered this useful data although it could not be included in this meta-analysis. The GDG discussed that the short term relief in pain could be as a result of the application of a rigid plastic brace restricting the individuals' movement after surgery. A long term benefit in function (measured on three different scales) was also shown to favour fusion. The GDG also noted the 17% complication rate and 8% reoperation rate for spinal fusion and that there was **significant potential harm to patients**.
  - **Spinal fusion versus other treatment (3-elements MBR, mixed modality exercise):** Clinical benefit in pain and function favouring spinal fusion was observed in the longer term follow up with serious uncertainty. This long term benefit in pain severity and function was observed in evidence from 1 small study comparing minimally treated patients as the control group to surgery. It was considered unlikely that improvements would be seen in the group receiving minimal treatment. The 3 larger studies in this comparison incorporated more rigorous MBR programmes as their comparator treatment; no clinically important difference in either pain or function was observed with this comparator. The GDG noted that 1 study had a very intensive MBR programme that involved 75 hours of intervention per week compared to 25 hours per week in the other 2 studies. However, evidence was consistent across all 3 studies, suggesting that the **outcomes for people receiving MBR programmes were no different those receiving surgery**. No clinically important difference in quality of life or healthcare utilisation (with some uncertainty) was seen between treatments in the long term follow-up for this comparison. The data for these 2 outcomes was taken from 1 study in which a high number of patients randomised to rehabilitation underwent surgical stabilisation of the spine; 10 subjects opted for this instead of rehabilitation, and 38 subjects in addition to rehabilitation, contributing to a >40% cross-over rate for patients who had both treatments. Overall it appeared that **MBR programmes perform as well as spinal fusion in terms of improving pain, function and quality of life, but are associated with a low risk of harm**.
  - **Spinal fusion versus different type of surgery (total disc replacement):** Evidence from 2 large trials demonstrated no clinically important difference in either pain or function between spinal fusion and disc replacement either in the short or the long term follow-up. A clinical benefit favouring disc replacement was demonstrated when assessed by the physical component of the SF-36 in both the and long term. However, no clinically important difference in the mental component of the SF-36 was observed at any time point. Very low quality evidence suggested a clinical benefit favouring disc replacement in terms of quality of life assessed by EQ-5D at the long term time point of 1 year which was not maintained at the 2 year follow-up. No clinically important difference between spinal fusion and disc replacement was seen in terms of adverse events (mortality and complications). The GDG noted that there was a **high rate of serious complications associated with both treatments**, for example 1 study reported that 345 out of 405 people experienced adverse events at 2 years following fusion surgery. However, it was noted that

intraoperative rates of serious complications differed at 14.6% for disc replacement compared to 8.7% for spinal fusion; the higher rate in disc replacement possibly attributed to its more invasive nature. The GDG understood there to be a roughly 10–20% rate of complications across trials, with approximately 4-5% serious complications. As a result, they did not feel that the clinical benefit favouring disc replacement assessed by the physical component of the SF-36 in both the short term and long term was significant enough to outweigh the potential harms associated with the procedure despite the effect being maintained at 1 and 2 year follow-up. Very low quality evidence demonstrated a clinical benefit favouring disc replacement for further surgery required at an adjacent level at 2 years. However, the study did not report treatment effect at different levels, so the GDG did not feel that this information was useful for decision making. Furthermore, data from the same study suggested no clinically important difference between spinal fusion and disc replacement for revision rate (reoperations) at the long term time points of 2 and 5 years.

- **Summary:** Overall the GDG considered that there was **no consistent benefit of spinal fusion over comparator treatments and evidence of potential harm**. Given this and the **limited number of studies** from which data could be evaluated, the GDG agreed that **spinal fusion should only be recommended for people with non-specific low back pain in the context of a randomised controlled trial**.

- **Trade-off between net clinical effects and costs**
  - Two cost-utility analyses were identified for spinal fusion, both concluding that spinal fusion is **not cost effective** in the base case.
  - The unit cost for spinal fusion surgery was estimated to be £7,337 per patient. This cost is based on the weighted average for complications and co-morbidities of the following HRG codes: Extradural Spine Major 2 with CC Score 5+ (HC01A); Extradural Spine Major 2 with CC Score 2-4 (HC01B); Extradural Spine Major 2 with CC Score 0-1 (HC01C); Extradural Spine Major 1 with CC Score 5+ (HC02D); Extradural Spine Major 1 with CC Score 2-4 (HC02E); Extradural Spine Major 1 with CC Score 0-1 (HC02F). The cost of total disc replacement surgery was also discussed by the GDG. This surgical procedure is included in the same HRG codes as spinal fusion and therefore the 2 surgeries do not differ in unit cost.
  - Taking into account the overall body of clinical effectiveness evidence for spinal fusion, the GDG concluded there was **no consistent benefit of spinal fusion** over comparator treatments and there was **considerable evidence of harm**. When combined with the cost-effectiveness evidence which indicated that spinal fusion was **not a cost-effective intervention** for the treatment of low back pain, the GDG agreed that **spinal fusion should not be routinely recommended for people with non-specific low back pain.**
- **Quality of evidence**
  - Evidence from 9 RCTS, quality ranged from low to very low, mainly downgraded for high risk of bias and uncertainty of the effect size.
  - In the study comparing spinal fusion versus usual care, population was randomised to more of the same treatment (physiotherapy and advice) or surgery. The GDG discussed that the control group appeared to be a **severely disadvantaged group** that had not been offered a new treatment and had been selected on the grounds of strict inclusion criteria of mandatory sick leave or equivalent disability for a year, as well as previous failure of non-surgical treatments. The GDG felt that this could result in a risk of bias due to a 'negative contextual effect' and also raised concerns that the study only reported outcomes at 2 years. The surgical group in this study was also much larger than the usual care group (n=211 versus n=72). It was also noted that **Million Visual Analogue Scale** (MVAS) used to measure function in the study reported a final score of 0-100 whereas commonly the MVAS comprises of 15 questions with a scale of 0-150.
  - In the comparison to other treatments (3-elements MBR programmes with **varying intensity** and mixed modality exercise), one study in particular was noted by the GDG to be a very small trial and used a less intensive comparator than the other trials. The GDG were not convinced by the small benefit in pain and function favouring spinal fusion reported in this study, which was not observed in the larger studies with more intensive comparator interventions.
  - In the comparison with other types of surgery (total disc replacement), the larger of the 2 studies was an industry funded investigational device exemption trial for an artificial lumbar disc and had an **incomplete outcome data rate** of 15.1% in the control arm compared to 5.7% in the disc replacement group which cast doubt on the results reported.
  - The **economic evidence** was assessed as partially applicable with **potentially serious limitations**.
- **Other considerations**

- The GDG agreed there were causes of low back pain for which spinal fusion might be an appropriate treatment (beyond the scope of this guideline*), however for non-specific low back pain* ***the evidence of benefit was outweighed by the potential harms****.*

NEW. The GDG noted that if spinal fusion was being undertaken, patient outcome information should be submitted to a national registry.

- The GDG were aware of NICE Interventional procedures guidance for Non rigid stabilisation techniques for the treatment of low back pain, IP366 which recommend normal arrangements for clinical governance, consent and audit for this procedure.
- The GDG were also aware of existing NICE interventional procedure guidance for Transaxial interbody lumbosacral fusion (IPG 387) and Lateral (including extreme, extra and direct lateral) interbody fusion in the lumbar spine (IPG321) which both recommend special arrangement for clinical governance, consent, audit and research. These procedures were excluded from the review and if considered for people with non-specific low back pain, the existing guidance should be followed.

- **Research recommendation**
  - Non-specific low back pain affects a large number of individuals in UK. The condition has a huge cost to the individual, society and the country's economy. Over the past 2 decades, increasing number of procedures have been proposed for the surgical management of LBP. These include but are not limited to surgical fixation with internal metal-work applied from the back, front, side or any combination of the three routes. The **costs of these operations have escalated** and with the advent of minimally invasive approaches more of the operations are performed with uncertain benefit. As well as the monetary cost, there are **complications associated with the surgical approaches** with some studies reporting around 20% complication rate in the short to medium term. There have been several studies looking at the clinical effectiveness of spinal fusion versus usual care, no surgery, different surgeries, and other treatments. The studies collectively fail to show clear advantage of fusion but do show some modest benefit in some elements of pain, function and quality of life as well a reduction in healthcare utilisation. It is not known what treatments should have been tried prior to the consideration of surgery. Some patients who respond positively to surgery demonstrate a large treatment effect and the ability to predict responders would improve options available to patients. The studies generally suffer from low number of patients, large cross over and in case selection bias. We therefore propose **a large, multi-centre randomized trial with sufficient power** to answer these important questions.

NICE 2016 first version of recommendations: 1 clinical recommendation and 1 research recommendation (March 2016)

37. Do not offer spinal fusion for people with non-specific low back pain unless as part of a randomised controlled trial.

Research recommendation:

7. Should individuals with non-specific low back pain be offered spinal fusion as a surgical option?

Belgian GDG considerations mentioned in the Lime survey in October 2016

<u>NICE draft recommendation 37. Do not offer spinal fusion for people with non-specific low back pain unless as part of a randomised controlled trial.</u>

Agreement with the content of the NICE recommendation 37: 9 Agree, 2 Disagree, 1 no opinion, 1 out of competence, 1 no answer, 4 not completed

- **Comments from those who do not agree:**
  - Here the definition of non-specific pain becomes important: Some studies show benefits for pain and the FDA approved surgical treatments and more specifically prosthesis. The cost benefit is debatable. What about a last option salvage treatment, after failure of MBR programs? High cross over in negative studies! Finally: does non-specific remains non-specific after diagnostic testing, in the presence of "minor" signs of instability...? Overestimation of complication rate.
  - Spinale fusie is te uitgebreid om als een topic te behandelen. Voor een "klassieke ALIF of PLIF" kan men een zelfde argument gebruiken als hierboven (afhankelijk van restricties). Voor nieuwere technieken moeten deze toegepast worden binnen het kader van een gerandomiseerde studie. Er werd een selectieve en verouderde lezing gemaakt van de bestaande literatuur.
- **Other comments:**
  - I suppose that in the report you will also indicate something like "There are causes of low back pain for which spinal fusion might be an appropriate treatment (e.g. ....) but they are beyond the scope of this guideline)"

- Maybe only in selected cases (after multidisciplinary evaluation)?
- We all know so many patient of whom the pain status could only worsen after spinal fusion...
- We have to add, however, the inclusion criteria in the studies were not 100% precise. There are some rare subgroups of patients (eg. degenerative anterolisthesis with marked instability, degenerative severe deformities) that can benefit from fusion surgery if well selected and after failed accurate conservative management.

Strength of the recommendation 14 on TENS: According to NICE formulation, it is a strong recommendation

GRADE Factors	
Balance between desirable and undesirable effects	Overall the GDG considered that there was no consistent benefit of spinal fusion over comparator treatments and evidence of potential harm. Given this and the limited number of studies from which data could be evaluated, the GDG agreed that spinal fusion should only be recommended for people with non-specific low back pain in the context of a randomised controlled trial.
Quality of evidence	Low to very low
Values and preferences	Taking into account the overall body of clinical effectiveness evidence for spinal fusion, the GDG concluded there was no consistent benefit of spinal fusion over comparator treatments and there was considerable evidence of harm. When combined with the cost-effectiveness evidence which indicated that spinal fusion was not a cost-effective intervention for the treatment of low back pain, the GDG agreed that spinal fusion should not be routinely recommended for people with non-specific low back pain.
Costs (resource allocation)	Two cost-utility analyses were identified for spinal fusion, both concluding that spinal fusion is not cost effective in the base case.

Agreement with the strength of the NICE draft recommendation 37: 7 strong, 2 weak, 0 no opinion, 0 no answer, 9 not completed

- No added comments

Research recommendation 7. Should individuals with non-specific low back pain be offered spinal fusion as a surgical option?

Agreement with the content of the NICE research recommendation 7: 7 Agree, 1 Disagree, 4 no opinion, 1 out of competence, 1 no answer, 4 not completed

- **Comments from those who do not agree:**
  - I would prefer studies about disc prothesis or further studies investigating the prediction factors of success
- **Other comments:**
  - Onder welbepaalde restricties.
  - Should 'selected' individuals...?

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30th November 2016)

Other NICE guidance

- Johnson and Johnson. The recommendations made by the GDG are contradictory to recommendations made by IPAC on spinal fusion and disc replacement surgery. For example, lateral interbody fusion in the lumbar spine (IPG321) and transaxial interbody lumbosacral fusion (IPG387) both have special arrangements for use recommendations, not research only. In addition, IP guidance on non-rigid stabilization techniques for the treatment of low back pain (IPG366) makes normal arrangements for use i.e. the procedure is safe and efficacious. With regards to intervertebral disc replacement in the lumbar spine (IPG306), this has normal arrangements for use. Yes, this difference is "noted" within the GDG considerations but with no indication of how this discrepancy will be resolved by NICE. Which recommendations should patients and commissioners use to inform their decision making? How will this discrepancy be resolved by NICE to avoid any misunderstanding or confusion amongst stakeholders? **NICE reply**: The

GDG were aware of the existing **IP guidance** and have been in communication with the IPG team to highlight the differences within the evidence reviews. Both IPG321 and IPG387 recommend special arrangements for the procedures covered and therefore are not considered to conflict with the recommendation that fusion should only take place in the context of an RCT. Although as you state IPG366 and IPG306 do recommend normal arrangements, the evidence reviewed in this guideline does not demonstrate sufficient evidence of effectiveness for spinal fusion or disc replacement that would enable a recommendation in a clinical guideline for their use. Given the finding from this guideline that neither spinal fusion nor disc replacement are clinically effective for low back pain, these treatments should not be offered (unless in the case of an RCT for spinal fusion as stated in the recommendation).(p66/222)

- United Kingdom Spinal Societies Board and British Orthopaedic association: The GDG noted the existing guidance on non-rigid stabilisation recommending "normal arrangements for clinical governance, consent and audit for this procedure". Non-rigid stabilisation as a technique has fallen out of favour in spinal surgery owing to a substantial re-operation rate and less satisfactory long term results. The GDG is requested to consider whether by effectively recommending against fusion surgery that a large patient population may then be subjected to a recrudescence of less satisfactory technique. The GDG noted the guidance on trans-axial interbody lumbosacral fusion (IPG387) and lateral (including extreme extra and direct lateral) interbody fusion IPG321. The GDG are requested to consider whether their advice is internally consistent with recommending against the majority of fusions but permitting these form of fusion which have a significant lower evidence based. **NICE reply**. The GDG were aware of the existing IP guidance and have been in communication with the IPG team.. Both IPG321 and IPG387 recommend special arrangements for the procedures covered and therefore are not considered to conflict with the recommendation that fusion should only take place in the context of an RCT.(p129/222)

Some indications of fusion

- Society for Back Pain Research: The recommendation is based on low evidence – very low from a small number of trials. The quality rating is significantly affected by the fact that blinding in fusion surgery is highly unlikely to ever be given ethical approval. The evidence demonstrate clinical benefit in a difficult client group at the end of the pathway and The concern is the complication rate (Given the limitations of the RCT literature it would be appropriate to seek clarification on the complication rate from the spine registries. (Swedish Spine registry (www.4s.nu), Spine Tango and the British Spine Registry). It is highly likely that the complication rate will be lower in specialist spine centres; given the importance of this It is worthy of GDG to revisit and consider prospective cohorts, the registry data is closest to this.
  Error: The algorithm advises that additional treatment is unlikely to be of benefit. This is not true. For a small subgroup spinal fusion is beneficial but has risks. Should patients be given a choice based on a very clear informed discussion of the trade-off between risk and benefit? Give patients the opportunity to make decisions autonomously about the risks they would be prepared to undertake**.** Otherwise this highly affected sub-group have no other options**. NICE reply:** This guideline recommends against the use of spinal fusion for people with non-specific low back pain, unless in the context of a randomised controlled trial. The GDG recognises that due to the nature of spinal fusion, the evidence is unlikely to achieve a high quality rating, and took this into account when considering the evidence and recommendations. Please note that the GDG prioritised a research recommendation on fusion as a surgical option in people with non-specific low back pain. Data from spinal registries was not used to inform this review as the GDG agreed when setting the protocol that studies design would be restricted to RCTs in the first instance, and then observational studies if there were limited evidence available, to ensure the best available evidence was used to inform the review question. Observational data was considered and used within the review, but no published analysis of registry data was identified. We are aware that it is difficult to get an accurate estimate of adverse event occurrence from clinical trial data, however this applies to all of the interventions studied in the guideline, and where adverse event data was limited, GDG expert opinion and knowledge of adverse event occurrence in clinical practice has further informed the recommendations in this area. The GDG have noted in the LETR that where fusion is carried out in the context of a randomised controlled trial, they would advise that data should be entered in spinal registries. Regarding the algorithm, the wording had now been updated. The GDG agreed that there was considerable concern regarding the risk of complications and harm, outweighing any potential benefits from the procedure. Therefore agree it is appropriate to restrict the scenarios under which spinal fusion for people with non-specific low back pain is offered to those that are part of a randomised controlled trial only.
  All patient treatment decisions would be discussed with the patient. Please see the introduction on page 4 of the short version about patient decisions, and the linked 'Your Care' web page. (p68/222)
- University Hospitals Birmingham NHS Foundation Trust: Whilst we recognise that there is no place for spinal fusion surgery in the management of non-specific lower back pain, could the GDG comment on specific lower back conditions for which spinal fusion could still be considered, for example, spondylolisthesis. Such omission creates the impression that there is no place for spinal fusion surgery at all. **NICE reply**: Other considerations paragraph') states that the GDG acknowledged there were causes of low back pain for which spinal fusion might be an appropriate treatment. These causes of low back pain, including spondylolisthesis, are beyond the scope of this guideline and

the GDG was unable to comment on them. However the reviewed evidence for non-specific low back pain showed that potential harms outweighed potential benefits and for this reason spinal fusion was recommended only in the context of a randomised controlled trial in this population. (p218/222)

Disagreement with the recommendation against

- United Kingdom Spinal Societies Board and British Orthopaedic association:
  - First paragraph, the GDG note that anterior lumbar interbody fusion is not commonly performed "due to a perceived lack of effectiveness". This statement appears supported only by the collected expert opinion, which may have been coloured by a trial against fusion **with BAK cages** which were subsequently demonstrated to have unsatisfactory results. An unmatched cohort series of 150 anterior fusions and 150 postero-lateral fusions indicated superiority of anterior fusion over instrumented postero-lateral fusion in function and return to work. **NICE reply**: The GDG was concerned about the use of **BAK cages to** achieve anterior lumbar interbody fusion in the control group of the Gornet 2011 trial. The GDG was aware that anterior procedures in the lumbar spine for back pain are not commonly performed in the UK setting, and that the BAK cages technique shows a low fusion rate and would not be considered appropriate for a stand-alone anterior fusion in clinical practice. For this reason, as most of the evidence in favour of disc replacement in the review came from the Gornet 2011 trial, the GDG wished to stress that such evidence should be regarded with caution. The comparison of different spinal fusion routes was outside the scope of the guideline.
  - The **GRADE quality rating** in surgical trials is usually low because of the inevitable risk of bias owing to the lack of blinding. The GDG may wish to consider the value of lower quality evidence in surgical studies to inform the expressed opinion**. NICE reply:** Regarding the quality rating of included studies, the protocol for this, and all intervention reviews in the guideline included both RCTs and observational studies where RCT evidence was lacking. In this review 2 cohort studies were included. GRADE quality rating informs the overall confidence in the evidence due to factors including risk of bias, and therefore ratings for outcomes where blinding is more problematic are still downgraded. It is noted that double blinded trials are less common in surgery, however this is also true of other interventions included in the guideline and the approach to evidence quality appraisal and consideration is consistent as stated in the methods, section 4.3.2.
  - The GDG expressed concern over the risk of **patient harm** from surgical intervention and quote figures from one study with 80 participants in the disc replacement arm, noting that it was not powered to detect harm. This imprecision must be in both directions however, the risk of an excess of serious complications by chance in a small group is higher. Many of the studies referred to by the GDG were included in the systemic review by Wei in 2013 (10). This systemic review examined the reported complications in five randomised controlled trials comprising of 1081 total disc replacement operations. The complication rate reported was 5.8 percent and in the 500 fusion patients of the same trials, the complication rate was 10.8 percent. In this review the re-operation rate was 5.2 percent for total disc replacement and six percent for spinal fusion. It is acknowledged that spinal surgery is a major intervention and will carry a significantly greater risk of patient harm than conservative management. These data were considered in the original NICE guidance IP 306. It is suggested that the GDG may wish to re-consider their presentation and evaluation of the risk of complications. **NICE reply**: The GDG were aware of the Hellum 2011 study, which reported the serious adverse events related with disc replacement, in particular 1 lower leg amputation and 4 cases of considerable blood loss out of 80 participants. It was the GDG concern that this was a high rate of adverse events in a study not powered to detect harm, but believed that this high adverse event rate was reflective of the risks observed in practice. This is detailed in the LETR (section 26.6). Wei et al (2013) was not included in our review as all primary studies included in the systematic review were available and included in this review. Some of the included studies were conducted in populations that were not relevant to our review protocol, however the relevant studies were included and did inform the recommendation. (p112/222)

Treatment before

- Society for Back Pain Research: The national back pain pathway (aligned with CG88) recommend referral for consideration of spinal fusion after patients have completed a combined physical and psychological programme. There is no RCT data on this subgroup to inform effectiveness post CPPP. **NICE reply**: The algorithm included in the guideline has been edited to include a statement to say that if an inadequate response to treatment has been observed, there should be a consideration as to whether every appropriate treatment above has been explored and the risks and benefits of ongoing treatment.. (p68/222)
- United Kingdom Spinal Societies Board and British Orthopaedic association: It is clear that any form of spinal surgery for axial lumbar spine pain is a much larger intervention with significant risk of complications. As such it is appropriate that spinal fusion should be considered only after an inadequate response to an appropriate NBR (CPPP). No answer from NICE. (p128/222)

Appropriate imaging

- Medtronic: We ask you to consider that appropriate imaging is required to attribute a diagnosis of specific versus non-specific low back pain**. NICE reply:** As detailed in the Introduction (chapter 2), this guideline only covers non-specific low back pain, and excludes the evaluation of serious spinal pathology. The clinical and cost effectiveness of imaging to improve functional disability, pain or psychological distress in people with low back pain and/or sciatica has been reviewed in chapter 7. (p125/222)

Multidisciplinary team

- NHS England: Multi-disciplinary Team review is accepted as good clinical practice and the GDG is asked to consider adding this to their recommendation. Quality RCTs in this area are unlikely to gain ethical approval as a double blind situation requiring sham surgery will probably not be approved. There is good evidence that observational studies from prospectively collected Register data give comparable results to RCTs. A suggestion is to change the recommendation in "'Do not offer spinal fusion for people with non-specific low back pain unless the patient has been discussed at a Spinal MDT meeting and prospective diagnostic, operative, complications and patient reported outcome and experience measures entered into a suitable Registry such as the British Spine Registry . **NICE reply:** We are unable to specify this in a recommendation however we have added a statement to the 'evidence and link to recommendations' section of the review to state that the GDG suggest where fusion is carried out in the context of a randomised controlled trial, data should be entered in spinal registries. It is noted in the 'evidence and link to recommendations' table that there are causes of low back pain for which spinal fusion might be an appropriate treatment, however these are beyond the scope of this guideline. (p125/222)

Patient' choice

- United Kingdom Spinal Societies Board and British Orthopaedic association: All health care delivery is patient centred and is undertaken in partnership with the patient themselves. It is perhaps inappropriate that the choice of an effective treatment should be denied to patients without their involvement. The uptake of a surgical option after full and open discussion of potential benefits and potential risks is a decision which should be made by patients. It is requested that the GDG consider whether patient choice should take a higher priority. **NICE reply:** It is done in Introduction p4 short version and the link "Your Care' web page".(p128/222)

Research recommendation: Problems with the trial

- United Kingdom Spinal Societies Board and British Orthopaedic association: The GDG recommend "a large multi-centre randomised trial with sufficient power to answer these important questions". It is inherent in the design of trial between surgical and non-surgical care that there can be no blinding of the patient or of the investigator. This risk of bias cannot be eliminated as the undertaking of sham surgery under general anaesthesia is outside the ethical compass. This will inevitably result in a low GRADE evaluation for randomised surgical trials**.** The GDG also suggest within the trial investigating possible predictors of response. It is clear that the trial size would be significantly larger than the Oxford Stabilisation Trial (Fairbank et al). The Fairbank study came under the auspices of the MRC, cost £1.8 million and took 9 years. The study included 349 subjects and achieved a GRADE quality rating of low due to risk of bias. As the risk of bias cannot be eliminated it seems extremely unlikely that funding could be obtained for any such further study and indeed it would appear difficult to justify such a use of research resources. **NICE reply**: The GDG believe that a good quality trial can be undertaken in surgery and the difficulties of blinding should not be an obstacle to such trials being undertaken. The review of the evidence did not suggest that this should be routinely considered on the NHS. As detailed in section 4.5.1 of the Methods chapter, when areas were identified for which good evidence was lacking, the GDG considered making recommendations for future research. The GDG is unable to comment about the funding of further trials, but the feasibility is considered in the writing of the research recommendation. Based on the evidence reviewed, showing no consistent benefit of spinal fusion over comparator treatments and potential harm, the GDG agreed it was appropriate to recommend against the use of spinal fusion for non-specific low back pain unless as part of a randomised controlled trial. (p130/222)

Registry instead of RCTs for the research recommendation

- Society for Back Pain Research: The concern is the complication rate (Given the limitations of the RCT literature it would be appropriate to seek clarification on the complication rate from the spine registries. (Swedish Spine registry (www.4s.nu), Spine Tango and the British Spine Registry). It is highly likely that the complication rate will be lower in specialist spine centres; given the importance of this It is worthy of GDG to revisit and consider prospective cohorts, the registry data is closest to this. **NICE reply**: The GDG discussed the wording of the recommendation, however agreed that there was considerable concern regarding the risk of complications and harm from this procedure, and therefore agree it is appropriate to restrict the scenarios under which spinal fusion for people with non-specific low back pain is offered to those that are part of a randomised controlled trial only. It was noted that at present in the UK submission to registries is voluntary, although this is in the process of changing. However, the GDG considered that at the present time being part of a registry would not reduce the concerns regarding risk of complications. It is noted in the 'evidence and link to recommendations' table that there are causes of low back pain for which spinal fusion might be an appropriate treatment, however these are beyond the scope of this guideline.(p68/222)

- United Kingdom Spinal Societies Board and British Orthopaedic association: It is plain that the risk of complications is potentially correlated with the experience of the surgeon and of the system. Lumbar fusion is a specialist procedure. The potential for complications might be addressed by performing such surgery only under the auspices of a specialist spinal surgeon. All specialised spinal surgery is now mandated to be entered on the British Spine Registry. In addition the entry of lumbar spinal fusion into the British Spine Registry would provide a thorough evaluation of the outcomes, the important predictive factors, the complications and the cost effectiveness of the procedure. With the increasing evidence for the utility of registries, this might meet the requirement for further evaluation and research in an effective but achievable manner. The GDG may wish to consider whether improved safeguards and the improved audit, research and governance which is available through the registry might be sufficient reason to modify the recommendation and allow patient choice. **NICE reply:** Regarding registry, we are unable to make a recommendation that data should be submitted to a registry, but have added a statement to the 'evidence and link to recommendations' section to state that the GDG suggest if done within an RCT data should be submitted to a registry. The GDG is unable to comment about how changes in audit and governance may affect the outcomes of surgery.(p130/222)
- Guy's and St. Thomas NHS Foundation: We agree that fusion for purely non specific LBP should not be recommended within any standard management pathway. Within our organization, at a specialist level, coexisting pathologies like degenerative listhesis and or incidental stenosis are often present in fusion cases and are therefore outside the scope of this guidance**. NICE reply:** We have included a statement in the 'evidence and link to recommendations' sections of the relevant chapters to highlight that when surgical procedures are undertaken, information should be submitted to a registry. (p190/222)

Cost

- Medtronic: Non-specific back pain affects a large number of individuals in UK. The condition has a huge cost to the individual, society and the country's economy. Over the past 2 decades, increasing numbers of procedures have been proposed for the surgical management of LBP. These include but are not limited to surgical fixation with internal metal-work applied from the back, front, side or any combination of the three routes. The costs of these operations have escalated and with the advent of minimally invasive approaches more of the operations are performed with uncertain benefit. As well as the monetary cost, there are complications associated with the surgical approaches with some studies reporting around 20% complication rate in the short to medium term. We agree that the overall number of operations have increased due to the ageing population and this will have a financial impact however we question whether minimally invasive procedures, which are performed in a limited number of centres, are having a significant impact on the escalating costs or overall increase in operations. This sentence also seems to allude that the benefit is more uncertain with minimally invasive procedures. We ask you to consider that literature shows that mid-term benefits are the same when comparing open fusion surgery to minimally invasive fusion with fewer perioperative complications in favour of the minimally invasive technique. **NICE reply**: The paragraph has now been edited as follows: 'The costs of these operations have escalated, and as well as the monetary cost, there are complications associated with the surgical approaches with some studies reporting around 20% complication rate in the short to medium term'.

NICE changes in the final version of the guideline (November 2016)

In the chapter Clinical evidence, a sentence was added:

One Cochrane review was identified but was not included as the stratification of the people with low back pain, low back pain with/without sciatica and sciatica was unclear, however the study included were individually assessed and included in this review if they matched the review protocol.

In other considerations, a sentence was added and a part of another removed:

~~however for non-specific low back pain the evidence of benefit was outweighed by the potential harms.~~

The GDG noted that if spinal fusion was being undertaken, patient outcome information should be submitted to a national registry.

In other consideration, research recommendation,

"The costs of these operations have escalated and with the advent of minimally invasive approaches more of the operations are performed with uncertain benefit. As well as the monetary cost, there are complications associated with the surgical approaches with some studies reporting around 20% complication rate in the short to medium term." Have been replaced by "The costs of these operations have escalated, and as well as the monetary cost, there are complications associated with the surgical approaches with some studies reporting around 20% complication rate in the short to medium term".

NICE final recommendations on spinal fusion(November 2016)
40. Do not offer spinal fusion for people with low back pain unless as part of a randomised controlled trial.
R5. Should people with low back pain be offered spinal fusion as a surgical option?

Belgian GDG comments during the GDG meeting on the 14th December 2016
NICE recommendation 40: Do not offer spinal fusion for people with non-specific low back pain unless as part of a randomised controlled trial.

- In the final version of the NICE guideline, "non-specific" has been removed.
- For some patient groups, spinal fusion could be an option. But this concerns very few patients. And it is not easy to define the LBP patients in which surgery will be useful. A multidisciplinary consultation would be necessary before taking the decision.
- Surgery might also be proposed after a conservative management.
- The restriction of only as part of a randomised controlled trial would not help these small patient subgroups, for whom no RCT will be set up.
- The GDG members agree that a register is more feasible than a RCT and that a multidisciplinary consultation should precede the decision to offer spinal fusion.
- Therefore it is proposed to specify the conditions in which spinal fusion can be offered and to prefer register instead of RCT.

⇨ **The NICE recommendation 40 has been accepted with following changes:**
⇨ **"***Do not offer spinal fusion for people with low back pain unless within following preconditions*
- *after failure of a non-surgical evidence-based multimodal management and*
- *after evaluation in a multidisciplinary consultation and*
- *preferably with data registration in a register*

NICE research recommendation 5: Should individuals with non-specific low back pain be offered spinal fusion as a surgical option?

- In the final version of the NICE guideline, "non-specific" has been removed.
- Since the Belgian GDG members prefer a register instead of a RCT, this research recommendation could be interpreted as the analysis of this register.
- Moreover the GDG members are more interested which patients could benefit from this surgery.
- The GDG members agree on the research recommendation 5 but with following modification: "Based on an analysis of the register of patients who underwent spinal fusion, in which patient subgroups spinal fusion could be offered as a surgical option?"

⇨ **The NICE research recommendation 5 has been changed in:**
⇨ *"In which patient subgroups spinal fusion could be offered as a surgical option?"*

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017. No comments

KCE 2017 final recommendations on spinal fusion (February 2017)
23. Do not offer spinal fusion for people with low back pain unless within following preconditions
• after failure of a non-surgical evidence-based multimodal management, and
• after evaluation in a multidisciplinary consultation and
• preferably with data registration in a register
(strong recommendation based on low to very low evidence from RCTs & cohort studies)

7.21. Spinal decompression for radicular pain

Spinal decompression in patients with radicular pain

NICE search question
"What is the clinical and cost-effectiveness of spinal decompression in people with sciatica?"

Introduction based on the draft version of NICE guideline (March 2016)

- Spinal decompression refers to removal of pressure from the nervous structures within the spinal column. This circumferential structure consists of vertebral body, disc and ligaments at the front, facet joints and foramen at the sides, and the lamina and ligaments at the back. Compression may be due to an abnormality of any of these structures and their removal results in spinal decompression. An example of spinal decompression, laminectomy, is the removal of the lamina either unilaterally (hemi-laminectomy) or bilaterally, which is usually accompanied by the removal of the attached yellow ligament (*ligamentum flavum*). This can also include enlarging the foramen (foraminotomy) or undercutting facetectomy (trimming of the overgrown facets) and/or discectomy. The ultimate aim is to make more room for the neural elements.
- The most common cause of the narrowing of the spinal canal is degenerative lumbar disease otherwise known as spondylosis. The symptoms associated with degenerative lumbar disease are leg symptoms (often pain, but also numbness and weakness) usually made worse by prolonged standing and walking. This is known as neurogenic claudication. At a very late stage of the condition people can develop bladder and bowel incontinence. In contrast to this, disc prolapse usually causes leg pain and sciatica. These 2 conditions often coexist in people suffering from back pain.
- There have been several advances in the techniques of laminectomy and discectomy. With the improvements in optics and illumination, surgical loops, microscopes and endoscopes, the procedures are thought to be less invasive. There has also been the introduction of different methods of removing disc material including laser, thermo-coagulation radiofrequency and many others. Despite controversy surrounding the best method for discectomy, we have not reviewed the comparative effectiveness of these methods and suggest that this be determined by the individual surgeon and by clinical appropriateness.

PICO used by NICE (March 2016)

Population	• People aged 16 or above with sciatica • Populations with neurogenic claudication causing leg pain will be included
Intervention(s)	• Spinal decompression 1. Laminectomy 2. Discectomy
Comparison(s)	• Usual care • Other treatment (interventions listed in our guideline review protocols)
Outcomes	**Critical** • Health-related quality of life (for example, SF-12, SF-36 or EQ-5D). • Pain severity (for example, visual analogue scale [VAS] or numeric rating scale [NRS]). • Function (for example, the Roland Morris Disability Questionnaire or the Oswestry disability index). • Psychological distress (HADS, GHQ, BDI, STAI) **Important** • Responder criteria (>30% improvement in pain or function)

	• Adverse events: morbidity; mortality. • Revision rate • Failure rate • Healthcare utilisation (prescribing, investigations, hospitalisation or health professional visit) Outcomes to be recorded at: o Short term (≤4 months) (8 weeks to 4 months) o Long-term: - > 4 months (4 months to 1 year) for all outcomes - 1-2 years for critical outcomes - 0-10 years for failure rates and revision rates (recurrence / repeat surgery at adjacent segments or at the same segment, will be reported narratively only, for GDG

Literature quoted by NICE 2016 guideline (March 2016)

- **Nine randomised controlled trials and 4 cohort studies were included in the review.** The search was extended to cohort studies for comparisons where there was insufficient evidence 4 (specific forms of decompression versus a valid comparator) and 4 further studies were included 5 (published in 6 papers). Four technics were analysed with different comparators: discectomy versus usual care (2 RCTs and 2 cohort studies), discectomy versus combined intervention (4 RCTs), discectomy versus fusion (1 cohort study); Percutaneous disc decompression versus usual care (1 RCT); plasma disc decompression versus other treatment (epidural steroid injection) (1 RCT) and laminectomy versus usual care (1 RCT and 1 cohort study).

Discectomy (see Table 49)

- **Discectomy versus usual care**
  - **Randomised trials** (Peul 2007 - usual care: conservative treatment to resume daily activities; and Weinstein 2006 - usual care: active physical therapy, education, NSAIDs): At short term (<4mo), clinical benefit in **QOL** for discectomy was demonstrated in the SF-36 0-100 domains of bodily pain, physical function (2 RCTs; very low quality; n=696), mental health, vitality and general health (1 RCT; low quality; n=281) (no difference in the three other subdomains). QoL measured with the EQ-5D 0-1 showed a clinical benefit in favour of discectomy (1 RCT; low quality; n=283). At long term (4mo-1y), no clinical difference was found in the SF-36 0-100 subdomains of physical function, emotional role and mental health (a clinical benefit in the 5 other subdomains) (2 RCTs; low to very low quality; n=696-281). Also no clinical difference was measured with the EQ-5D 0-1 (1 RCT; low quality; n=283). At 2 years, only the results were reported for bodily pain, indicating a clinical benefit in favour of discectomy and for physical function, in which no clinical difference was found (SF-36 0-100; 1 RCT; very low quality; n=373). A short term (<4months) clinical benefit was seen in leg and back **pain** in the discectomy group, but at long term (1y and 2y) no clinical difference was anymore seen between discectomy and usual care (VAS 0-10; 2 RCTs, low to very low quality; n=333-50). Pain measured with the sciatica bothersomeness index 0-24 showed no clinical difference at any time point (1 RCT; very low quality; n=409-373). One RCT showed a clinical benefit in number of patients who reported a complete or nearly complete disappearance of symptoms in the discectomy group (**responder criteria**) both at short term and at long term (1 RCT; low quality; n=281). Only a short term clinical benefit in **function**, measured by RMDQ 0-24, for discectomy was seen (1 RCT; low quality; n=281). Assessment with ODI O-100 (2 RCTs; low quality; n=467) or assessments at long term by either scale showed no clinical differences. No differences were found in number of patients with additional physical therapy visits (**healthcare utilisation**) (at 2y; 1 RCT; very low quality; n=50).
  - **Cohort study** (Weinstein 2006 – usual care: active physical therapy, education, NSAIDs): A cohort study reported two subdomains of the **QoL** SF-36 0-100, showing a clinical benefit in bodily pain and in physical function in favour of discectomy at any time point (very low quality; n=656-621). Also for leg and back **pain** a clinical benefit in favour of discectomy was reported (sciatica bothersomeness index 0-24; 1 study; very low quality; n=656 and back pain bothersomeness 0-6; 1 study; very low quality; n=1191) at short term and at 1y, only at 2y no clinical difference was anymore found for back pain. A clinical benefit in **function**

favouring discectomy was found at any time point (ODI 0-100; 1 study; very low quality; n=656-621). A higher number of patients with more reported diagnostic test use was found in the discectomy group (1 study; low quality; n=1191), but no differences were found in the other measures of **healthcare utilisation** (number of patients with additional physical therapy visits, number of patients with reported healthcare visits and medication use) (1 study; very low quality; n=1191).
    - Not reported outcomes: psychological distress, healthcare utilisation
- **Discectomy versus combined intervention (manual therapy + biomechanical exercise + self-management)**
    - Conflicting evidence from 1 RCT for **QoL** at short term (<4mo): clinical benefit for discectomy was found for the subdomains of bodily pain, vitality, physical function and general health but clinical harm for discectomy for the domains of physical role, emotional role and social function and no difference for the subdomain mental health (SF-36 0-100; low to very low quality; n=40). No clinical difference was found for **pain** (McGill 0-78; 1 RCT; low quality; n=40) and **function** (RMDQ 0-24; 1 RCT; low quality; n=40). No long term data were presented for the reported outcomes.
    - Not reported outcomes: revision rate, healthcare utilisation, responder criteria
- **Discectomy versus fusion**
    - A single cohort study reported no clinical difference at long term (1y) in **function** (ODI 0-100; very low quality; n=55) and in **revision rate** between discectomy and fusion (very low quality; n=55). No short term data were reported.
    - Not reported outcomes: QoL, pain, psychological distress, healthcare utilisation, adverse events, failure rate, responder criteria

Table 49 – Clinical effectiveness of discectomy in patients with sciatica

Discectomy in patients with sciatica				
Outcomes	**Discectomy versus usual care (RCTs)**	**Discectomy versus usual care (cohort studies)**	**Discectomy versus combined intervention (manual therapy + biomechanical exercise + self-management)**	**Discectomy versus fusion (cohort studies)**
QoL	At short term (<4mo): • **SF-36 0-100: No diff in 3 of 8 domains** (2 RCTs; low to very low; n=690-281) • **EQ-5D 0-1: CIB favouring discectomy** (1 RCT; low; n=283) At long term (4mo-1y): • **SF-36 0-100: No diff in 3 of 8 domains** (2 RCTs; low to very low; n=696-281) • **EQ-5D 0-1: no diff** (1 RCT; low; n=283)	At short term (<4mo): • **SF-36 0-100 bodily pain: CIB favouring discectomy** (1 RCT; very low; n=656) • **SF-36 0-100 physical functioning: CIB favouring discectomy** (1 RCT; very low; n=656) At long term (4mo-1y): • **SF-36 0-100 bodily pain: CIB favouring discectomy** (1 study; very low; n=631) • **SF-36 0-100 physical functioning: CIB favouring discectomy** (1 study; very low; n=631)	At short term (<4mo): • **SF-36 0-100: conflicting results** o **CIB favouring discectomy in subdomains bodily pain, vitality, physical function, general health** o **CIB favouring combined intervention in physical role, emotional role, social function** o **No diff in mental health** (1 RCT; low to very low; n=40) At long term: Not reported	

	At long term (2y): • **SF-36 0-100: CIB favouring discectomy in subdomain bodily pain, no diff in subdomain physical function** (1 RCT; very low; n=373) (only 2 subdomains reported)	At long term (2y): • **SF-36 0-100 bodily pain: CIB favouring discectomy** (1 RCT; very low; n=621) • **SF-36 0-100 physical functioning: CIB favouring discectomy** (1 RCT; very low; n=621)		
Pain	At short term (<4mo): • **Leg pain VAS 0-10: CIB favouring discectomy** (2 RCTs; very low; n=333) • **Back pain VAS 0-10: CIB favouring discectomy** (2 RCTs; low; n=333) • **Sciatica bothersomeness index 0-24: no diff** (1 RCT; very low; n=409) At long term (4mo-1y): • **Leg pain VAS 0-10: no diff** (2 RCTs; low; n=333) • **Back pain VAS 0-10: no diff** (2 RCTs; low; n=332) • **Sciatica bothersomeness index 0-24: no diff** (1 RCT; low; n=413) At long term (2y): • **Leg pain VAS 0-10: no diff** (1 RCT; very low; n=50) • **Back pain VAS 0-10: no diff** (1 RCT; very low; n=50) • **Sciatica bothersomeness index 0-24: no diff** (1 RCT; low; n=373)	At short term (<4mo): • **Sciatica bothersomeness index 0-24: CIB favouring discectomy** (1 study; very low; n=656) • **Back pain bothersomeness 0-6: CIB favouring discectomy** (1 study; very low; n=1191) At long term (4mo-1y): • **Sciatica bothersomeness index 0-24: CIB favouring discectomy** (1 study; very low; n=631) • **Back pain bothersomeness 0-6: CIB favouring discectomy** (1 study; very low; n=1191) At long term (2y): • **Sciatica bothersomeness index 0-24: CIB favouring discectomy** (1 study; very low; n=621) • **Back pain bothersomeness 0-6: no diff** (1 study; very low; n=1191)	At short term (<4mo): • **McGill 0-78: no diff** (1 RCT; low; n=40) At long term: Not reported	

Function	At short term (<4mo): • **RMDQ 0-24 (final score): CIB favouring discectomy** (1 RCT; low; n=281) • **ODI 0-100 (change score): no diff** (2 RCTs; low; n=461) At long term (4mo-1y): • **RMDQ 0-24 (final score): no diff** (1 RCT; low; n=281) • **ODI 0-100 (change score): no diff** (2 RCTs; low; n=467) At long term (2y): • **ODI 0-100 (change score): no diff** (2 RCTs; low; n=423)	At short term (<4mo): • **ODI 0-100: CIB favouring discectomy** (1 study; very low; n=656) At long term (4mo-1y): • **ODI 0-100: CIB favouring discectomy** (1 study; very low; n=631) At long term (2y): • **ODI 0-100: CIB favouring discectomy** (1 study; very low; n=621)	At short term (<4mo): • **RMDQ 0-24: no diff** (1 RCT; low; n=40) At long term: Not reported	At short term (<4mo): Not reported At long term (4mo-1y): • **ODI 0-100: no diff** (1 study; very low; n=55)
Revision rate				At short term (<4mo): Not reported At long term (2y): • **Revision surgery: no diff** (1 study; very low; n=55)
Healthcare utilisation	At short term (<4mo): Not reported At long term (2y): • **Number of patn with additional physical therapy visits: no diff** (1 RCT; very low; n=50)	At short term (<4mo): Not reported At long term (2y): • **Number of patn with more reported diagnostic test use: CIB favouring UC** (1 RCT; low; n=1191) • **Number of patn with additional physical therapy visits: no diff** (1 RCT; very low; n=1191) • **Number of patn with reported healthcare visits: no diff**		

		(1 RCT; very low; n=1191) • **Medication use: no diff** (1 RCT; very low; n=1191)		
Responder criteria	At short term (<4mo): • **(nearly) complete disappearance of symptoms: CIB favouring discectomy** (1 RCT; low; n=281) At long term (>4mo): • **(nearly) complete disappearance of symptoms: CIB favouring discectomy** (1 RCT; very low; n=281)			

CIB: clinically important benefit

Disc decompression

- **Percutaneous disc decompression versus usual care (conservative therapy of analgesics, NSAIDs, muscle relaxants, physiotherapy, education)**
  - A single RCT reported only results for the **pain** outcome: a clinical benefit in leg pain was found at short term (<4months) and at long term (1y and at 2y) in favour of the percutaneous disc decompression (NVS 0-10; low to very low quality; n=62).
  - Not reported outcomes: QoL, function, psychological distress, responder criteria, adverse events, revision rate, failure rate, healthcare utilisation
- **Plasma disc decompression versus other treatment (epidural steroid injection)**
  - A single RCT compared plasma disc decompression to epidural steroid injection and found a clinical benefit in leg and back **pain** (VAS 0-10; 1 RCT; low to moderate quality; n=85) at both short term (3 months) and long term (6 months) in favour of the plasma disc decompression. However, there was no clinical difference in **function** at any time point (low to moderate quality; n=85) or in procedure related **adverse events** (at 6 months; very low quality; n=55).
  - Not reported outcomes: QoL, psychological distress, responder criteria, revision rate, failure rate, healthcare utilisation

Laminectomy

- **Laminectomy versus usual care (active physical therapy, education, NSAIDs)**
  - **Randomised trial** (Weinstein 2008): Conflicting evidence from 1 RCT for **QOL** showed for bodily pain no clinical difference at short term, however at long term a clinical benefit was found in favour of laminectomy (at 1 y and ta 2y; 1 RCT; low quality; n=246). In the contrary, for the SF-36 0-100 submain of physical function a short term clinical benefit in favour of usual care was found and no differences at long term (1 RCT; low quality; n=246). No differences for **pain** (both leg and back pain) (low back pain bothersomeness index 0-24; sciatica bothersomeness index 0-24; 1 RCT; low quality; n=246-221) and for **function** (ODI 0-100; 1 RCT; low quality; n=251-221) were found at any time point.
  - **Cohort study** (Weinstein 2008): The combined cohort-RCT study showed a clinical benefit in **QoL** (for subdomains of bodily pain and physical function) (SF-30 0-100; very low quality; n=691-448) and **function** both at short and long term in favour of laminectomy (ODI 0-100; 1 study; very low quality; n=691-532). For **pain**, only a clinical benefit in favour of laminectomy was found for back pain (Back pain bothersomeness index 0-24; 1 study; low to very low quality; n=691-532). For the

other time points (short term and at 2y) and for leg pain at any time point, no differences could be found between laminectomy and usual care (sciatica bothersomeness index 0-24; 1 study; very low quality; n=691-533).

- **Not reported outcomes:** psychological distress, responder criteria, adverse events, revision rate, failure rate, healthcare utilisation

Economic evidence

- Three economic evaluations were identified on the comparison of laminectomy versus usual care (Tosteson 2008 (USA), Tosteson 2008a (USA), Van den Hout 2008 (NL)):
  - The studies from the USA reported a higher incremental cost for surgery compared to the study conducted in the Netherlands. The unit cost of surgery used in the USA study was $12,754 for surgery with no complications, which is equal to £8,071 using the purchasing power parities. This figure is very high compared to the cost reported in the NHS Reference Cost (£3,582) for the HRG code HC04F – Extradural Spine Intermediate 1, which includes spinal decompression surgery. If a lower cost estimate for surgery was used in the analysis, the estimated ICER would be lower too.
  - The three cost–utility analyses found that spinal decompression was not cost-effective compared to usual care treating patients with disc herniation or spinal stenosis. These analyses were assessed as partially applicable with potentially serious limitations.

NICE GDG considerations (March 2016)

- **Relative values of different outcomes:**
  - Critical outcomes were health-related QoL, pain severity, function, psychological distress
  - Important outcome were responder criteria for pain and function, adverse events, revision rate, failure rate and healthcare utilisation
  - No evidence was found for psychological distress and failure rate. The GDG felt there was sufficient evidence for all of the outcomes that were considered important for this review.
- **Trade-off between clinical benefits and harms**
  - **Discectomy versus usual care:** Overall, the evidence suggested a clinical benefit in favour of discectomy when performed in people with sciatica due to a herniated intervertebral disc for quality of life assessed by the SF-36 (in 5 of the 8 subdomains) in the short term. This benefit was also supported by EQ-5D data at the short term follow-up. Some benefit for discectomy was also seen at the long term follow up of 1 year in 5 of the 8 SF-36 domains as well. As with quality of life data, clinical benefit favouring discectomy was observed for both back and leg pain in the short term. The GDG noted that although the benefits were maintained in the long term, the between group difference was not. The GDG noted that sciatic symptoms usually improve over the course of the first 3 months in the majority of people without treatment but this **evidence suggested people undergoing discectomy improve quicker**. The GDG agreed that in some individuals the pain severity may warrant an earlier intervention. In terms of function, the randomised evidence showed no difference between treatments, although the non-randomised data suggested a clinically important difference favouring discectomy in both the short and long term. In terms of healthcare utilisation, there was no evidence for a difference other than a suggestion that more diagnostic tests were required in those undergoing discectomy; however the GDG agreed that this did not outweigh the possible short term benefits observed. The group noted that **discectomy was a relatively safe procedure**, and that the most common surgical complication in the discectomy group was a dural tear. The GDG thought this could possibly increase hospital length of stay, and that a tear may result in CNS infection. Reoperation rates were low with discectomy, and mainly due to recurrent disc herniation. The GDG noted that re-operations may not be considered as adverse events following surgery, but may be a natural history of the condition, since about 5% of patients will suffer from a recurrence of disc prolapse. The GDG noted that there was a **high rate of cross-over** from the control group arm into the discectomy group in the included trials, and those that crossed over had high pain scores post usual care treatment. Results were usually reported as intention to treat analysis and therefore the effects seen in the usual care group may have been over-estimated. This was noted as an inevitable consequence of surgical trials that do not utilise a placebo control. If cross-over isn't offered as an option in a trial, a high drop-out rate from the usual care arm would also be expected. It was also considered that had the people who crossed over to receive discectomy been removed from the analysis, the effect size in favour of discectomy would likely have been larger than observed, though the GDG recognised that this introduces a risk of bias. There was also concern raised about the uncertainty surrounding the amount of physiotherapy sessions received by the treatment groups in 1 study. It was unclear if this treatment was offered at baseline or as additional sessions. Equally, It was not possible to establish whether the proportion of patients referred

for additional physiotherapy was the same in the discectomy and the control groups. The GDG felt this could have affected the outcomes of pain and function reported and therefore did not have much confidence in the effects reported. The GDG agreed that although there was **concern about the reliability of the evidence** due to a high cross-over rate, the cross-over of patients was more predominant in 1 arm of the trial (from the usual care group to surgery), and occurred mostly after the short term outcome data was collected. This gave the GDG some confidence in the results reported as the benefit seen in the discectomy group would have been even larger had the usual care cross-over patients not been considered in this arm. However as this very low quality evidence was from a single trial with a small sample size, it did not contribute significantly to informing the recommendation.

- **Discectomy versus combined intervention (manual therapy + biomechanical exercise + self-management):** Contrasting results were seen amongst the individual domains of quality of life in the short term. There were no obvious baseline differences between the arms for these domains that may have explained this. Evidence for pain and function showed no clinically important difference between the 2 groups. The GDG noted that the study reported baseline pain scores and the "present pain intensity" values separately with 2 values for each group varying significantly from each other. The present pain intensity scores were reported to be ~2.5 for both the discectomy and combination treatment groups (baseline McGill scores were reported as ~30). The GDG considered this to be an anomaly and therefore interpreted the results with caution.
- **Percutaneous disc decompression versus usual care:** The evidence showed a clinically important difference favouring percutaneous disc decompression for the outcome of pain in both the short term (≤ 4 months) and long term (> 4 months; at both 1 year and 2 year follow up). However as this finding came from a single, low quality study with a small sample size, the GDG could not be confident enough to make a recommendation based on this limited evidence.
- **Plasma disc decompression versus epidural steroid injection:** A clinical benefit in pain favouring decompression was reported for both leg and back pain in the short term and long term. However, no clinically important difference between treatments was seen in function at either time-point. The GDG noted that 1 of the criteria for inclusion in the trial was that the participants had to have failed a previous epidural injection for the same symptoms between 3 weeks to 6 months previously. They considered this to be **a serious flaw of the trial**, which lowered their confidence in the evidence reported. When weighing up the balance between benefits and harms, the GDG considered the adverse events associated with plasma decompression. The evidence showed that there was no clinically important difference in adverse events reported between the 2 treatment groups. The group felt that the **majority of adverse events reported were not a cause for concern**, except possibly increased weakness seen in the decompression group. However, as this was a single event and there was no additional information provided; the GDG could not derive conclusive evidence of harm from the study.
- **Discectomy versus fusion:** The GDG discussed that the majority of the evidence was in favour of discectomy in terms of quality of life and pain in the short term, however these effects were not always maintained at long term followed up. The evidence also showed no clinically important difference between the 2 surgical treatments for function (assessed by ODI) in the long term.
- **Summary:** The GDG considered that discectomy for people suffering from sciatica offered a **good prognosis** and was **successful in providing long-term pain relief**. However, they also noted that sciatic symptoms tend to improve naturally with time without treatment. Despite the good long term prognosis with or without treatment, the GDG felt that earlier symptom resolution with **surgical intervention should be an option for people**. It was agreed that there was sufficient evidence to suggest that discectomy should be considered for a **subgroup of people with sciatica who had failed to respond to conservative management of their symptoms**.

- **Trade-off between net clinical effects and costs**
  - Three cost-utility analyses were identified for comparison of spinal decompression versus usual care, all concluding that it is not cost effective in the base case.
  - The USA studies were based on both randomised and observational cohorts of the SPORT trial; in the first study the population was adults with a diagnosis of intervertebral disc herniation, while in the second the population was adults with spinal stenosis without degenerative spondylolisthesis (the study presented results separately for people with and without degenerative spondylolisthesis but we only focused on the latter). In both studies surgery was **more effective but more costly** than usual care with a resulting ICER of more than £40,000 per QALY. In the second study, a probabilistic sensitivity analysis resulted in 95% confidence interval around the ICER of £31,617 to £66,191 per QALY gained.
  - The third study was a within-trial analysis (associated clinical paper Peul 2008) conducted in the Netherlands on a population with disc herniation and lumbosacral radicular syndrome where early micro-discectomy was compared to prolonged conservative care provided by the GP followed by surgery if sciatica persisted at 6

months. However, people in the conservative care group could also receive surgery earlier than 6 months if they had increasing leg pain that was not responsive to drugs and progressive neurological deficit. Again, in this study surgery was more effective but more costly than usual care, with an ICER of £31,932 per QALY gained. The 95% confidence interval around the ICER was £10,817 to £332,249 per QALY gained.

- It was noted that in the first 2 studies conducted in the USA the cost of surgery was significantly higher compared to the cost reported in the study from the Netherlands. The unit cost of surgery in the USA studies (£8,071) was also compared to the NHS Reference cost of spinal decompression surgery in the UK (£3,582). Conducting a simple threshold analysis using the intervention cost of £3,582 reported in the NHS Reference Cost; spinal decompression surgery would need to generate at least an additional 0.179 QALYs compared to no surgery for it to be considered cost effective at the £20,000 per QALY threshold. The observed QALY gain in the USA studies was 0.21 and 0.17. However, in the European study, the effectiveness was much lower compared to the USA studies (0.044 QALYs). The GDG discussed this evidence and concluded that this could be due to a high cross-over between arms in this study: during the first year surgery was performed in 89% of patients in the early surgery group and 40% of the prolonged conservative care group. If the effectiveness was similar to that reported in the USA studies then spinal decompression is likely to be cost-effective.
- The GDG concluded that there was a **high uncertainty around the conclusions of the economic studies** as the cost of surgery is overestimated in the USA studies and the effectiveness is likely to be underestimated in the European study. **Therefore overall the GDG concluded that decompression surgery is likely to be cost effective in patients with sciatica when other treatments have failed.**

- **Quality of evidence**
  - Evidence from 9 RCTS and 4 cohort studies, quality ranged from low to very low, mainly downgraded for high risk of bias due to lack of appropriate blinding.
  - The non-randomised evidence was rated as very low quality, due to inherent selection bias in non-randomised studies as well as a lack of appropriate blinding. This meant it was considered to be at serious risk of bias and therefore the group placed low confidence in the effects reported.
- **Other considerations**
  - The issue regarding **optimal time to offer spinal decompression** to patients was discussed. Whilst the GDG agreed that in the majority of cases, sciatic symptoms would improve naturally with time, they recognised that the option for earlier pain relief should be available for a **subset of patients that suffer from severe, acute sciatic pain**. The group agreed that surgical intervention following a period of conservative management for **around 6 weeks** would be reasonable. However, it was noted that there was little evidence to support this time-point and that the 6 week conservative treatment interval was largely historical and consensus based. The GDG agreed that as non-surgical management should be pursued prior to surgery, this would negate the need to specify a specific time point in the recommendation as it is likely that it would be at least 3-6 months before surgery was offered.
  - The GDG agreed that this recommendation would equally apply for pregnant women and this should be considered on a case by case basis.
  - The GDG were aware of the NICE clinical guideline for pharmacological management of neuropathic pain (CG173) which covers the pharmacological management of sciatica and therefore was outside of the remit for this guideline to do a systematic review of the evidence for this. Conservative management for sciatica should therefore be guided by the recommendations set in CG173 before discectomy is considered as an option.
  - It was also noted that in the non-randomised study included in the review, patients had to pay for their own treatment which the group agreed was a serious limitation of the trial, since the costs of spinal fusion far outweigh those of discectomy. This could potentially skew the results in favour of the cheaper surgical option.
  - The GDG were aware of existing NICE interventional procedure guidance for Interspinous distraction procedures for lumbar spinal stenosis causing neurogenic claudication (IPG365) and Percutaneous intradiscal laser ablation in the lumbar spine (IPG357) which recommend normal arrangements for clinical governance, consent and audit. This specific procedure was excluded from this review and therefore this existing guidance should be followed for people with sciatica. Interventional procedure guidance also exists for Percutaneous intradiscal laser ablation in the lumbar spine (IPG357) which recommends normal arrangements for clinical governance, consent and audit, Automated percutaneous mechanical lumbar discectomy (IPG141), Endoscopic laser foraminoplasty (IPG31) Insertion of an annular disc implant lumbar discectomy (IPG506) and Percutaneous endoscopic laser lumbar discectomy (IPG300) which all recommend special arrangements for clinical governance, consent, audit and research. These procedures were excluded from the review due to being inappropriate to pool with decompression techniques in general, and therefore if being considered for people with sciatica, existing guidance should be followed. The GDG were also aware of IPG guidance for Percutaneous coblation of the intervertebral disc for low back pain and sciatica (IPG543) which recommends normal arrangements, however it

was noted that this review considered different evidence and followed different methodology to that included within this review. At the time of consultation IPG300 was being updated. Information on the update is available here: http://www.nice.org.uk/guidance/indevelopment/gid-ip2806.

NICE 2016 first version of recommendation: 1 clinical recommendation (March 2016)

38. Consider spinal decompression for people with sciatica when non-surgical treatment has not improved pain or function. (For recommendations on pharmacological management of sciatica see NICE's guideline on Neuropathic pain in adults)

Belgian GDG considerations mentioned in the Lime survey in October 2016

Agreement with the content of the NICE recommendation 38: 10 Agree, 2 Disagree, 1 no opinion, 0 out of competence, 1 no answer, 4 not completed

- **Comments from those who do not agree:**
  - Shouldn't we add "and if an important disability remains"? Furthermore, we should also add "or if neurological deficits"
  - Although this is out of my competence, again what is meant with non-surgical treatment!! We need to avoid ambiguity as much as possible
- **Other comments:**

Again, this seems to be out of the topic of the recommendation

Strength of the recommendation 37 on spinal decompression: According to NICE formulation, it is a weak recommendation

GRADE Factors	
Balance between desirable and undesirable effects	The GDG considered that discectomy for people suffering from sciatica offered a good prognosis and was successful in providing long-term pain relief. However, they also noted that sciatic symptoms tend to improve naturally with time without treatment. Despite the good long term prognosis with or without treatment, the GDG felt that earlier symptom resolution with surgical intervention should be an option for people. It was agreed that there was sufficient evidence to suggest that discectomy should be considered for a subgroup of people with sciatica who had failed to respond to conservative management of their symptoms.
Quality of evidence	Low to very low
Values and preferences	Whilst the GDG agreed that in the majority of cases, sciatic symptoms would improve naturally with time, they recognised that the option for earlier pain relief should be available for a subset of patients that suffer from severe, acute sciatic pain. The group agreed that surgical intervention following a period of conservative management for around 6 weeks would be reasonable.
Costs (resource allocation)	The GDG concluded that there was a high uncertainty around the conclusions of the economic studies as the cost of surgery is overestimated in the USA studies and the effectiveness is likely to be underestimated in the European study. Therefore overall the GDG concluded that decompression surgery is likely to be cost effective in patients with sciatica when other treatments have failed.

Agreement with the strength of the NICE draft recommendation 38: 4 strong, 5 weak, 0 no opinion, 1 no answer, 8 not completed

- **Comments for a weak recommendation**
  - Depending of the values of the patients as the global assessment of the risks, including a psychological assessment.
  - Because the majority of cases improves naturally in time or with conservative management.
- **Comments for a strong recommendation**

- Balance between desirable and undesirable effects. Values and preferences.

NICE final version of recommendation (30 November 2016): addition of imaging issue

41. Consider spinal decompression for people with sciatica when non-surgical treatment has not improved pain or function and their radiological findings are consistent with sciatic symptoms.

Stakeholders' comments and replies from NICE team on draft of March 2016 (edited the 30th November 2016)

Indication for decompression to vague or not sufficient

- Arthritis Research UK: Consider spinal decompression for sciatica when non-surgical treatment has not improved pain and function. This is rather vague as there is no timeline attached to it – when should clinicians consider spinal decompression in the timeline of sciatica if there is no improvement? Trials of surgery versus conservative care suggest that timing is important. **NICE reply**: The issue regarding **optimal timing to offer spinal decompression** was not specifically considered by the review question. However, the GDG discussed attaching a timeline to the recommendation. It was GDG opinion that a reasonable period of conservative management could be around 6 weeks, however it was felt that the evidence was not strong enough to specify a time point. Furthermore, the GDG agreed that as non-surgical management should be pursued prior to surgery, this would negate the need to specify a specific time point.(p3/222)
- Warwick Clinical Trials Unit**:** Here there seem to be some evidence for **short term benefits** from decompression surgery that are not maintained in the long term. The benefits, as for all recommendations in this guideline, are modest. We think that the guidance needs to more clearly linked to the potential short term benefits, the apparent absence of long term benefits and risk of serious adverse events. This recommendation also needs to recognise that surgical de-compression is only a treatment option when there is radiological evidence of compression. There may also be time window here for when surgical decompression is likely to be most effective. Suggesting this approach for those with very long standing symptoms of sciatica may be raising unrealistic expectations. At the other extreme we doubt that surgery is a sensible option for most people with acute sciatica that may well largely resolve in the short term irrespective of treatment. Setting the pros and cons of surgery for individual patients is, we think, beyond scope of this guideline. Also we think that before there is a surgical consultation that there should be evidence of surgically treatable lesion. We therefore suggest editing the recommendation to something like: 'Consider referral to a spinal surgeon for possible spinal decompression for people with persistent sciatica when non-surgical treatment has not improved pain or function and there are radiological findings congruent with their sciatic symptoms'. **NICE reply:** The evidence reviewed showed that discectomy provided good prognosis and long-term pain relief in people suffering from sciatica. Sciatic symptoms tend to improve naturally with time without treatment; however, the GDG felt that earlier symptom resolution with surgical intervention should be an option. It was therefore recommended that spinal decompression is considered for a subgroup of people with sciatica who had failed to respond to conservative management of their symptoms. This is detailed in section 28.6 (Recommendations and link to evidence). The GDG discussed the need of imaging prior to spinal decompression and observed that prior imaging was an inclusion criteria for all the studies included in the review. The GDG was also aware that operating without concordant imaging would carry a significant risk of harm, because such patients would be exposed to the risks of surgery and general anaesthetics with little chance of any benefit. The GDG therefore decided it was appropriate to restrict the use of spinal decompression in people in whom radiological findings are concordant with sciatic symptoms. The GDG noted that if spinal decompression was being performed, patient outcome information should be submitted to a national registry. The wording of the recommendation has now been updated as follows: Consider spinal decompression for people with sciatica when non-surgical treatment has not improved pain or function and in whom radiological findings are concordant with sciatic symptoms.(p138/222)

Only for some people

- Homerton University Hospital NHS Foundation Trust: These simplistic statements imply that surgery should be considered for anyone with chronic low back pain (such as those whose persistent pain has not been cured by pain management). It suggests a lack of understanding of both chronic pain physiology and pain management research. Surgery has a place however it has not been justified in a coherent way. **NICE reply**: Both the surgery and prognostic factors review and the spinal decompression review deal with people who have failed to respond to appropriate conservative treatment. The GDG agreed that management of people with sciatica should be guided by the recommendations set in CG173 before discectomy is considered as an option. Discectomy should be considered for a subgroup of people with sciatica who had failed to respond to conservative management of their symptoms**.** (p217/222)
- Spine Intervention Society: Surgical decompression should be performed only if mechanical compression of a nerve root by a large disc herniation is proven to be the cause of this pain. Several authors reported significantly worse outcomes after discectomy in those with small, contained disc herniations, and some even excluded from surgical

consideration patients with **small sized lumbar disc herniations**. This recommendation should also caution that surgical results are better if performed within 6 months, as per North American Spine Society guidelines. **NICE reply**: We have revised the surgical decompression recommendation to reflect the requirement for concordant imaging prior to surgical treatment. From the trials and data reviewed by the GDG, we were not able to ascertain whether the size of disc herniation had any measurable impact on patient outcomes. The evidence reviewed did not inform a time point to specify within the recommendation.

NICE changes in the final version of the guideline (November 2016)

In the chapter Clinical evidence, several sentences was added:

Two Cochrane reviews were identified by searches but could not be included for the following reasons:

- the review included studies on surgery techniques in disc prolapse and not just spinal decompression;
- the review compared different types of spinal decompression techniques and was therefore not relevant to the review protocol.

The studies included in these Cochrane reviews were individually assessed and included if they matched the review protocol.

In Trade-off between clinical benefits and harms, more explanation was provided on BAK cage techniques:

The GDG were concerned that the benefits observed came mainly from a study comparing disc replacement to anterior lumbar interbody fusion (BAK cages technique). The GDG was aware that anterior procedures in the lumbar spine for back pain are not commonly performed in the UK setting, and that the BAK cages technique shows a low fusion rate and would not be considered appropriate for a stand-alone anterior fusion in clinical practice. T

In the summary, a part of sentence was added: The GDG noted that there were some signs of benefit from disc replacement compared to other interventions, but this evidence was very limited and not consistent across outcomes.

In Trade-off between net clinical effects and costs, the terms “2 studies” was changed in “1 study”:

The GDG noted that the comparators in the ~~2 studies~~ first study may have affected the overall conclusions as they may not be cost effective interventions ~~themselves~~ itself. Therefore, disc replacement could have been shown to be cost effective in the studies only because it was compared to cost ineffective interventions.

A sentence was also reformulated:

~~However in the study comparing disc replacement with multidisciplinary rehabilitation, when SF6D was used as a quality of life measure instead of EQ5D, the ICER was around £29,000 and the intervention was not cost effective anymore.~~

One way sensitivity analysis was undertaken in the study comparing disc replacement with 3-element MBR, where SF6D was used as a quality of life measure instead of EQ5D.The ICER was around £29,000 and the intervention was not cost effective anymore

And a part of sentence added:

Overall, the GDG were concerned about the lack of evidence of effect and the safety of the procedure.

In Other considerations, a sentence was added:

The GDG agreed there may be specific causes of low back pain for which disc replacement might be an appropriate treatment which are beyond the scope of this guideline.

And some words were inserted:

However, evidence reviewed by this GDG suggests that there was very limited evidence available of effectiveness of these procedures does not outweigh the risks and therefore the GDG agreed that it is appropriate to recommend against the use of disc replacement techniques for this population~~.~~

NICE final recommendations on spinal fusion(November 2016)

41. Consider spinal decompression for people with sciatica when non-surgical treatment has not improved pain or function and their radiological findings are consistent with sciatic symptoms

Belgian GDG comments during the GDG meeting on the 14th December 2016

NICE recommendation 41: Consider spinal decompression for people with sciatica when non-surgical treatment has not improved pain or function. (For recommendations on pharmacological management of sciatica see NICE's guideline on Neuropathic pain in adults)

- In the final version of the NICE guideline this recommendation has been changed: "*Consider spinal decompression for people with sciatica when non-surgical treatment has not improved pain or function and their radiological findings are consistent with sciatic symptoms."*
  "*and their radiological findings are consistent with sciatic symptoms*" has been added.
- *The NICE GDG decided that there is a need for imaging prior to spinal decompression:*
  - *Prior imaging was an inclusion criteria for all of the included studies because:*
  - *Operating without concordant imaging would carry a significant risk of harm, because such patients would be exposed to the risks of surgery and general anaesthetics with little change of any benefit.*
- Additional comments of the NICE stakeholders were on the timing of surgery. However the Belgian GDG members agreed that this should not be specified but determined case by case.
- The GDG members emphasised that the radiological findings should be consistent with the current clinical findings (klinisch beeld/tableau clinique).
- Also "non-surgical treatment" should be replaced by "multimodal management", which is in line with the wording in previous recommendations.
- The KCE researchers will analyse the recommendations on pharmacological interventions for neuropathic pain and will discuss them with the GDG members via mail or lime survey.

⇨ The final NICE recommendation 41 has been accepted with following changes:
⇨ "*Consider spinal decompression for people with radicular pain when non-surgical multimodal management has not improved pain or function and their radiological findings are consistent with the current clinical symptoms."*

Belgian GDG comments on the last formulation during the meeting on the 24th January 2017

- It is rare that surgery is done before 6 weeks but sometimes patient does not have to wait until 3 months to undergo surgery. It is proposed to add "At least 6-12 weeks" within the recommendation.
- The place of electrophysiological diagnostic was questioned: it was not mentioned in NICE but widely used in Belgium. Electrophysiological diagnostic will be added in the table "no clear recommendation because not studied by NICE".

KCE 2017 final recommendations on spinal decompression (February 2017)

22. Consider spinal decompression for people with radicular pain (at least 6-12 weeks after the onset) when non-surgical evidence-based multimodal management has not improved pain or function and their radiological findings are consistent with the current clinical symptoms.
(weak recommendation based on low to very low quality evidence from RCTs and cohort studies)

8. EXTERNAL REVIEW

The recommendations prepared by the guideline development group were circulated to relevant representatives of professional associations and other clinical experts not involved in the GDG (see Appendix 1), invited to act as external reviewers of the draft guideline. All expert referees made declarations of interest.

REFERENCES

1. Scottish Intercollegiate Guidelines Network (SIGN). Management of chronic pain. A national clinical guideline. . 2013 Dec.
2. Delitto A, George SZ, Van Dillen LR, Whitman JM, Sowa G, Shekelle P, et al. Low back pain. J Orthop Sports Phys Ther. 2012;42(4):A1-57.
3. Bundesärztekammer (BÄK), Kassenärztliche Bundesvereinigung (KBV), Arbeitsgemeinschaft der Wissen-schaftlichen Medizinischen Fachgesellschaften (AWMF). Nationale VersorgungsLeitlinie Kreuzschmerz – Leitlinien-Report, 1. Auflage. Version 3. 2011. Available from: http://www.kreuzschmerz.versorgungsleitlinien.de
4. American College of Occupational and Environmental Medicine (ACOEM). Low back disorders. In: editor(s) HK, editor. Occupational medicine practice guidelines. Evaluation and management of common health problems and functional recovery in workers: 3rd ed. Elk Grove Village (IL); 2011. p. 333-796.
5. Staal JB, Hendriks EJM, Heijmans M, Kiers H, Lutgers-Boomsma AM, Rutten G, et al. KNGF-richtlijn Lage rugpijn. 2013. Koninklijk Nederlands Genootschap voor Fysiotherapie (KNGF)
6. Goertz M, Thorson D, Bonsell J, Bonte B, Campbell R, Haake B, et al. Adult acute and subacute low back pain. 2012 Nov. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI)
7. Hooten WM, Timming R, Belgrade M, Gaul J, Goertz M, Haake B, et al. Assessment and management of chronic pain. 2013 Nov. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI)
8. Dubinsky RM, Miyasaki J. Assessment: efficacy of transcutaneous electric nerve stimulation in the treatment of pain in neurologic disorders (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2010;74(2):173-6.
9. Clinical Practice Guidelines Subcommittees, Orthopedic Surgery Department, King Khalid University Hospital, King Saud University. Evidence-Based Clinical Practice Guideline for Management of Persistent non-specific low back pain. 2013.

10. American Society of Anesthesiologists Task Force on Chronic Pain Management, American Society of Regional Anesthesia and Pain Medicine. Practice guidelines for chronic pain management: an updated report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine. Anesthesiology. 2010 Apr;112(4):810-33.
11. Harrison DD, Siskin LA, Betz JW. Best practices & practice guidelines. 2013 Nov. Arlington (VA): International Chiropractors Association (ICA)
12. Work Loss Data Institute. Low back - lumbar & thoracic (acute & chronic). 2013 Dec. Encinitas (CA)
13. Work Loss Data Institute. Pain (chronic). 2013 Nov. Encinitas (CA)
14. Toward Optimized Practice. Guideline for the evidence-informed primary care management of low back pain. 2011. Edmonton (AB)
15. Colorado Division of Workers' Compensation. Chronic pain disorder medical treatment guidelines. 2011 Dec. Denver (CO): Colorado Division of Workers' Compensation
16. Braddock EJ, Greenlee J, Hammer RE, Johnson SF, Martello MJ, O'Connell MR, et al. Manual medicine guidelines for musculoskeletal injuries. 2013 Dec 1.
17. Gordon R, Cremata E, Hawk C. Guidelines for the practice and performance of manipulation under anesthesia. Chiropr Man Therap. 2014;22(1):7.
18. Cohen S, Huang J, Brummett C. Facet joint pain-advances in patient selection and treatment. Nat. Rev. Rheumatol. 2013(9):101-16.
19. Lakemeier S, Lind M, Schultz W, Fuchs-Winkerlmann S, Timmesfeld N, Foelsch C, et al. A comparison of intraarticular lumbar facet joint steroid injections and lumbar facet joint radiofrequency denervation in the treatment of low back pain: a randomized, controlled, double-blind trial. Anesthesia and Analgesia. 2013;117(1):228-35.
20. National Spinal Taskforce. Commissioning spinal services-getting the service back on track. A guide for commissioners of spinal services. 2013. Available from: http://www.nationalspinaltaskforce.co.uk/pdfs/NHSSpinalReport_vis7%2030.01.13.pdf