



Contents lists available at ScienceDirect

Research in Social and Administrative Pharmacy

journal homepage: www.elsevier.com/locate/rsap

Original Research Paper

Equipping physicians for benzodiazepine receptor agonists deprescription in older adults: theory-based development of the BE-SAFE intervention

François-Xavier Sibille^{a,b,c,*}, Joanna Salbert^d, Lucy Bolt^{e,f}, Vagioula Tsoutsis^g, Enrico Callegari^{i,r}, Olivia Dalleur^{a,j}, Tokandji Adda^a, Thomas Agoritsas^{k,l,m}, Thomas Bergerⁿ, Carole E. Aubert^{e,f}, Dimitris Dikeos^g, Antoni Salvà^o, Begoña Pascual^p, Ramon Miralles^q, Torgeir Bruun Wyller^{h,r}, Andrea M. Patey^s, Jeremy M. Grimshaw^{s,t}, Adam Wichniak^d, Anne Spinewine^{a,u,1}, Marie de Saint Hubert^{b,c,1}

^a Clinical Pharmacy and Pharmacoepidemiology Research Group, Louvain Drug Research Institute, UCLouvain Belgium^b Geriatric Department, CHU UCL Namur, Yvoir, Belgium^c Institute of Health and Society, UCLouvain, Belgium^d Third Department of Psychiatry and Sleep Medicine Center, Institute of Psychiatry and Neurology, Warsaw, Poland^e Department of General Internal Medicine, Inselspital, Bern University Hospital, University of Bern, Switzerland^f Institute of Primary Health Care (BIHAM), University of Bern, Switzerland^g Sleep Research Unit, First Department of Psychiatry, Eginition Hospital, Medical School, National & Kapodistrian University of Athens, Athens, Greece^h Institute of Clinical Medicine, University of Oslo, Oslo, Norwayⁱ Department of Old Age Psychiatry, Østfold Hospital Trust, Grålum, Norway^j Pharmacy Department, Cliniques Universitaires Saint-Luc, Brussels, Belgium^k Division of General Internal Medicine, Department of Medicine, Geneva University Hospitals, University of Geneva, Switzerland^l Department of Health Research Methods, Evidence, and Impact, McMaster University, Canada^m MAGIC Evidence Ecosystem Foundation, Oslo, Norwayⁿ Department of Clinical Psychology and Psychotherapy, Institute of Psychology, University of Bern, Switzerland^o Fundació Salut i Entornament - Universidad Autònoma de Barcelona, Spain^p Badalona Serveis Assistencials, Badalona, Spain^q Hospital Germans Trias i Pujol, Badalona (Barcelona), Spain^r Department of Geriatric Medicine, Oslo University Hospital, Oslo, Norway^s Methodology and Implementation Research, Ottawa Hospital Research Institute, Canada^t Department of Medicine, University of Ottawa, Canada^u Pharmacy Department, CHU UCL Namur, Yvoir, Belgium

ARTICLE INFO

Keywords:

Benzodiazepine receptor agonists

Older adults

Deprescription

Hospital physicians

Intervention development

ABSTRACT

Background: Benzodiazepine receptor agonists (BZRA) are still widely used for sleep problems in older adults despite an unfavourable risk-benefit ratio. The hospital setting presents an opportunity for optimising medication use in older adults. The BE-SAFE project follows a rigorous sequential approach for developing a theory-informed intervention towards BZRA deprescription initiated in the hospital setting in 6 European countries (Belgium, Greece, Norway, Poland, Spain, and Switzerland).

Objectives: The objectives of this paper are to describe the development of the physicians' intervention, the results of on the acceptability and perceived feasibility with physicians, and the finalised BE-SAFE intervention.

Methods: The intervention was built upon preliminary work and developed in four main steps: selection of behaviour change techniques; identification of existing resources and assessment of needs and preferences of hospital physicians; development of intervention components and modes of delivery; and end-users' evaluation and refinement of intervention.

Results: A total of 11 behaviour change techniques were selected, addressing 6 main barriers into a 6-component intervention: senior physician endorsement, training, self-monitoring, deprescription algorithm, communication to patients and other healthcare professionals. These core elements will be delivered allowing local adaptability.

* Corresponding author. Avenue Dr Gaston Therasse, 1 5530 Yvoir Belgium,
E-mail address: francois-xavier.sibille@chuclouvain.be (F.-X. Sibille).

¹ Equally contributing last authors.

<https://doi.org/10.1016/j.sapharm.2025.05.002>

Received 15 January 2025; Received in revised form 28 April 2025; Accepted 6 May 2025

Available online 21 May 2025

1551-7411/© 2025 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0/>).

Twenty-four physicians evaluated the intervention. They confirmed that the intervention effectively targets the barriers highlighted in preliminary work and provided feedback for improvement regarding clarity and time issues.

Conclusions: A 6-component physician's intervention to enhance BZRA deprescription initiated in hospital settings was developed by systematically addressing implementation issues in a theory informed manner. This intervention will be evaluated in a multi-country cluster randomised controlled trial.

1. Background

Benzodiazepine receptor agonists (BZRA) are frequently prescribed for sleep problems in adults aged 65 and older. Yet, they present an unfavourable risk (e.g., falls, hip fractures, delirium) - benefit (reduced sleep latency onset, reduced awakenings) balance.¹ Moreover, although it is widely recommended that BZRA use should be limited to a maximum of 4 weeks, long-term use is often observed.² Several international guidelines consider BZRAs as potentially inappropriate medications in older adults and recommend avoiding them, or, when already used, considering deprescription.^{3,4} Despite these recommendations, the prevalence of BZRA use in Europe remains high.^{5,6}

Deprescription is the process of cessation or dose reduction of a medication, supervised by a healthcare professional (HCP), with the goals of improving health outcomes and minimizing risks.⁷ Evidence shows that BZRA deprescription can reduce the harms associated with chronic BZRA use, without significantly worsening sleep quality, anxiety, or depression.^{8,9}

The hospital setting presents an important opportunity for optimising BZRA use in older adults.¹⁰ BZRA prevalence rates in hospitals are high,^{11,12} and admission or specialist consultation provides an opportunity for medication review.¹³ Limited evidence supports the feasibility of deprescription initiated in the hospital. In the Canadian MedSafer study, for instance, electronic decision support for deprescription in hospitalised older adults improved BZRA deprescription at discharge with an adjusted risk difference of 22.7 % (40.0 % in the intervention versus 20.4 % in the control group).⁹ However, deprescription in hospitals faces unique challenges, including high staff turnover, communication issues during care transitions, and the non-sleep-friendly hospital environment.¹⁴ Data from Europe are limited,¹⁵ and contextual factors may also influence effectiveness.

BE-SAFE (Implementing a patient-centred and evidence-based intervention to reduce BZRA use to improve patient SAFETY and quality of care), is a HORIZON Europe-funded project whose goal is to improve patient safety by reducing BZRA use throughout Europe (Supplementary Material 1).¹⁶ It follows a rigorous sequential approach to develop a BZRA-specific deprescription intervention and relies on the Choosing Wisely De-implementation Framework (CWDIF).¹⁷ The approach aims to develop an intervention that overcomes previously identified barriers and fits with the care settings in the six participating countries (Belgium, Greece, Norway, Poland, Spain, and Switzerland) where it will be implemented.

1.1. Objectives

The primary objective of this paper is to describe the development of the physicians' intervention. Secondary objectives are to provide the results of the evaluation on the acceptability and perceived feasibility of the planned intervention with end-users, and to present the finalised BE-SAFE intervention.

2. Methods

2.1. Overall approach

This work followed international recommendations for complex intervention development.^{17,18} Specific attention was paid to several

key elements highlighted by the Medical Research Council guidance: considering context, using a theory-based approach, and engaging stakeholders. The description below follows the GUIDED recommendations for intervention development reporting (Supplementary Material 2).^{19,20}

The AACTT (Action, Actor, Context, Target, Time) Framework²¹ helped define who needs to do what differently. The target behaviour was defined as BZRA deprescription initiated by physicians in the hospital setting (primary target for the BE-SAFE intervention). This includes several sub-actions such as identifying eligible patients, exploring the patient's preferences and values to make a shared decision, defining a tapering scheme whenever relevant, planning and performing follow-up often in collaboration with the general practitioner (GP).

The development of the intervention was built upon preliminary work performed in BE-SAFE and occurred in 4 main steps, as described below and illustrated in Fig. 1. The BE-SAFE consortium responsible for intervention development included clinicians and researchers with expertise in geriatric medicine, sleep medicine, and implementation science.

2.2. Preliminary work

Firstly, a qualitative study was performed to describe care trajectories and healthcare organisations relevant to BZRA deprescription in the 6 countries.²² Those interviews provided several findings relevant to intervention development. Deprescribing is not linear or sequential, and the care trajectory of BZRA deprescribing initiated at the hospital level is unlikely to occur with one professional and in one setting. As different HCPs may have a role in BZRA deprescription, communication strategies should be improved inside and outside of the hospital setting. Many contextual factors that can influence deprescription, highlighting the need for local adaptability in delivering the intervention.

Secondly, a multicountry survey explored the main barriers to BZRA deprescription from the perspective of hospital physicians and GPs.²³ Those were sorted into several domains representing barriers to changing behaviour, using the Theoretical Domains Framework (TDF).²⁴ TDF is a structured framework for identifying and analysing behavioural change drivers.²⁵ In total, 240 hospital physicians and 96 GPs working in the 6 countries where the BE-SAFE RCT will occur answered the survey. Major barriers were found in six TDF domains: Skills, Beliefs about capabilities, Goals, Social influence, Emotion, and Environmental context and resources (Table 1). These were considered priorities to address in the BE-SAFE intervention to change physicians' behaviour regarding BZRA deprescribing. Major barriers were overall similar across countries, as well as between hospital physicians and GPs, allowing developing an intervention with common core components.

Thirdly, the MAGIC Evidence Ecosystem Foundation led the development of a trustworthy clinical guideline on BZRA deprescription in insomnia disorder. Its panel issued a guideline in three layers.²⁶ It suggests offering BZRA deprescription rather than usual care for patients taking BZRA (first layer) and highlights the importance of shared decision making (SDM). The guideline then issues a conditional recommendation to offer a multifaceted rather than single intervention (second layer). Finally (third layer), it suggests applying the following types of interventions: patients' education, physicians' education, tapering and cognitive behavioural therapy for insomnia (CBT-I); while it issues a conditional recommendation against pharma

cologically-assisted intervention.

Step 1: Selection of behaviour change techniques

Step 1 aimed to select behaviour change techniques (BCTs) addressing the major barriers identified for physicians in the six TDF domains. A BCT is defined as an “observable, replicable, and irreducible component of an intervention designed to change behaviour, and a postulated active ingredient within the intervention”.^{27,28} The TDF domains were mapped with BCTs using the Theory and Technique Tool and expertise in implementation science within the consortium.²⁹ Selection of BCTs was based on the APEASE criteria (Acceptability, Practicability, Effectiveness, Affordability, Side effects, and Ethics).³⁰ BCTs were excluded if - in all 6 countries - they could not be performed by the physician (practicability), were not acceptable, not ethical, and not replicable or had no potential for scaling up (affordability). Preselection of BCTs was validated by all BE-SAFE partners.

Step 2: Identification of existing materials, end-users’ needs and preferences

Step 2 focused on identifying existing materials to support physicians in BZRA deprescription and evaluating the needs and preferences of end-users.

Firstly, existing resources were identified through several channels: materials used in trials included in the systematic review performed by MAGIC to develop the guideline³¹; request to the international community of deprescription researchers through posts on social media; request to professional organisations and personal contacts.

Then, the needs and opinions of physicians about educational materials to support BZRA deprescription were identified. A convenience sample of Belgian physicians working in hospital wards expected to participate in the BE-SAFE randomised controlled trial (RCT) and one general practice was invited. Two researchers conducted group discussions and discussions were audio recorded after consent of all participants. Participants were first asked about their expectations about the content and format of materials to support BZRA deprescription. Following this, they commented on 4 materials purposively selected to have different formats, contents and origins (Supplementary Material 3).

Table 1

Priority Theoretical Domain Framework domains and selected Behaviour Change Techniques.

Priority TDF domains	Barriers identified in BE-SAFE settings	Priority BCTs for the intervention development
Skills	Lack of training on - how to deprescribe BZRA; - how to engage with patients about BZRA deprescription; - how to implement alternative approaches.	4.1. Instruction on how to perform behaviour 8.1. Behavioural practice and rehearsal
Beliefs about capabilities	- Low confidence that they can deprescribe even when limited time. - Moderate confidence that they can deprescribe BZRA if they want to.	1.2. Problem solving 2.3 Self-monitoring of the behaviour 6.1. Demonstration of the behaviour 8.1. Behavioural practice and rehearsal
Goals	- More important health problems to address than BZRA deprescribing. - Not seeing BZRA deprescription as a priority for them.	1.1. Goal setting (behaviour)
Social influence	- Feeling a lot of pressure from older adults to renew/extend their BZRA prescriptions. - Perception that most patients are reluctant to stop their BZRA. - Moderate support from colleagues.	3.2. Social support (practical) 6.3 Information about others’ approval
Environment and resources	- Lack of guidelines and tools for BZRA deprescription. - Lack of time to educate and inform patients about BZRA deprescription. - Lack of goals/policies in the department/institution that encourage deprescription.	9.1 Credible source 12.5 Adding objects to the environment.
Emotion	- Frustration with challenges of BZRA deprescription - Stress about BZRA deprescription	6.3 Information about others’ approval 11.2 Reduce negative emotions

BZRA = benzodiazepine receptor agonist; BCT = behaviour change technique; TDF= Theoretical Domain Framework.

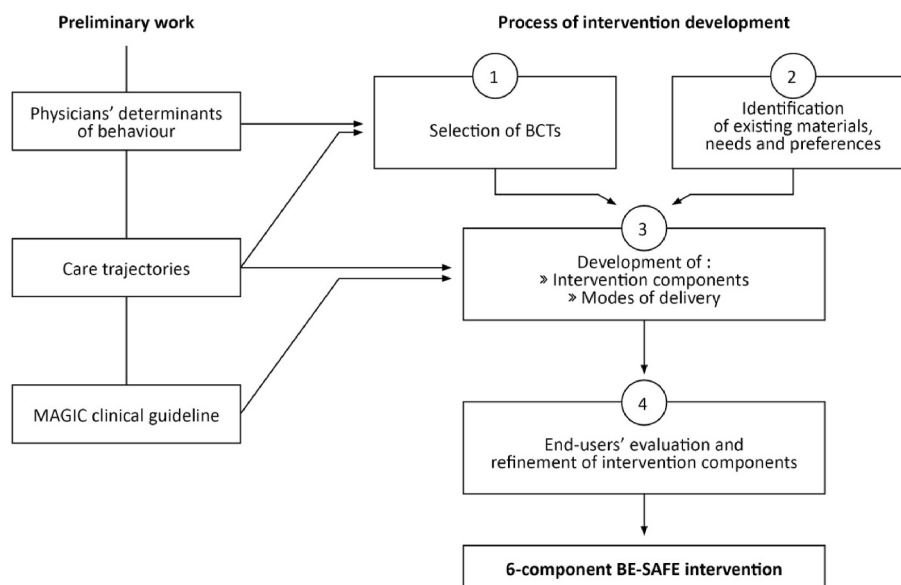


Fig. 1. Overview of the development of the BE-SAFE intervention.

Step 3: Development of intervention components and modes of delivery

The list of BCTs selected in Step 1 was operationalised into a set of intervention components, and the content, format and modes of delivery were defined based on results from Step 2 and from preliminary work. Intervention components were refined iteratively based on feedback from research team members.

Specific attention was given to developing intervention components that would be acceptable and practical to use in all trial sites. For example, several countries considered that an educational session longer than 30 min would not be feasible. So, to keep the intervention pragmatic and replicable, training modules do not exceed 30 min in total. On the other hand, flexibility was allowed to operationalise the modes of delivery of the intervention to fit with the local context. For instance, regarding the mode of communication with GPs, each partner was invited to decide between a phone call, a written communication (standardised online form sent by a secured health messaging system or by post or given on a paper form to the participant to be passed on to other HCPs).

Step 4: End-users' evaluation

Feedback was requested from potential end-users on an English preliminary version of the intervention components. Each partner was asked to recruit 3 to 6 participants at their site, including hospital physicians from the medical specialities that will be involved in the trial and at least one GP. Participants were asked to review each component, either by reading or watching, and provide feedback through an online survey. Initially, they were asked to comment on the length, their most and least preferred aspects, and to offer suggestions for improvement in free text. Following this, they were asked to rate on a 5-point Likert scale 9 statements which addressed key behavioural elements targeted by the intervention.

3. Results

3.1. Selected behaviour change techniques

Eleven BCTs and 1-4 BCTs targeting each of the six TDF domains were selected (Table 1): Goal setting (behaviour), Problem solving, Self-monitoring of the behaviour, Social support (practical), Instruction on how to perform behaviour, Demonstration of the behaviour, Information about others' approval, Behavioural practice and rehearsal, Credible source, Reduce negative emotions and Adding objects to the environment.

3.2. Existing interventions and end-users' needs and preferences

We identified 23 resources supporting HCPs in BZRA deprescription (Supplementary Material 4). They vary greatly regarding format (written document, e-learning, video), length (from a 2-page to a 12-page document), content (communication tips, rationale, alternatives), target population (physicians or pharmacists only, or HCPs in general), validation and dissemination (from one hospital to a whole country or more).

Five group discussions gathered a total of 10 hospital physicians (5 males and 5 females) and 8 GPs (4 males and 4 females). The discussions were based on a guide and lasted between 60 and 95 min. Participants agreed on easy-to-access materials in various formats (paper, online, integrated into the electronic medical record or prescription module). The deprescribing algorithm format was unanimously appreciated. Participants insisted on limiting the time for the initial training and to perform BZRA deprescribing. Participants agreed that materials should be available in the local language and that the presentation of clinical cases was interesting. On the contrary, opinions differed regarding the

way of delivering the materials (live training or online and on-demand), the acceptable length of the initial training and the level of detail provided on the BZRA-related adverse effects. This work was performed in Belgium only for pragmatic reasons, but the results were discussed with the partners of the other countries.

3.3. Description of intervention components and modes of delivery

The BE-SAFE intervention is described following the Template for Intervention Description and Replication (TidieR, Supplementary Material 5)²⁰ and has 6 components (Table 2). A senior physician will encourage intervention physicians to take the training and use the other components to implement deprescription in clinical practice (Component I: senior physician endorsement). The training consists of 3 short videos (Component II: physician education) covering the importance of BZRA deprescription in older adults and how to use the algorithm, SDM and a demonstration of deprescription including SDM through clinical cases. Physicians will be encouraged to reflect on how they performed, using a one-page monitoring tool (Component III: self-monitoring). The core component is the deprescription algorithm (Component IV). The front side provides a 5-step process that guides physicians through BZRA deprescription, based on SDM. It was developed based on the format of the Canadian BZRA deprescription algorithm.³² It guides HCPs through a flowchart on the front and provides additional information such as expected benefits and non-pharmacological support measures on the back. Expert consensus informed the approach where evidence was lacking, such as tapering pace, managing adverse effects, and the type of CBT-I (individual, group, or self-help). The Three-Talk model (Team--Option-Decision) was chosen to structure SDM.³³ When a decision has been made, to improve continuity of care, physicians should provide written communication of the discussion and the decision made to the patient or the caregiver (Component V: Patient/caregiver communication) and other HCPs, mainly the GP (Component VI: HCP communication). All components will be available online for intervention physicians and GPs.

The BE-SAFE intervention was designed as a whole: attention was paid to the alignment of the content of the components and their explicit interconnection. For instance, tips for SDM are provided in the algorithm (Component IV) but are also addressed in training modules (Component II). The expected benefits of BZRA deprescription are highlighted in training modules (Component II) and reminded in the communication form for patients (Component V). Fig. 2 summarises how the components work together.

3.4. End-users' evaluation and refinement of intervention components

The survey was completed by 24 respondents (14 women and 10 men, 15 hospital physicians and 9 GPs, 3 to 6 per country) over 3 weeks. The median number of years of practice was 10 (first quartile 3 years; third quartile 16 years).

The respondents globally agreed that the barriers targeted were improved (Table 3). Yet, 37.5 % of the respondents stated they would not consider BZRA deprescription for all older adults irrespective of adverse events. Moreover, free-text comments identified some opportunities for improvement in the following areas: additional content (e.g., non-pharmacological support measures), clarity, time issues, layout and audio. The components were adapted accordingly (Supplementary Material 6).

4. Discussion

This work describes the theory-based development of the BE-SAFE intervention that aims to support physicians from 6 European countries in BZRA deprescription in older adults. This intervention comprises core elements common to all settings but allows for some local adaptations to favour implementation. It will be used with material (brochures and

Table 2

Overview of BE-SAFE intervention components.

Intervention components	Description of intervention components	Modes of delivery	Main Behaviour Change Techniques
I. Senior physician endorsement	At each study site, a senior hospital physician (e.g., head of the department or direct superior) encourages intervention physicians to consider BZRA deprescription in all older adults on long-term BZRA, encourages them to take the training modules and reinforces that this is an important goal for the department	Written communication (form provided, paper or e-mail) or Individual or group face-to-face discussion Also available on the website (hidden page)	1.1. Goal setting (behaviour). 3.2 Social support (practical). 6.3 Information about others' approval. 9.1 Credible source.
II. Training Modules	Module 1 addresses the importance of considering BZRA deprescription for all older adults on long-term BZRAs; explains how to overcome initial physician and patient inertia; provides information about CBT-I; and explains how to use the deprescription algorithm. Module 2 describes what SDM is, and why it is important; tackles myths about SDM for BZRA deprescription and gives practical instructions. Module 3 presents 2 clinical vignettes reflecting different participant typologies; different styles of conversation; and different decisions taken.	Individual or group sessions to watch a video + Availability on the website (hidden page)	1.1. Goal setting (behaviour). 3.2 Social support (practical). 4.1 Instruction on how to perform the behaviour. 6.3 Information about others' approval. 8.1 Behavioural practice and rehearsal. 9.1 Credible source. 11.2 Reduce negative emotions.
III. Self-monitoring	-Checklist of the steps proposed in the algorithm. -Reflection on 1 action to improve their behaviour regarding BZRA deprescription.	Paper or electronic version provided to the physician, available on the website (hidden page)	2.3 Self-monitoring of the behaviour. 12.5 Adding objects to the environment.
IV. Deprescription algorithm	5-step method: - Check for any reason why BZRA should be continued - Engage with the patient- SDM - Reach a decision - Plan follow-up - Perform follow-up	2-page document electronic and/or paper version provided to the physician. Also available on the website (hidden page)	1.2 Problem solving. 4.1 Instruction on how to perform the behaviour. 6.1 Demonstration of the behaviour. 9.1 Credible

Table 2 (continued)

Intervention components	Description of intervention components	Modes of delivery	Main Behaviour Change Techniques
	Practical information - Clinical triggers - Current evidence and recommendations - Expected benefits - Potential risks - Communication tips to address frequent barriers - (non) pharmacological support measures		source. 12.5 Adding objects to the environment.
V. Patient/caregiver communication	Transfer tool with information on place and time of discussion, participant values and preferences, and practical tapering scheme. Reminder of resources and potential risks.	Recording in the participant record + Paper or electronic version handled to the patient/caregiver	3.2 Social support (practical). 9.1 Credible source 12.5 Adding objects to the environment.
VI. HCP communication	Transfer tool with information on clinical aspects and participant values and preferences, summary of decisions taken and actions, and follow-up recommendations. Reminder of rational, expected benefits, potential risks, and tapering instructions.	Recording in the participant record + Paper or electronic version sent directly or through the participant and/or phone call to selected HCPs	3.2 Social support (practical). 6.3 Information about others' approval. 12.5 Adding objects to the environment.

BZRA = benzodiazepine receptor agonist; CBT-I = cognitive and behavioural therapy for insomnia; GP = general practitioner; HCP = healthcare professionals; SDM = shared-decision making.

videos) developed for patients.

4.1. BE-SAFE intervention

Our intervention tackles existing barriers and addresses communication, education, and coordination challenges identified in our preliminary work and in other researches.³⁴ SDM is a central concept of the intervention because BZRA deprescription is a preference-sensitive decision.^{26,35} The deprescription algorithm integrates the assessment of patients' values and preferences, allowing informed decisions that may include postponing decision (e.g., after discharge) or deciding not to deprescribe. The training tackles 3 misconceptions hindering the implementation of SDM in daily practice, including the well-known perception-reality gap.^{36,37} Non-pharmacological measures might be overlooked in sleep problems, but CBT-I is indisputably the first-line treatment of sleep problems because of long-term efficacy and safety.³⁸ The aim of the BE-SAFE intervention is not to provide extensive training, but rather to raise awareness to CBT-I in sleep problems. Specific attention was paid to care transition, often the weak link in hospital interventions but crucial for BZRA deprescription which often exceeds the hospital stay and needs the combined efforts of all HCPs.³⁴ Time concerns raised by the stakeholders regarding the training and the process for each patient are consistent with the evidence^{34,39,40} and

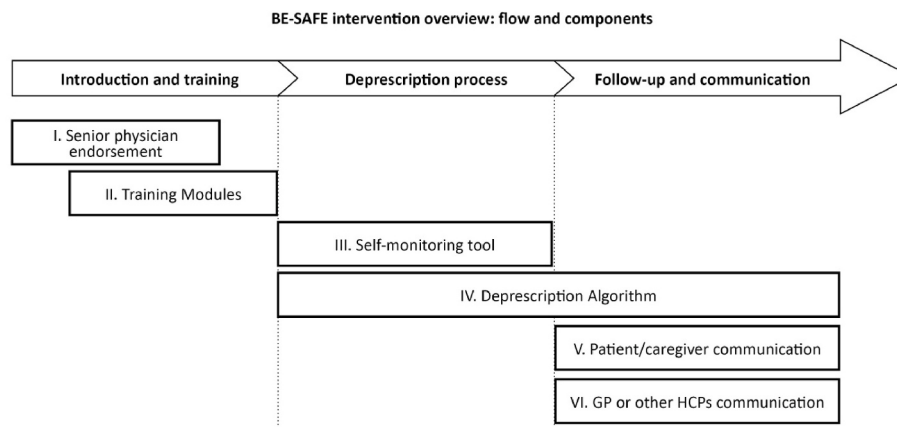


Fig. 2. BE-SAFE intervention overview: flow and components.

were specifically addressed.

4.2. Comparison with other hospital-based deprescribing intervention

Recent deprescription interventions in hospitalised older adults – although not specific to BZRA – exhibit both similarities and differences in context, development, or content. The CHARMER intervention targets geriatricians and pharmacists in English hospitals and promotes proactive deprescription.⁴¹ It was developed using theory and extensive stakeholder involvement, and allows for adaptation through local implementation teams. Although the number of BCTs and components is similar between CHARMER and BE-SAFE, no BCT is common. CHARMER selected BCTs relating to organisational changes (such as Social comparison and Restructuring the social environment), while BE-SAFE mainly targets individual physicians.¹⁸ The MedSafer study aimed to reduce adverse drug events among Canadian older adults with polypharmacy.⁴² It relied mainly on software generated reports of deprescription opportunities, which addresses automated processes. Previous research highlights the need to address non-reflective processes including Emotions (TDF domain).^{23,43,44} Like BE-SAFE, MedSafer provided tapering instructions, patient educational material, and discharge reports, but did not include physician training.

4.3. Strengths and limitations

This work systematically addressed implementation issues in a theory-informed manner and identified appropriate BCTs to target the context-specific barriers of BZRA deprescription in older adults. This increases the likelihood that the designed intervention will change behaviour, will likely improve scalability if the intervention is successful and also will inform the process evaluation.⁴⁵

This work has several limitations. Firstly, the BE-SAFE intervention does not aim for healthcare or organisational changes, although raised as barriers by the participants in the preliminary work. This choice was made to provide an intervention replicable in other contexts and to limit the risk of contamination, as the RCT will be clustered at physician level. Moreover, although other HCPs such as nurses are involved in the care pathways and can influence deprescription, their role and available resources vary significantly across sites. The decision was thus made not to develop intervention components directly targeting other HCPs for the trial. Finally, the end-user evaluation was limited in scope. A feasibility study would have been preferable but was not possible to implement given project's constraints. A further assessment of the intervention is planned further in a process evaluation embedded in the trial.

5. Conclusion

A 6-component physician's intervention to enhance BZRA deprescription initiated in hospital settings was developed by systematically addressing implementation issues in a theory informed manner. This intervention will be evaluated in the coming cluster RCT, process evaluation and case studies in 6 European countries.

CRediT authorship contribution statement

François-Xavier Sibille: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Joanna Salbert:** Writing – review & editing, Validation, Methodology. **Lucy Bolt:** Writing – review & editing, Validation, Methodology. **Vagioula Tsoutsis:** Writing – review & editing, Validation, Methodology. **Enrico Callegari:** Writing – review & editing, Validation, Methodology, Conceptualization. **Olivia Dalleur:** Writing – review & editing, Validation, Methodology, Conceptualization. **Tokandji Adda:** Writing – review & editing, Visualization, Validation, Methodology, Data curation. **Thomas Agoritsas:** Writing – review & editing, Validation, Methodology. **Thomas Berger:** Writing – review & editing, Validation, Methodology, Conceptualization. **Carole E. Aubert:** Writing – review & editing, Validation, Methodology, Funding acquisition, Conceptualization. **Dimitris Dikeos:** Writing – review & editing, Validation, Methodology. **Antoni Salvà:** Writing – review & editing, Validation, Methodology. **Begoña Pascual:** Writing – review & editing, Validation, Methodology. **Ramon Miralles:** Writing – review & editing, Validation, Methodology. **Torgeir Bruun Wyller:** Writing – review & editing, Validation, Methodology, Conceptualization. **Andrea M. Patey:** Writing – review & editing, Validation, Methodology. **Jeremy M. Grimshaw:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Adam Wichniak:** Writing – review & editing, Validation, Supervision, Methodology, Funding acquisition. **Anne Spine-wine:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Funding acquisition, Conceptualization. **Marie de Saint Hubert:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Conceptualization.

Ethics

Approval from the Ethics Committee was not mandatory. Physicians agreed to participate verbally to the group discussions or by connecting and answering the online survey.

Table 3

Results of the end-users' evaluation (N = 24).

How much do you agree with the following statements?	Strongly disagree N (%)	Disagree N (%)	Neutral N (%)	Agree N (%)	Strongly agree N (%)
With these materials, I would be better prepared to engage in BZRA deprescription in older adults using it for sleep problems.	0 (0.0 %)	1 (4.2 %)	0 (0.0 %)	9 (37.5 %)	14 (58.3 %)
With these materials, I would consider BZRA deprescription for all older adults irrespective of the presence of adverse events.	2 (8.3 %)	7 (29.2 %)	2 (8.3 %)	12 (50.0 %)	1 (4.2 %)
With these materials, I would feel better prepared to select and implement a tapering plan.	0 (0.0 %)	0 (0.0 %)	2 (8.3 %)	11 (45.8 %)	11 (45.8 %)
With these materials, I would be more confident that I can deprescribe with limited time.	1 (4.2 %)	4 (16.7 %)	4 (16.7 %)	11 (45.8 %)	4 (16.7 %)
With these materials, I would feel better prepared to implement non-pharmacological support measures.	0 (0.0 %)	2 (8.3 %)	8 (33.3 %)	9 (37.5 %)	5 (20.8 %)
With these materials, I would feel better equipped to cope with patients' reluctance to discontinue their BZRA	0 (0.0 %)	0 (0.0 %)	7 (29.2 %)	11 (45.8 %)	6 (25.0 %)
With these materials, I would feel better prepared to communicate about BZRA deprescription with other healthcare professionals inside or outside my department/ practice.	0 (0.0 %)	3 (12.5 %)	1 (4.2 %)	13 (54.2 %)	7 (29.2 %)
If I received that kind of e-mail from a senior physician, I would consider that BZRA deprescription in older adults is a priority in my clinical work.*	0 (0.0 %)	1 (4.2 %)	5 (20.8 %)	10 (41.7 %)	8 (33.3 %)
If I received that kind of e-mail from a senior physician, I would be more prone to watch the training modules and read the tools.*	0 (0.0 %)	0 (0.0 %)	4 (16.7 %)	14 (58.3 %)	6 (25.0 %)

BZRA = benzodiazepine receptor agonist. *Refers only to the senior physician endorsement.

Availability of data and materials

Complete data are not openly available due to ongoing work and are available from the corresponding author upon reasonable request.

Funding

François-Xavier Sibille was supported by a grant "Clinical Master Specialist Applicant for a Ph.D." of the Fonds de la Recherche Scientifique – FNRS (Belgium). The funder had no role in study design, data collection, data analysis, data interpretation, or report writing. Carole E. Aubert was supported by the Swiss National Science Foundation (grant PZ00P3_201672/1).

This work is part of the BE-SAFE project supported by the European Union Horizon Europe research and innovation program under the grant agreement No 101057123, and by the Swiss State Secretariat for Education, Research and Innovation (SERI) (contract No 22.00116). Views and opinions expressed are however those of the authors only and do not necessarily reflect those of the European Union or the SERI. Neither the European Union nor the SERI can be held responsible for them.

Acknowledgements

We warmly thank the participants in the group discussions and the survey. We are also grateful to the members of the local and international Patient Partnership Advisory Councils and the Advisory Board of BE-SAFE for their valuable input at the various steps of the intervention development.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.sapharm.2025.05.002>.

References

- Glass J, Lanctôt KL, Herrmann N, Sproule BA, Busto UE. *Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits*. *BMJ*. 2005;331(7526):1169.
- Olsson M, King M, Schoenbaum M. Benzodiazepine use in the United States. *JAMA Psychiatry*. 2015;72(2):136–142.
- O'Mahony D, A. Cherubini, A.R. Guiteras, et al., *STOPP/START criteria for potentially inappropriate prescribing in older people: version 3*. European Geriatric Medicine, 2023.O'Mahony D., et al. *STOPP/START Criteria for Potentially Inappropriate Prescribing in Older People: Version 3*. European Geriatric Medicine. 2023.
- Pazan F, Weiss C, Wehling M. The FORTA (fit FOR the aged) list 2018: third version of a validated clinical tool for improved drug treatment in older people. *Drugs Aging*. 2019;36(5):481–484.
- Huerta C, Abbing-Karahagopian V, Requena G, et al. *Exposure to benzodiazepines (anxiolytics, hypnotics and related drugs) in seven European electronic healthcare databases: a cross-national descriptive study from the PROTECT-EU Project*. *Pharmacoepidemiol Drug Saf*. 2016;25(Suppl 1):56–65.
- OCDE. *Panorama de la santé 2017 : Les indicateurs de l'OCDE*. Éditions OCDE; 2017.
- Reeve E, Gnjdic D, Long J, Hilmer S. A systematic review of the emerging definition of "deprescribing" with network analysis: implications for future research and clinical practice. *Br J Clin Pharmacol*. 2015;80(6):1254–1268.
- Ng BJ, Le Couteur DG, Hilmer SN. Deprescribing benzodiazepines in older patients: impact of interventions targeting physicians, pharmacists, and patients. *Drugs Aging*. 2018;35(6):493–521.
- McDonald EG, Wu PE, Rashidi B, et al. *The MedSafer Study-Electronic Decision Support for Deprescribing in Hospitalized Older Adults: A Cluster Randomized Clinical Trial*. *JAMA Intern Med*. 2022;182(3):265–273.
- Sawan M, Reeve E, Turner J, et al. A systems approach to identifying the challenges of implementing deprescribing in older adults across different health-care settings and countries: a narrative review. *Expert Rev Clin Pharmacol*. 2020;13(3):233–245.
- Beuscart JB, Ficheur G, Miquieu M, et al. Co-prescriptions of psychotropic drugs to older patients in a general hospital. *European Geriatric Medicine*. 2017;8(1):84–89.
- Sibille F-X, Spinewine A, Zerah L, et al. Current practice in benzodiazepine receptor agonists deprescribing on acute geriatric wards: a cohort study. *BMC Geriatrics*. 2022;22(1):88.
- Petrovic M, Somers A, Onder G. Optimization of geriatric pharmacotherapy: role of multifaceted cooperation in the hospital setting. *Drugs Aging*. 2016;33(3):179–188.
- Neville HL, Granter C, Adibi P, et al. *Interventions to reduce benzodiazepine and sedative-hypnotic drug use in acute care hospitals: A scoping review*. *Res Social Adm Pharm*. 2022;18(5):2874–2886.
- Saeed D, Carter G, Parsons C. Interventions to improve medicines optimisation in frail older patients in secondary and acute care settings: a systematic review of randomised controlled trials and non-randomised studies. *Int J Clin Pharm*. 2022;44(1):15–26.
- Innovation, D.-G.f.R.a. *Horizon Europe*. 21/08/2024]; Available from: https://research-and-innovation.ec.europa.eu/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe_en.

17. Grimshaw JM, Patey AM, Kirkham KR, et al. *De-implementing wisely: developing the evidence base to reduce low-value care*. *BMJ Qual Saf*. 2020;29(5):409–417.
18. Skivington K, Matthews L, Simpson SA, et al. *A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance*. *BMJ*. 2021;374:n2061.
19. Duncan E, O'Cathain A, Rousseau N, et al. *Guidance for reporting intervention development studies in health research (GUIDED): an evidence-based consensus study*. *BMJ Open*. 2020;10(4):e033516.
20. Hoffmann TC, Glasziou PP, Boutron I, et al. *Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide*. *Bmj*. 2014;348:g1687.
21. Presseau J, McCleary N, Lorencatto F, et al. *Action, actor, context, target, time (AACTT): a framework for specifying behaviour*. *Implement Sci*. 2019;14(1):102.
22. López-Toribio M, et al. *Description of care pathways for benzodiazepine and sedative hypnotic discontinuation in older adults: protocol of a multicentre qualitative study*. *Int J Integrated Care*. 2023;23(S1).
23. Shapoval, V., M. de Saint Hubert, P. Evrard, et al., *Barriers to Deprescribing Benzodiazepines in Older Adults in a Survey of European Physicians*. *JAMA Network Open*. 2025. 8(3): p. e2459883–e2459883.
24. Alharthi M, Wright D, Scott S, Birt L. *Barriers and enablers to deprescribing for older people in care homes: The theory-based perspectives of pharmacist independent prescribers*. *Res Social Adm Pharm*. 2023;19(5):746–752.
25. Cane J, O'Connor D, Michie S. *Validation of the theoretical domains framework for use in behaviour change and implementation research*. *Implement Sci*. 2012;7:37.
26. App, M. *BE-SAFE: Deprescription of benzodiazepine and sedative hypnotics (BSHs) in insomnia disorder*. 2023 10/10/2023; Available from: <https://app.magicapp.org/#/guideline/7507>.
27. Cane J, Richardson M, Johnston M, Ladha R, Michie S. *From lists of behaviour change techniques (BCTs) to structured hierarchies: comparison of two methods of developing a hierarchy of BCTs*. *Br J Health Psychol*. 2015;20(1):130–150.
28. Michie S, Richardson M, Johnston M, et al. *The Behavior Change Technique Taxonomy (v1) of 93 Hierarchically Clustered Techniques: Building an International Consensus for the Reporting of Behavior Change Interventions*. *Annals of Behavioral Medicine*. 2013;46(1):81–95.
29. Project, H.B.C. *The Theory & Techniques Tool*. [cited 2023; Available from: <http://theoryandtechniquetool.humanbehaviourchange.org/>].
30. Michie S, Atkins L, West R. *The Behaviour Change Wheel: A Guide to Designing Interventions*. 2014.
31. al, Z.D.e., *The comparative Effectiveness of Interventions to Facilitate Deprescription of Benzodiazepines and Other Sedative Hypnotics: A Systematic Review and Meta-Analysis in Review*.
32. Institute, B.R. *Deprescribing Guidelines and Algorithms*. [cited 2023; Available from: <https://deprescribing.org/resources/deprescribing-guidelines-algorithms/>].
33. Elwyn G, Frosch D, Thomson R, et al. *Shared decision making: a model for clinical practice*. *J Gen Intern Med*. 2012;27(10):1361–1367.
34. Pavon JM, Zhang AD, Fish LJ, et al. *Factors influencing central nervous system medication deprescribing and behavior change in hospitalized older adults*. *J Am Geriatr Soc*. 2024;72(8):2359–2371.
35. Elwyn G, Laitner S, Coulter A, et al. *Implementing shared decision making in the NHS*. *Bmj*. 2010;341:c5146.
36. Thevelin S, Petein C, Metry B, et al. *Experience of hospital-initiated medication changes in older people with multimorbidity: a multicentre mixed-methods study embedded in the OPTimising thERapy to prevent Avoidable hospital admissions in Multimorbid older people (OPERAM) trial*. *BMJ Qual Saf*. 2022;31(12):888–898.
37. Rognan SE, Jørgensen MJ, Mathiesen L, et al. *'The way you talk, do I have a choice?' Patient narratives of medication decision-making during hospitalization*. *International Journal of Qualitative Studies on Health and Well-being*. 2023;18(1):2250084.
38. Riemann D, Espie CA, Altena E, et al. *The European Insomnia Guideline: An update on the diagnosis and treatment of insomnia 2023*. *Journal of Sleep Research*. 2023;32(6):e14035.
39. AlRasheed MM, Alhawassi TM, Alanazi A, et al. *Knowledge and willingness of physicians about deprescribing among older patients: a qualitative study*. *Clin Interv Aging*. 2018;13:1401–1408.
40. Sheehan OC, Gleason KS, Bayliss EA, et al. *Intervention design in cognitively impaired populations-Lessons learned from the OPTIMIZE deprescribing pragmatic trial*. *J Am Geriatr Soc*. 2023;71(3):774–784.
41. Scott S, Atkins B, Kellar I, et al. *Co-design of a behaviour change intervention to equip geriatricians and pharmacists to proactively deprescribe medicines that are no longer needed or are risky to continue in hospital*. *Res Social Adm Pharm*. 2023;19(5):707–716.
42. McDonald EG, Wu PE, Rashidi B, et al. *The MedSafer Study: A Controlled Trial of an Electronic Decision Support Tool for Deprescribing in Acute Care*. *Journal of the American Geriatrics Society*. 2019;67(9):1843–1850.
43. Potthoff S, Kwasnicka D, Avery L, et al. *Changing healthcare professionals' non-reflective processes to improve the quality of care*. *Soc Sci Med*. 2022;298:114840.
44. Helfrich CD, Rose AJ, Hartmann CW, et al. *How the dual process model of human cognition can inform efforts to de-implement ineffective and harmful clinical practices: A preliminary model of unlearning and substitution*. *J Eval Clin Pract*. 2018;24(1):198–205.
45. Helsingen LM, Vandvik PO, Jodal HC, et al. *Colorectal cancer screening with faecal immunochemical testing, sigmoidoscopy or colonoscopy: a clinical practice guideline*. *Bmj*. 2019;367:l5515.