Physicians' perceptions of palliative sedation for existential suffering: a systematic review

Paulo Rodrigues,[1] Johan Menten,[2] Chris Gastmans[2]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/bmjspcare-2019-001865).

[1]ETHICS 7446 - Centre d'éthique médicale, Université Catholique de Lille, Lille, France
[2]Interfaculty Centre for Biomedical Ethics and Law, Katholieke Universiteit Leuven, Leuven, Belgium

Correspondence to
Dr Paulo Rodrigues, ETHICS 7446 - Centre d'éthique médicale, Universite Catholique de Lille, Lille 59800, France; paulusrod@gmail.com

Received 17 April 2019
Revised 26 July 2019
Accepted 14 August 2019

To cite: Rodrigues P, Menten J, Gastmans C. *BMJ Supportive & Palliative Care* Epub ahead of print: [please include Day Month Year]. doi:10.1136/bmjspcare-2019-001865

ABSTRACT

Background Palliative sedation for existential suffering (PS-ES) is a controversial clinical intervention. Empirical studies about physicians' perceptions do not converge in a clear position and current clinical practice guidelines do not agree either regarding this kind of intervention.

Aim To gain deeper insight into physicians' perceptions of PS-ES, the factors influencing it, the conditions for implementing it and the alternatives to it.

Design Systematic review of qualitative, quantitative and mixed-methods studies following the *Peer Review Electronic Search Strategies* and *Preferred Reporting Items for Systematic Reviews and Meta-analyses* protocols; quality appraisal and thematic synthesis methodology.

Data sources Seven electronic databases (PubMed, CINAHL, Embase, Scopus, Web of Science, PsycINFO, PsycARTICLES) were exhaustively searched from inception through March 2019. Two reviewers screened paper titles, abstracts and full texts. We included only peer-reviewed journal articles published in English, French, German, Dutch, Spanish, Italian or Portuguese that focused on physicians' perceptions of PS-ES.

Results The search yielded 17 publications published between 2002 and 2017. Physicians do not hold clear views or agree if and when PS-ES is appropriate. Case-related and individual-related factors that influenced physicians' perceptions were identified. There is still no consensus regarding criteria to distinguish between necessary and sufficient conditions for invoking PS-ES. Some alternatives to PS-ES were identified.

Conclusions To date, there is still no consensus on physicians' perceptions of PS-ES. Further research is necessary to understand factors that influence physicians' perceptions and philosophical-ethical presuppositions underlying this perceptions.

BACKGROUND

Palliative sedation (PS) is an exceptional last-resort treatment to alleviate refractory symptoms at the end of a patient's life. This kind of intervention should not be conflated with the practices of hastening death, euthanasia or physician-assisted suicide.[1] PS is defined here as 'the monitored use of medications intended to induce a state of decreased or absent awareness (unconsciousness) in order to relieve the burden of otherwise intractable suffering in a manner that is ethically acceptable to the patient, family, and healthcare providers'.[2] p. 581 PS is used to mitigate physical refractory symptoms (eg, dyspnoea, nausea, vomiting, physical pain) and psychological distress (eg, anxiety, anguish, depression, delirium). Intractable suffering or refractory symptoms refer 'to symptoms that cannot be adequately controlled despite aggressive efforts to identify a tolerable therapy that does not compromise consciousness'.[3] p. 143

The complex nature of existential suffering (ES)[4–7] continues to fuel the controversy about whether it is a main indication for PS or not (especially if physical pain is under control).[8–10] Distinguishing kinds of suffering is problematic in itself, and objective or subjective assessment of different kinds of suffering is a hotly debated topic in the medical literature.[11] The definition of ES is elusive, because the boundaries between it and other kinds of suffering (psychological, social and spiritual) are blurred.[12] In the medical literature, ES has been discussed in terms of loss of dignity, demoralisation, dependency, fear, panic, death anxiety, hopelessness, worthlessness, meaninglessness, loneliness, isolation, loss of control, lack of social support, being battle-weary, being mentally exhausted or worn out. For our purposes, we assume that ES is

pain, distress or hardship due to a loss or interruption of meaning, purpose or hope in life.[13]

Physicians have a primary, personal responsibility in clarifying the decision-making for patients, families and caregivers considering palliative sedation for existential suffering (PS-ES), and they play a key role in the discussions. A review of ethical aspects of PS-ES revealed that physicians' anthropological models and philosophical presuppositions underpin the ethical debate on PS-ES.[14]

To better understand how physicians really feel about PS-ES and what causes them either to apply it or not, requires further elucidation through an interdisciplinary approach. A previous non-systematic review of seven qualitative studies concluded that there is a general disapproval from physicians regarding the use of PS-ES.[15] Nevertheless, an in-depth analysis and review of physicians' perceptions of PS-ES in qualitative, quantitative and mixed-methods studies has not been performed yet. Such an analysis, bringing together these results, is an important step in reaching a better understanding of PS-ES, in establishing more robust evidence regarding factors that influence physicians' perceptions of PS-ES, as much as conditions for implementing and alternatives to PS-ES.

Aims and research question

This systematic review intends to appraise evidence in the international literature on how physicians perceive PS-ES, the factors that influence their perceptions, how do they perceive the conditions for implementing it and the alternatives to PS-ES. Our research question can be formulated as follows :

What are palliative care physicians' perceptions of PS-ES?

METHODS

Design

We followed systematic-review best practices to formulate a search strategy and conduct a systematic review of quantitative, qualitative and mixed-methods studies.[16] The search protocol was bolstered by clear study objectives and inclusion criteria. The search protocol comprised four steps:

1. A systematic search of relevant literature databases was done, followed by the snowball method and citation chasing;[17] the Peer Review Electronic Search Strategies (PRESS) electronic search protocol was used,[18] and Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) was used for reporting systematic reviews.[19 20]
2. Identification and selection of pertinent publications using predefined inclusion and exclusion criteria.
3. Quality appraisal of research evidence from the selected publications using the Critical Appraisal Skills Programme[21] and assessment criteria of Hawker's tool.[22]
4. Data extraction and synthetisation of results from selected publications using thematic synthesis.[23 24]

Search strategy

We performed electronic queries in PubMed, CINAHL, Embase, Scopus, Web of Science, PsycINFO, PsycARTICLES, aiming to achieve full coverage of the PS-ES subject. We developed the search strategies and search strings in collaboration with a professional librarian having expertise in the biomedical sciences databases. The search strings combined four main concepts (online supplementary table 1): PS, subjective dimension, population, ES. We performed and completed the electronic database search on first March 2019, without any lower limit for publication date.

The references identified were merged and managed in a unique EndNote V.X8.2 (Clarivate Analytics, Philadelphia, Pennsylvania, USA) reference library. Duplicate records were removed prior to applying the following filters: type of document (peer-reviewed journal article); publication language (English, French, German, Dutch, Italian, Spanish, Portuguese). Two authors independently conducted both title-abstract and full-text screening of the final reference list. If disagreements arose about including an article, the two screeners discussed and resolved the disagreements until consensus was reached. To ensure the maximum coverage possible, we also used snowball and citation chasing methods to identify additional candidate articles for inclusion.

Inclusion and exclusion criteria

Studies reporting on empirical research using quantitative, qualitative or mixed-methods approaches were eligible for inclusion. We included only peer-reviewed journal articles published in English, French, German, Dutch, Spanish, Italian or Portuguese.

Publications were eligible for inclusion if the study included physicians as participants. If other healthcare professionals were also included, we required that the reported data clearly distinguish physicians' perceptions, attitudes, opinions, and so on. If physicians' data in a candidate article was not clearly tabulated separately, then we required that physicians comprised the majority of the study sample (>60%).

We focused on studies reporting on physicians' perceptions of PS reporting at least partially on aspects of PS-ES, but we excluded articles reporting only on actual physicians' experiences.

Quality assessment

Two researchers independently assessed the quality of candidate publications that met the inclusion criteria. The researchers compared their assessment of the selected full-text publications and sought consensus in case of disagreement. The quality assessment is indicative and does not constitute an inclusion/exclusion criterion determining the eligibility of the articles for this systematic review.

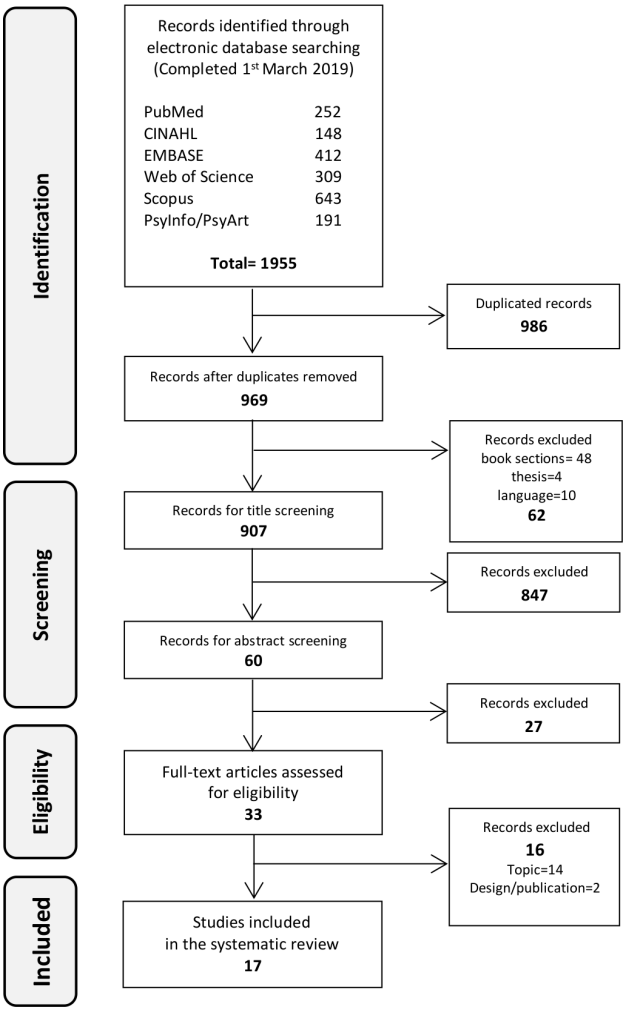

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram.

Data extraction and synthesis

We extracted data from the included articles using a standardised form (online supplementary table 2abc), and we used a thematic synthesis method for synthesising evidence. This synthesis consisted of: (A) Identifying the findings in the results section. (B) Coding passages using categories extracted from the studies having the highest methodological quality. (C) Adapting the coding tree (D) Developing descriptive categories and grouping those having similar codes.

RESULTS

Included studies

A total of 1955 papers was screened (figure 1), but only 17 met our inclusion criteria. Seven studies were reports of quantitative studies,[25–31] seven were reports of qualitative studies[32–38] and three[39–41] were reports of mixed-methods studies. The included articles were published between 2002 and 2017. The studies were conducted in USA (n=4); Canada (n=3); Switzerland (n=2); the Netherlands (n=2); Belgium (n=1); Germany (n=1); Japan (n=1); and in some cases, multiple countries (n=3). Two articles used data from the same quantitative study.[25 26] One mixed-methods study[39] compared the results of two other studies.[40 41] Qualitative studies used semi-structured interviews (n=6) or a focus group (n=1);[32] the quantitative studies (n=7) and two mixed-methods studies used a questionnaire, sometimes along with vignettes (n=4).[25 27 40 41]

In qualitative studies, sample sizes ranged from 19 to 54 participants; in quantitative studies, from 81 to 1156 participants; and in mixed-methods studies, from 74 to 175 participants. Most studies (n=13) focused exclusively on physicians' perceptions, but some additionally included perceptions of nurses (32), pharmacists,[41] or professionals in several fields (eg, philosophy, theology, ethics, sociology, law).[28 34] One qualitative study[35] and three quantitative studies[26 29 30] focused exclusively on PS-ES, while other studies had wider foci related to PS.

Quality assessment

All the qualitative studies obtained a good overall assessment (15–18/20) in our analysis (online supplementary table 3). They expanded what was then known about perspectives on PS-ES, offered insight on factors influencing perspectives on PS-ES, suggested new ideas for further research, and had implications for policy and practice. However, all articles failed to adequately consider the relationship between the researcher and participants.

Our quality assessment of the quantitative and mixed-methods studies supported their relevance (19–23/27) in determining physicians' perspectives of PS-ES (online supplementary table 4). Nevertheless, transferability and generalisability of the findings and impact on theory, policies and practice were weakly addressed in these quantitative and mixed-method studies.

Thematic synthesis

We categorised the results of our study by using thematic synthesis: (A) General attitudes towards and arguments for and against PS-ES. (B) Factors that influence general attitudes. (C) Conditions for implementing PS-ES. (D) Alternatives to PS-ES.

General attitudes towards and arguments for and against PS-ES

Seven studies described the general attitudes of physicians towards PS-ES, and 11 studies described arguments for or against PS-ES.

General attitudes

Positive attitudes towards PS-ES varied widely, with the following percentage of the physicians showing positive attitudes: 6.8%,[29] 22%,[30] 31%,[25 26] 42.1%,[31] 37%–61%[28] and 68% positive attitudes.[27] The range of negative attitudes varied widely also, with the following percentage of physicians showing negative attitudes: 14.3%,[29] 17.1%,[31] 34%,[25 26] 23%–43%[28]

and 64% negative attitudes.[30] The percentages of participants having neutral or undecided attitudes were 14%,[30] 16%–20%,[28] 29.6%[31] and 47%.[29] The heterogeneity of the quantitative results reveals a lack of consensus that is also manifested by the variety of arguments for and against PS-ES.

Arguments for PS-ES

Explicit arguments in support of PS-ES stated that drug treatment for psychological symptoms requires 2–4 weeks to take effect and that the patient's body needs to be able to adequately metabolise the drug(s); moreover, psychological interventions are not appropriate for all patients, because this kind of intervention requires that the patient have sufficient energy, be competent, desire to engage in psychotherapy and should not be physically exhausted.[35] Some physicians said that it would be unethical to refuse PS-ES if patients request it.[39] They thought that PS-ES is a more humane solution than euthanasia and physician-assisted suicide, because physicians can accompany and care for their patients until death.[36]

Arguments against PS-ES

A major argument against PS-ES is the complex nature of ES and the implications of not fully understanding its nature.[30 32–35 37 38] Physicians against PS-ES appealed to the inconsistency in symptom classification and the complex interaction between physical and psycho-existential suffering,[34] the difficulty to assess ES objectively,[32 34] the refractoriness of ES and the appropriateness of PS.[40 41] PS-ES does not seem justified when physical symptoms are under control, when the patient does not request it from the care team, and when the family physically and emotionally supports the patient.[40]

One quantitative study found that 36% of physicians believed that PS-ES hastens death.[30] For other physicians, PS-ES represented abandonment of the patient,[41] essentially a form of euthanasia,[30 36 39–41] a semieuthanasic act[36] or a form of physician-assisted suicide.[30 39] PS-ES can also be difficult to manage when the prognosis suggests the patient will live for a long time, when the patient will be a burden for health professionals or when implementing PS-ES will make communicating with the patient difficult.[36 40] Some physicians also have an unfavourable attitude towards PS-ES, because relatives and the care team sometimes are excluded from the decision-making process.[36 40] The possibility of PS-ES becoming common practice might ultimately lead to a 'slippery slope' in healthcare decision-making that should be avoided.[32] For others protective safeguards are needed.[34]

Factors that influence general attitudes

Eleven studies reported on case-related or individual-related factors that influence physicians' attitudes about PS-ES. Ten studies examined correlations between case-related or individual-related factors and PS-ES support (table 1).

Case-related factors

Type of suffering

One quantitative study[29] provided statistical support (table 1) for the idea that there are less favourable attitudes towards PS-ES than PS for refractory physical pain. This result is consistent with those of two mixed-methods studies from Quebec and Switzerland,[40 41] in which the authors examined cases of prognoses conveying short-term and long-term survival. These two studies confirmed (table 1) that only the type of suffering had a significant impact on physicians' attitudes towards sedation. However, other studies[26 27] suggest that some physicians possess similar attitudes towards PS for physical pain and PS-ES, although this relationship was not examined quantitatively.

Prognosis

Two mixed-methods studies[40 41] compared by Dumond[39] showed that neither the prognosis nor the interaction between prognosis and type of suffering influence physicians' attitudes towards PS-ES (table 1). One quantitative study[28] showed that physician-ethicists in a German setting are more favourable towards applying PS-ES for a terminal patient (61%) than for a non-terminal patient but with an unfavourable prognosis (37%). Others in this study thought that PS-ES is unacceptable for either situation (23% vs 43%, respectively).

Individual-related factors

Training

Some factors are related to characteristics of the physician being assessed. One study[29] showed that postgraduate physician residents (postgraduate year 2–4) were more supportive of PS-ES than first-year postgraduate residents (87% vs 30.2%; table 1). Voeuk *et al*[30] showed (table 1) that additional training in palliative medicine does not significantly affect physicians' views on PS-ES (no additional training vs 1 year of additional training).

Experience

Voeuk *et al*'s study[30] also showed (table 1) that participants' views on PS-ES were not significantly different based on the amount of clinical experience (<15 years vs 15–35 years). Another study[25] revealed that physicians who induced intentional sedation to the point of unconsciousness were more likely to agree to the statement that ES should be treated with PS (table 1). Morita *et al*'s study[27] showed that physicians with modest end-of-life experience in their practice and with less general clinical experience would be more likely to consider euthanasia or physician-assisted suicide as alternatives to PS-ES (table 1).

Table 1 Tested whether various case-related and individual-related factors of participants were associated with PS-ES support

Publication	Type of suffering	Prognosis	Interaction between type of suffering and prognosis	Training	Experience	Specialty	Country	Psychological factors	Religiosity and spirituality
Quantitative studies									
Cripe *et al*[29] (2017)	p<0.001			p=0.011					OR=0.21 95% CI 0.05 to 0.89, p=0.03
Maiser *et al*[31] (2017)							p=0.270		p=0.289
Morita *et al*[27] (2002)					OR=0.63 95% CI 0.43 to 0.94, p=0.023			OR=1.02; 95% CI 1.00 to 1.04, p=0.060	
Putman *et al*[25] (2013)					p<0.001				OR=0.4 95% CI 0.2 to 0.9
Simon *et al*[28] (2007)									
Smyre *et al* [26] (2015)						OR=2.2 95% CI 1.3 to 3.6 OR=3.5 95% CI 1.5 to 8.4			OR=2.7 95% CI 1.2 to 5.7 OR=2.6 95% CI 1.2 to 5.5
Voeuk *et al*[30] (2017)				p>0.05	p>0.05				
Mixed-methods studies									
Dumont *et al*[39] (2015) Comparing [40] and [41]							Wilcoxon LP-ES=0.0577 LP-PP=0.5730 SP-ES=0.3260 SP-PP=0.0914		
Beauverd *et al*[40] (2014)	F=33.92 df=1 p<0.000[1]	F=0.406 df=1 p=0.526	F=1.308 df=1 p=0.257						
Blondeau *et al*[41] (2005)	F=63.17 df=1 p<0.0001	F=2.84 df=1 p=0.0944	F=0.13 df=1 p=0.7238						

df, degrees of freedom; ES, existential suffering; LP, long-term prognosis;PP, physical pain; PS, palliative sedation; SP, short-term prognosis.

Specialty

Smyre *et al*'s study[26] tested differences among physicians' specialties with regard to attitudes towards PS-ES (table 1) and found that geriatricians, hospice and palliative care physicians were significantly likely to agree that they should seek to relieve ES as much as physical pain. By contrast, nephrologists were at higher odds of strongly disagreeing that it was their duty to treat, even sometimes, the psychological and spiritual suffering of terminally ill patients with PS (table 1).

Differences between countries

Some studies established comparisons between physicians' attitudes from different countries or nationalities. Maiser *et al*'s study[31] failed to find a statistically significant difference (table 1) in attitudes towards PS-ES among physicians of different nationalities (US clinicians vs non-US). In another study,[39] the attitudes of physicians in Quebec (where physician-assisted suicide was illegal at the time of the study) and those from Switzerland (where physician-assisted suicide is legal) tended to be different (but statistically non-significant; table 1) when a patient had a long-term prognosis with ES and for a short-term prognosis accompanied by physical suffering. In both cases Swiss physicians were less disposed to employ PS.

Psychological factors

Morita *et al*'s study[27] on physicians in Japan showed (table 1) that a higher level of emotional exhaustion influenced physicians' attitudes towards PS-ES. A qualitative study[32] suggested that some physicians might be willing to consider using PS-ES if they could empathise with and understand the patient's suffering.

Religiosity and spirituality

One study[29] found support to the hypothesis that in physician residents having higher intrinsic religious motivation, greater optimism was associated with less support for PS-ES (table 1). Another study[26] showed (table 1) that physicians identifying themselves as Protestant evangelical more strongly agreed when compared with physicians having no affiliation, that 'physicians should seek to relieve patients' spiritual suffering just as much as patients' physical pain' (table 1). On the other hand, the former group more strongly disagreed compared with the latter group that 'doctors should sometimes treat the psychological and spiritual suffering of terminally ill patients by sedating the patient to unconsciousness' (table 1). Along the same lines, another study[25] tested the hypothesis (table 1) that physicians identifying themselves as Hindu were less likely to agree with the statement that physicians should sometimes treat ES by sedating the patient to unconsciousness. They also found support for the hypothesis that Hindu physicians as well as physicians identifying themselves with other religions would be less likely to opt for PS-ES compared with physicians who had no religion.

By contrast, another study[31] failed to find statistically a significant difference in the attitudes towards PS-ES of physicians who worked in religiously affiliated institutions (table 1). Cripe *et al*'s study[29] also showed that moral guidelines based on religious tradition do not significantly influence complex medical decisions.

Conditions for implementing PS-ES

Twelve studies identified certain conditions under which physicians would likely consider using PS-ES. These conditions will be considered in turn.

Prognosis and refractoriness

In two qualitative studies physicians would only support PS-ES if the patient presented physical deterioration[33] and short life expectancy.[35] Even if refractory symptoms are usually a condition for PS, it is still controversial among physician participants whether refractoriness of ES is a condition for implementing PS.[34 35 37 40] Sometimes assessment of refractoriness by a psychiatrist would be deemed suitable by physicians,[35] as would the involvement of a multidisciplinary team to assess the nature and the true refractoriness of ES.[34]

Conjunction with physical suffering and withdrawal of nutrition

In some studies, physician participants stated that ES should be accompanied by physical suffering to consider PS.[32–35 38] However, in a study conducted in Canada, 43% of physicians stated they would agree to use PS-ES in the absence of physical refractory pain, while 40% would disagree.[30]

In a study conducted in Germany, 55% of physicians[28] reported that PS-ES accompanied by withdrawal of nutrition in a dying patient would be acceptable, while 29% would consider it unacceptable. However, with a patient having an unfavourable prognosis, 32% said it would be acceptable, and 48% said it would be unacceptable.

Patients' request, family involvement and team decision

Compared with physician experience, guideline indications and religious beliefs, a patient's expressed wishes are considered by physicians in postgraduate training to be the most important factor that influences complex medical decisions.[29] Regarding the decision-making process, some physicians stressed the importance of considering the patient's explicit request for sedation,[35 39 40] consultation and involvement of the family in the decision,[36 40] decision of the primary care team[40] or the consultation with a multidisciplinary team.[34]

Alternatives to PS-ES

Seven studies reported results on physicians' views of alternatives to PS-ES that they might consider using.

Palliative care, mild and intermittent sedation, withdrawal of nutrition

As an alternative to using PS-ES, another approach to treating ES is to evaluate other medications to manage ES[39–41] or to use intermittent sedation in modified PS-ES.[35 36 40 41] Morita *et al*'s study[27] revealed that while some physicians (49%) would consider using palliative care without PS-ES, others (83%) would propose intermittent-deep sedation, or mild sedation with psychotropics (79.6%) or opioids (71.8%) as an alternative to PS-ES.

Sixty-eight per cent of physicians in Germany who were surveyed[28] have favourable attitudes towards using nutrition withdrawal (without accompanying PS) in a dying patient, while 21% would consider it to be an unacceptable way of managing refractory ES. With a patient having an unfavourable prognosis, 52% would find PS-ES to be acceptable, while 34% would consider it still unacceptable.

Psychological and spiritual care

For a sample of physicians practising in Japan, 42% reported that they would consider psychiatric treatment for managing ES without intentional sedation; 15% of the physician's sample said it would be a strong possibility for them.[27] Nevertheless, this same study revealed that physicians choosing PS-ES as a strong possibility are less confident about recommending psychological care as a treatment possibility compared with other possibilities (p=0.058).

Given the complex nature of ES, psychological and spiritual intervention is sometimes an alternative to PS-ES, especially for patients with ES having a long-term survival prognosis.[40 41] In one study[35] it was found that, for some physicians, using PS-ES might be considered after failed attempts using pharmacological and psychological interventions; psychological interventions were not considered to be suitable in circumstances in which the patient has little energy, is incompetent or does not want to get involved with psychotherapy; sometimes, talking and spending extra time with the patient was considered by some physicians to be an alternative to PS-ES. In another study physicians proposed simply waiting for resolution of ES could be an alternative to PS-ES.[40]

Physician-assisted suicide and euthanasia

Some physicians said that they would sometimes propose physician-assisted suicide or euthanasia as a more adequate intervention to deal with ES.[36 39 40] However, Morita *et al*'s study[27] revealed that only 8.4% of physicians in Japan would consider physician-assisted suicide or euthanasia to be adequate for dealing with ES (8% possibly thought so; 0.4% thought it was a strong possibility). The physicians sustaining this position were less involved in end-of-life care (table 1). A study comparing the attitudes of physicians in Québec and Switzerland[39] revealed that where physician-assisted suicide is legally permitted, as with Switzerland, physicians would be more inclined to discuss physician-assisted suicide than PS with patients having refractory ES.

DISCUSSION

Main findings

We set out to better understand how physicians perceive PS-ES and the factors that affect those perceptions. Our results from a systematic literature review showed that physicians do not hold clear views or consensus on under which circumstances and conditions PS-ES is appropriate. Our results support the observation that PS-ES is still a very controversial issue among physicians.

A major difficulty in moving forward concerns unambiguously characterising and understanding the nature of suffering, in general, and of ES, in particular. Among the several approaches advanced on the nature of suffering, which one should guide decision-making about PS? A subjective holistic approach[42] considers suffering to be present when a disruption in a person's existential integrity is the dominant subjective experience. This means that physicians should address every instance of a patient's suffering, whether it be perceived or even ES. On the other hand, an objective teleological approach of suffering[43] argues that physicians should only relieve suffering that can only be objectively assessed using reliable clinical methods. In this case, PS would be considered only for physical pain, meaning that ES should be preferably relieved by psychotherapeutic or spiritual kinds of interventions.

This conceptual problem on the nature and the objective/subjective assessment of ES is linked to the question of who has the prerogative to determine whether ES is present: the patient or the physician. Moreover, doubts about its refractory nature destabilises clinical-ethical decision-making regarding PS-ES. A lack of robust conceptual and ethical arguments grounding PS-ES decision-making and practices clearly contributes to the controversial status of PS-ES and the absence of consensus among physicians.[44] The above-mentioned systematic review on ethical aspects of PS-ES[14] revealed that implicit anthropological models and philosophical presuppositions underpin the ethical debate on PS-ES. However, considering the present systematic review of empirical evidence on physicians' perceptions of PS-ES, it is revealed that philosophical presuppositions and ethical arguments remain mostly unclear and unexpressed. The practical aspects of implementing PS-ES predominates in reporting physicians' attention.

Several factors seem to have an influence on general attitudes towards PS-ES, even though not all have been evaluated quantitatively (table 1). In studies where prognosis and interaction of prognosis and type of suffering did not influence physicians' attitudes towards PS-ES,[40 41] the type of suffering seemed to

determine their attitude: Physicians were more favourable towards PS for physical pain than to PS-ES.[29 40 41] The influence of individual-related factors (ie, those related to the individual characteristics of a physician) were inconclusive, because different studies are sometimes contradictory or because the studies were insufficient and thus failed to produce clear evidence. These individual-related factors include extent and type of training,[29 30] years of experience,[25 27 30] type of medical specialty,[26] country of practice[27–35 39–41] and psychological factors.[27]

The degree of physicians' religiosity and spirituality seems to affect their attitudes towards PS-ES.[25 26 29] Physicians having a religious affiliation tend to have a more negative attitude towards PS-ES. This outcome suggests that philosophical-ethical presuppositions—most of the time being tacit and implicit—influence physicians' attitudes towards PS-ES. This is a hypothesis that needs to be evaluated more rigorously by further research.

Conditions for implementing PS-ES were evident, but there is still no consensus regarding criteria to distinguish between necessary and sufficient conditions for invoking PS-ES. Similarly, alternatives to PS-ES are proposed without a strong ethical argumentation grounding them. In countries where euthanasia/physician-assisted suicide is legal, they are sometimes presented as more acceptable alternatives to PS-ES.[44] Attempts to avoid the complexity and controversial aspects of PS-ES by replacing it with euthanasia/physician-assisted suicide risks sliding down a slippery slope. Hence, more effort should be directed towards exploring the complexity behind physicians' perceptions towards PS-ES.

Strengths and weaknesses

This systematic review used robust methodology for evaluating the literature, following PRESS and PRISMA review protocols. The research process and quality appraisal of the 17 included articles were conducted by two independent researchers. Although articles published in seven languages were screened, assuring an international coverage of the subject, the articles meeting the inclusion criteria were in English. Different types of studies from many different countries were represented in the final group of selections, assuring that a wide range of cultural contexts and legal frameworks were sampled for physicians' perceptions.

Implications for practice, theory and policy

As of early 2019, there is no published solid and coherent guidance for clinical-ethical decision-making regarding the use of PS-ES. Moreover, existing clinical practice guidelines reveal much ambiguity and divergence surrounding PS-ES.[45–48] The controversial character of PS-ES that is now reflected in the diversity of physicians' attitudes towards it, as analysed in this systematic review, suggests that it is premature to try to establish clear guidance about PS-ES. More qualitative research is needed to explore and to make explicit the philosophical-ethical presuppositions underlying physicians' attitudes towards PS-ES. An in-depth analysis of these presuppositions, complemented by advanced philosophical reflection on the nature of ES, will advance a better understanding of what prevents physicians from expressing clear and well-thought-out attitudes towards PS-ES.

CONCLUSIONS

This study brings into light that there is no uniformity and consensus on physicians' perceptions of PS-ES, of conditions of application and of alternatives. Further research is needed to gain deeper insight into factors that influence physicians' perceptions of PS-ES as well as into the philosophical-ethical presuppositions underlying these perceptions.

Acknowledgements The authors thank Mrs Christine Lanners, specialist librarian of the Health Sciences Library for her contribution to the electronic database search.

Contributors Study concept and design, acquisition of data, title/abstract/full-text screening, analysis and interpretation of data: PR and CG; drafting of the manuscript, critical revision of the manuscript and approval: PR, CG and JM; Study supervision: CG.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Hahn MP. Review of palliative sedation and its distinction from euthanasia and lethal injection. *J Pain Palliat Care Pharmacother* 2012;26:30–9.
2 Cherny NI, Radbruch L, Board of the European Association for Palliative Care. European association for palliative care (EAPC) recommended framework for the use of sedation in palliative care. *Palliat Med* 2009;23:581–93.
3 Cherny NI, ESMO Guidelines Working Group. ESMO clinical practice guidelines for the management of refractory symptoms at the end of life and the use of palliative sedation. *Ann Oncol* 2014;25 Suppl 3(suppl 3):iii143–52.
4 Svenaeus F. The phenomenology of suffering in medicine and bioethics. *Theor Med Bioeth* 2014;35:407–20.
5 Bozzaro C. The concept of suffering in medicine: an investigation using the example of deep palliative sedation at the end of life. *Ethik Med* 2015;27:93–106.
6 Cassell EJ. The nature of suffering. In: Youngner S, Arnold R, eds. *The Oxford Handbook of ethics at the end of life*. Oxford University Press, 2016: 216–26.
7 Bueno-Gómez N. Conceptualizing suffering and pain. *Philos Ethics Humanit Med* 2017;12.
8 Sulmasy DP, Jansen LA. Terminal sedation: conceptual clarifications and moral controversies. *J Gen Intern Med* 2002;17.
9 Cassell EJ, Rich BA. Intractable end-of-life suffering and the ethics of palliative sedation. *Pain Med* 2010;11:435–8.
10 Rainone F. Palliative sedation: controversies and challenges. *Prog Palliat Care* 2015;23:153–62.

11 Bozzaro C, Schildmann J. "Suffering" in Palliative Sedation: Conceptual Analysis and Implications for Decision Making in Clinical Practice. *J Pain Symptom Manage* 2018;56:288–94.
12 Krikorian A, Limonero JT, Maté J. Suffering and distress at the end-of-life. *Psychooncology* 2012;21:799–808.
13 Kirk TW, Mahon MM. National hospice and palliative care organization (NHPCO) position statement and commentary on the use of palliative sedation in imminently dying terminally ill patients. *J Pain Symptom Manage* 2010;39:914–23.
14 Rodrigues P, Crokaert J, Gastmans C. Palliative sedation for Existential suffering: a systematic review of Argument-Based ethics literature. *J Pain Symptom Manage* 2018;55:1577–90.
15 Lam M, Lam H, Agarwal A, *et al*. Clinicians' views on palliative sedation for existential suffering: a systematic review and thematic synthesis of qualitative studies. *J Pain Manage* 2017;10:31–40.
16 Dixon-Woods M, Agarwal S, Jones D, *et al*. Synthesising qualitative and quantitative evidence: a review of possible methods. *J Health Serv Res Policy* 2005;10:45–53.
17 Greenhalgh T, Peacock R. Effectiveness and efficiency of search methods in systematic reviews of complex evidence: audit of primary sources. *BMJ* 2005;331:1064–5.
18 McGowan J, Sampson M, Salzwedel DM, *et al*. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. *J Clin Epidemiol* 2016;75:40–6.
19 Moher D, Liberati A, Tetzlaff J, *et al*. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *International Journal of Surgery* 2010;8:336–41.
20 Shamseer L, Moher D, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;349:g7647.
21 CASP. Critical appraisal skills programme (CASP), 2017. Available: http://docs.wixstatic.com/ugd/dded87_25658615020e427da194a325e7773d42.pdf
22 Hawker S, Payne S, Kerr C, *et al*. Appraising the evidence: reviewing disparate data systematically. *Qual Health Res* 2002;12:1284–99.
23 Thomas J, Harden A. Methods for the thematic synthesis of qualitative research in systematic reviews. *BMC Med Res Methodol* 2008;8:45.
24 Kavanagh J, Campbell F, Harden A. Mixed methods synthesis: A worked example. In: Hannes K, Lockwood C, eds. *Synthesizing qualitative research choosing the right approach*. Wiley-Blackwell, 2012: 113–36.
25 Putman MS, Yoon JD, Rasinski KA, *et al*. Intentional sedation to unconsciousness at the end of life: findings from a national physician survey. *J Pain Symptom Manage* 2013;46:326–34.
26 Smyre CL, Yoon JD, Rasinski KA, *et al*. Limits and responsibilities of physicians addressing spiritual suffering in terminally ill patients. *J Pain Symptom Manage* 2015;49:562–9.
27 Morita T, Akechi T, Sugawara Y, *et al*. Practices and attitudes of Japanese oncologists and palliative care physicians concerning terminal sedation: a nationwide survey. *JCO* 2002;20:758–64.
28 Simon A, Kar M, Hinz J, *et al*. Attitudes towards terminal sedation: an empirical survey among experts in the field of medical ethics. *BMC Palliat Care* 2007;6:1–7.
29 Cripe LD, Perkins SM, Cottingham A, *et al*. Physicians in postgraduate training characteristics and support of palliative sedation for Existential distress. *Am J Hosp Palliat Care* 2017;34:697–703.
30 Voeuk A, Nekolaichuk C, Fainsinger R, *et al*. Continuous Palliative Sedation for Existential Distress? A Survey of Canadian Palliative Care Physicians' Views. *J Palliat Care* 2017;32:26–33.
31 Maiser S, Estrada-Stephen K, Sahr N, *et al*. A survey of hospice and palliative care clinicians' experiences and attitudes regarding the use of palliative sedation. *J Palliat Med* 2017;20:915–21.
32 Rietjens JAC, Buiting HM, Pasman HRW, *et al*. Deciding about continuous deep sedation: physicians' perspectives: a focus group study. *Palliat Med* 2009;23:410–7.
33 Robijn L, Chambaere K, Raus K, *et al*. Reasons for continuous sedation until death in cancer patients: a qualitative interview study. *Eur J Cancer Care* 2017;26:e12405–9.
34 Papavasiliou E, Payne S, Brearley S. Current debates on end-of-life sedation: an international expert elicitation study. *Support Care Cancer* 2014;22:2141–9.
35 Anquinet L, Rietjens J, van der Heide A, *et al*. Physicians' experiences and perspectives regarding the use of continuous sedation until death for cancer patients in the context of psychological and existential suffering at the end of life. *Psychooncology* 2014;23:539–46.
36 Foley R-A, Johnston WS, Bernard M, *et al*. Attitudes regarding palliative sedation and death hastening among Swiss physicians: a contextually sensitive approach. *Death Stud* 2015;39:473–82.
37 Blondeau D, Dumont S, Roy L, *et al*. Attitudes of Quebec doctors toward sedation at the end of life: an exploratory study. *Pall Supp Care* 2009;7:331–7.
38 Swart SJ, van der Heide A, van Zuylen L, *et al*. Continuous palliative sedation: not only a response to physical suffering. *J Palliat Med* 2014;17:27–36.
39 Dumont S, Blondeau D, Turcotte V, *et al*. The use of palliative sedation: a comparison of attitudes of French-speaking physicians from Quebec and Switzerland. *Pall Supp Care* 2015;13:839–47.
40 Beauverd M, Bernard M, Currat T, *et al*. French Swiss physicians' attitude toward palliative sedation: influence of prognosis and type of suffering. *Pall Supp Care* 2014;12:345–50.
41 Blondeau D, Roy L, Dumont S, *et al*. Physicians' and Pharmacists' Attitudes toward the use of Sedation at the End of Life: Influence of Prognosis and Type of Suffering. *J Palliat Care* 2005;21:238–45.
42 Cassell EJ. *The nature of suffering and the goals of medicine*. 2nd edn. Oxford University Press, 2004.
43 van Hooft S. Suffering and the goals of medicine. *Med Health Care Philos* 1998;1:125–31.
44 Gaignard M-E, Hurst S. A qualitative study on existential suffering and assisted suicide in Switzerland. *BMC Med Ethics* 2019;20:34.
45 Abarshi E, Rietjens J, Robijn L, *et al*. International variations in clinical practice guidelines for palliative sedation: a systematic review. *BMJ Support Palliat Care* 2017;7:bmjspcare-2016-001159–9.
46 Gurschick L, Mayer DK, Hanson LC. Palliative sedation: an analysis of international guidelines and position statements. *Am J of Hosp & Palliat Med* 2015;32:660–71.
47 Schildmann E, Schildmann J. Palliative sedation therapy: a systematic literature review and critical appraisal of available guidance on indication and decision making. *J Palliat Med* 2014;17:601–11.
48 Ciancio AL, Mirza RM, Ciancio AA, *et al*. The use of palliative sedation to treat Existential suffering: a scoping review on practices, ethical considerations, and guidelines. *J Palliat Care* 2019:1–8.