

Review Article

Palliative Sedation for Existential Suffering: A Systematic Review of Argument-Based Ethics Literature



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Abstract

Context. Although unanimity exists on using palliative sedation (PS) for controlling refractory physical suffering in end-of-life situations, using it for controlling refractory existential suffering (PS-ES) is controversial. Complicating the debate is that definitions and terminology for existential suffering are unclear, ambiguous, and imprecise, leading to a lack of consensus for clinical practice.

Objectives. To systematically identify, describe, analyze, and discuss ethical arguments and concepts underpinning the argument-based bioethics literature on PS-ES.

Methods. We conducted a systematic search of the argument-based bioethics literature in PubMed, CINAHL, Embase®, The Philosopher's Index, PsycINFO®, PsycARTICLES®, Scopus, ScienceDirect, Web of Science, Pascal-Francis, and Cairn. We included articles published in peer-reviewed journals till December 31, 2016, written in English or French, which focused on ethical arguments related to PS-ES. We used *Peer Review of Electronic Search Strategies* protocol, *Preferred Reporting Items for Systematic Reviews and Meta-Analyses*, and *The Qualitative Analysis Guide of Leuven* for data extraction and synthesis of themes.

Results. We identified 18 articles that met the inclusion criteria. Our analysis revealed mind-body dualism, existential suffering, refractoriness, terminal condition, and imminent death as relevant concepts in the ethical debate on PS-ES. The ethical principles of double effect, proportionality, and the four principles of biomedical ethics were used in argumentations in the PS-ES debate.

Conclusion. There is a clear need to better define the terminology used in discussions of PS-ES and to ground ethical arguments in a more effective way. Anthropological presuppositions such as mind-body dualism underpin the debate and need to be more clearly elucidated using an interdisciplinary approach. *J Pain Symptom Manage* 2018;55:1577–1590. © 2018 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.

Key Words

Systematic review, deep sedation, ethics, palliative sedation, end-of-life care, existential suffering

Introduction

Palliative sedation (PS) is considered a treatment of last resort in end-of-life care for the management of intolerable and refractory symptoms in the final stages of life. The terminology used for sedation in end-of-life situations is confusing and needs clarification and systematization.^{1–7} Systematic reviews to date have covered the main findings related to specific issues in

PS, such as its definition^{8–10} and distinction from euthanasia, physician-assisted suicide and lethal injection,¹¹ indications¹² and decision making regarding its initiation and continuation,^{13–15} medication and monitoring during application,^{16–19} survival time once it has begun,^{20,21} guidelines to use,^{22,23} recommendations for standards,²⁴ perspectives of relatives²⁵ and caregivers,^{26,27} and ethical issues related to its use.^{28–32}

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Because PS is used to alleviate refractory symptoms at the end of life,³³ it is important to distinguish PS from minimal sedation (anxiolysis), moderate sedation (conscious sedation), and general anesthesia. This distinction becomes clearer when refractory symptoms and PS are precisely defined. As Cherny³⁴(p. 143) proposed, “refractory symptoms” refer to “symptoms that cannot be adequately controlled despite aggressive efforts to identify a tolerable therapy that does not compromise consciousness.” Broeckaert³⁵(p. 246) defined PS as “the intentional administration of sedatives in such dosages and combinations as required to reduce the terminal patient’s consciousness as much as needed to adequately control one or more refractory symptoms.”

PS has been used to deal with not only physical refractory symptoms (e.g., dyspnea, nausea, vomiting) but also nonphysiological refractory symptoms, such as psychological distress (anxiety, anguish, depression, delirium, etc.)³⁶ and existential suffering (e.g., hopelessness, meaninglessness, fear, panic, etc.).^{37,38} Applications of PS for nonphysiological refractory symptoms have provoked much debate because the nature of suffering (e.g., physical, psychological, social, existential, spiritual) is still controversial.³⁹ As existential suffering requires subjective assessment by a health professional and because a clear conceptual framework for understanding the full range of suffering and pain is still lacking, there are great differences in how physicians choose to control nonphysiological refractory symptoms at a patient’s end of life.⁴⁰

Indeed, the lack of a clear conceptual framework that includes the full range of suffering adds to the incoherence surrounding PS in the end of life. Murata⁴¹(p. 17) proposed a conceptual philosophical framework for spiritual suffering, defining it as “pain caused by extinction of the being and the meaning of the self.” He later assumed the broader expression psychoexistential or spiritual suffering⁴² for spiritual suffering. This definition drift well demonstrates how difficult it is to clearly establish terminology and to distinguish these kinds of suffering.

From a psychiatric perspective, Schuman-Olivier et al.³⁶ established a theoretical framework that differentiates existential suffering from existential distress. This framework acknowledges existential suffering as a special case that applies to persons with terminal illness or who are at the end of life.³⁶ Some typologies^{43–45} permit concepts included in existential suffering, such as loss of meaning and purpose of life, fear of death, despair, loss of dignity, hopelessness, helplessness, and others. Kirk and Mahon⁴⁶(p. 916) assume that “existential suffering is suffering that arises from a loss or interruption of meaning, purpose, or hope in life” and is not restricted to persons with terminal illness.

Two studies originating from The Netherlands^{47,48} revealed that existential suffering was the indication in 16%–26.4% of cases in which PS was applied. Another study⁴⁹ reported that patients require PS for refractory existential suffering (PS-ES) in a wide range of situations, such as having a feeling of meaninglessness and worthlessness, being a burden on others, dependency, inability to care for oneself, death anxiety, fear, panic, desire to control one’s time of death, isolation, and lack of social support. This indicates that a wider range of the kinds of patient distress is included in PS-ES applications.

This diversity in conceptual frameworks and clinical experience has produced uneasiness in health care professionals. Empirical studies indicate that clinicians still feel ambivalent about using PS-ES in their practice,^{50,51} and a consensus for PS-ES is far from being reached.^{27,52–54}

Although use of PS-ES lacks a clear consensus, competing conceptual frameworks have not matured, and definitions vary about what constitutes suffering. Still, PS has been continued to be recommended by clinical practice guidelines to relieve patients of refractory existential symptoms.^{55,56} However, an international panel of palliative care experts states that PS-ES is admissible only under exceptional circumstances and after consultation with palliative care experts.²⁴ Clearly, then, guidelines have not reached a consensus on PS-ES,^{46,57} and others even consider PS-ES to be inappropriate,⁵⁸ as other kind of interventions can indeed treat existential suffering in patients in advanced stages of illness.⁵⁹

To the best of our knowledge, no clear overview of the underlying concepts and arguments used in the ethical debate on PS-ES has been made available in the literature. Thus, to address this, we undertook a systematic review of argument-based bioethics literature on PS-ES.

Methods

Several models of systematic^{60,61} and nonsystematic⁶² literature reviews have been developed in the field of bioethics. We conducted a systematic review of argument-based bioethics literature that identifies ethical arguments and underlying concepts.^{63,64} We followed the *Peer Review of Electronic Search Strategies* (PRESS) guideline⁶⁵ for our literature search, and we used the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) statement^{66,67} for reporting our search process.

Research Question

We formulated the following research question to frame our article selections and analysis:

What are the ethical arguments and concepts underpinning the debate on PS-ES?

Our aim is to systematize the ethical arguments used in discussing PS-ES. Moreover, it is important to present an overview of the main concepts that ground an argument, so that we can understand how a certain concept is being used in the argumentation for or against PS-ES.

Literature Search

PubMed (1966-), CINAHL (1995-), Embase[®] (1974-), The Philosopher's Index (1940-), PsycINFO[®] (1806-), and PsycARTICLES[®] (1894-) electronic databases were queried to achieve full coverage of the subject. Additional searches were performed in Scopus[®] (1996-), ScienceDirect (1995-), and Web of Science (all databases; 1898). We also performed queries using French language search terms in the human sciences electronic databases Pascal-Francis (1972-) and Cairn (2001-), the latter integrating also biomedical journals.

Our research question was distilled first into three groups of concepts, separately in English and French (Table 1; A, B, and C). As the literature has not yet clearly established the distinction between psychological distress/suffering and existential suffering, we used broad concepts that extracted the notion of existential suffering (Group B).

Each group of concepts was then expressed in explicit one- or two-word search terms in English

and French (Table 2). These were then used in the database searches.

We performed a systematic search in electronic databases following the PRESS guideline.⁶⁵ The search strategy was later peer reviewed and validated by an independent librarian from the Health Sciences Library (Université Catholique de Louvain, Belgium).

We used Boolean search queries, following the general form of (A AND B) OR (A AND C). The first term (A AND B) was intended to target articles concerning PS-ES, and the second term (A AND C) was intended to target articles concerning ethical aspects of PS. These queries were restricted by using title and abstract field delimiters, adjusting the format of the search expressions to suite the particulars of the different database interfaces. This is indicated in Table 3 for the PubMed database.

The database search was performed by the first author (P. R.) in March 2017, using no lower-limit publication date restrictions or filters. Retrieved references were organized and managed in a unique EndNote[™] X8.2 (Clarivate Analytics, Beijing, China) reference library. Duplicate references were removed before applying the following filters: type of document (peer-reviewed journal article), language (English, French), and date (December 31, 2016, as upper limit).

The resulting reference list was subjected to both title and abstract screening using predefined inclusion and exclusion criteria. Peer-reviewed articles to be

Table 1
Search Terms and Concepts in English and the Corresponding French Versions

English		
Group A <i>Palliative sedation</i>	Group B <i>Existential suffering</i>	Group C <i>Ethics</i>
continuous deep sedation; continuous sedation; controlled sedation; deep sedation; end-of-life sedation; palliative sedation; sedation therapy; terminal sedation; total sedation	anxiety; depression; existential concerns; existential distress; existential pain; existential questions; existential suffering; intractable distress; intractable symptoms; mental suffering; moral distress; nonphysical symptoms; non-physiologic symptoms; psycho-existential suffering; psychological distress; psychological stress; refractory suffering; refractory symptoms; spiritual distress; terminal suffering; unbearable distress	argument; conflict; conscientious objection; controversy; debate; discussion; ethical issues; ethical reasons; ethics; justifications; moral reasons/arguments; philosophical arguments; philosophical reasons
French		
Group A <i>Sédation profonde</i>	Group B <i>Souffrance existentielle</i>	Group C <i>Éthique</i>
sédation continue; sédation profonde; sédation palliative; sédation terminale; sédation totale; sédation contrôlée; traitement palliatif par sédation; sédation pour détresse terminale; sédation terminale; sédation de répit	anxiété; dépression; détresse existentielle; souffrance existentielle; souffrance réfractaire; souffrance psychique; symptômes non-physiologiques; détresse psychologique; détresse morale; détresse spirituelle; symptômes réfractaires	argument; conflit; objection; controverse; débat; discussion; éthique; justification; raisons; arguments philosophiques; raisons philosophiques

Table 2
Search Terms in English and French

English	French				
Group A 'continuous sedation'; 'controlled sedation'; 'deep sedation'; 'end-of-life sedation'; 'palliative sedation'; 'sedation therapy'; 'terminal sedation'; 'total sedation'	Group B anxiety depression distress existential intractable mental* moral* nonphys* non-phys* psycho-existential psycholog* refractory spiritual* stress suffer* terminal*	Group C argument* conflict* controvers* debat* discussion* ethic* justification* moral* objection* philosoph* reason*	Group A 'sédation contrôlée' 'sédation terminale' 'sédation continue' 'sédation de répit' 'sédation palliative' 'sédation profonde' 'sédation totale'	Group B anxiété dépression détresse existent* moral non-phys* non phys* psych* réfractaire* souffrance spirit*	Group C argument* conflit* objection* controverse* débat* discussion* éthique* justification* raison* philosoph*

included in the full-text screening met the following criteria: 1) presented ethical argumentations about PS, or 2) addressed the topic of PS-ES.

In selecting articles for inclusion, we used definition of PS by Broeckeaert³⁵ and broad definition of existential suffering by Kirk and Mahon⁴⁶ (see Introduction section). We excluded publications dealing with clinical practice guidelines, ethics policies, protocols, reviews (without discussion), empirical studies, and ethics codes. On the other hand, we included letters to the editor, editorials, and commentaries for full-text screening, mainly because the controversial subject of PS-ES is often discussed in these publications. Title and abstract screening was performed by the first author (P. R.) and checked by the second author (J. C.); discrepancies were resolved through discussion and consensus.

The full-text screening was performed independently by two reviewers (P. R. and J. C.), and the third author (C. G.) acted as tiebreaker in cases of disagreement. Publications were included if they met the following criteria: 1) consisted of ethical arguments, and 2) related to PS-ES. Argument-based bioethics literature comprises literature that integrates normative principles, arguments, underlying concepts, tool analysis, and explores its implications for clinical practice.⁶⁴ The snowball method was applied to the reference lists of publications eligible for inclusion to ensure maximum coverage.

Table 3
Search Strategy (PubMed)

#1 A [title/abstract]
#2 B [title/abstract]
#3 C [title/abstract]
#4 Deep sedation/ethics (MESH terms)
#5 1 AND 2
#6 1 AND 3
#7 4 OR 5 OR 6

Data Extraction and Synthesis

We used the coding process of *The Qualitative Analysis Guide of Leuven*⁶⁸ for data extraction and synthesis method. Briefly, this includes the following sequential steps:

- Read and reread the selected articles to extract their essential features and identify the main arguments and concepts used.
- Develop a narrative summary for each article.
- Translate narrative summaries into mind maps that represent normative arguments and underlying concepts.
- Compare mind-map schemes to identify common arguments and concepts.
- Construct a final scheme synthesizing and structuring all the arguments and concepts collected.
- Iteratively read the selected texts to confirm, complete, and verify the analysis done and to re-contextualize the ethical arguments and the underlying concepts identified.
- Describe and report the results in a structured way in the Results section.

Results

The organization of the literature search is presented according to the PRISMA flowchart (Fig. 1).

The literature search yielded 18 publications meeting our eligibility criteria.^{36,69–85} These comprise 16 journal articles and two letters to journal editors. Most articles were published in English ($n = 17$), and one was in French. The articles were published in medical journals ($n = 9$), ethics/bioethics journals ($n = 6$), or nursing journals ($n = 3$). The first authors of the articles were physicians ($n = 8$), ethicists ($n = 5$), nurses ($n = 4$), or a psychologist ($n = 1$).

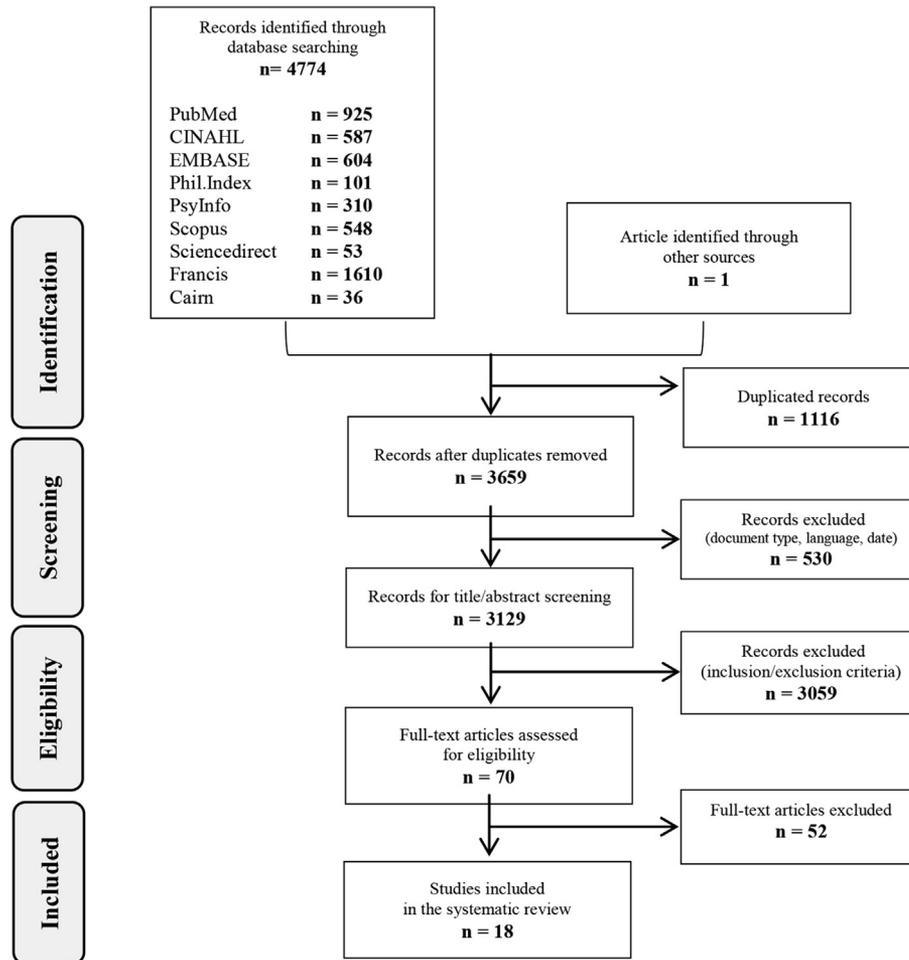


Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of the search process.

Countries for the main work affiliations of the first authors were U.S. ($n = 10$), Canada ($n = 3$), Europe (France, Germany, and Norway), Israel, or Japan.

In our presentation of the results, we organize them according to the underlying concepts emerging from our analysis and the ethical principles used to build the argumentations regarding PS-ES.

Underlying Concepts

We will now consider several concepts that emerged from our analysis of the included literature: mind-body dualism, existential suffering, refractoriness, terminal condition, and imminent death (Table 4).

Mind-Body Dualism. The arguments and concepts appealed to a background discussion about the philosophical mind-body problem. Opinions were divided between two anthropological models that presuppose conflicting philosophical stances: one viewing the mind and body as separate dimensions of a person (i.e., mind-body dualism), and the other viewing the person in a more holistic way. Jansen and Sulmasy^{69,70} subscribe to a dualistic view that leads to the

identification of different kinds of suffering affecting separately the mind and the body. Because palliative interventions should be made according to the nature of suffering, mind-body dualism led Jansen and Sulmasy to hold that PS is an inappropriate and ineffective intervention to deal with suffering related to the mind or nonphysiological refractory symptoms, such as psychological distress, existential, and spiritual suffering. Instead, they view psychotherapy and spiritual care as much more appropriate interventions for nonphysiological refractory symptoms.

Cassell and Rich,^{71–73} on the other hand, adopted the latter stance. They challenge mind-body dualism and argue for a holistic concept of human person. This perspective leads to deny the difference between kinds of suffering and to consider that suffering affects the person as a whole. Along the same lines, ten Have and Welie⁷⁴ hold that mind-body dualism leads to somatic reductionism that separates symptom distress from suffering.

Existential Suffering. Existential suffering was defined in multiple ways, and the opinions were divided on its

Table 4
Grounding Concepts in PS-ES Debate

Grounding Concepts	Used in Arguments	
	Pro PS-ES	Contra PS-ES
Mind-body dualism		
Affirmed	—	Jansen; ⁶⁹ Jansen & Sulmasy ⁷⁰
Denied	Cassell & Rich; ⁷¹ Rich; ^{72,73} ten Have & Welie ⁷⁴	
Existential suffering		
Specific kind of suffering	—	Schuman-Olivier et al.; ³⁶ Jansen; ⁶⁹ Jansen & Sulmasy; ⁷⁰ Wirth & Hurwitz; ⁷⁵ and Cherny ⁷⁷
Nonspecific kind of suffering	Cassell & Rich; ⁷¹ Rich ^{72,73}	Gamblin et al.; ⁷⁶ Hallenbeck; ⁷⁸ and Sadler ⁸⁰
Refractoriness		
Clear assessment	Rich; ^{72,73} ten Have & Welie ⁷⁴	—
Unclear assessment	—	Schuman-Olivier et al.; ³⁶ Jansen; ⁶⁹ Jansen & Sulmasy; ⁷⁰ ten Have and Welie; ⁷⁴ Gamblin et al.; ⁷⁶ Cherny; ⁷⁷ Sadler; ⁸⁰ Crenshaw ⁸¹
Terminal condition		
Sufficient	Schuman-Olivier et al.; ³⁶ ten Have & Welie; ⁷⁴ Hallenbeck ⁷⁸	—
Insufficient	—	Jansen; ⁶⁹ Jansen & Sulmasy; ⁷⁰ Sadler ⁸⁰

PS-ES = palliative sedation for refractory existential suffering.

nature, intensity, and refractoriness. Jansen and Sulmasy^{69,70} defined two kinds of suffering: 1) neurocognitive suffering (anxiety disorder, depression, psychosis, insomnia, bone pain, etc.), which is clinical and caused by the patient's underlying physical condition, and 2) agent-narrative suffering (i.e., existential suffering, including loneliness, hopelessness, meaninglessness, etc.), which is nonclinical and only indirectly related to the patient's medical condition. The nature of existential suffering (agent-narrative suffering) in this framework makes PS an unjustified and inappropriate intervention because it impairs the patient, preventing him or her from engaging his or her internal resources to respond to it.^{70,75}

Cassell and Rich⁷¹⁻⁷³ argue that the precedent classification of suffering—one grounded in dualist anthropology and insufficiently established—wrongly leads to two understandings of suffering. One is that suffering is seen as subjective and thus beyond the scope of medicine. The second reduces suffering to its physiological dimension. Instead, they argue for a holistic conception of suffering that goes beyond the mind-body dichotomy. They consider suffering in general to originate as a threat to personal integrity. Thus, suffering is an affliction of persons, not bodies.⁷¹(p. 436)

Gamblin et al.⁷⁶ find difficult to distinguish normal concerns at end of life from psychological distress/existential refractory suffering. This means that the use of adequate assessment tools is necessary to avoid the risk of a subjective evaluation of it by health care providers.

Cherny⁷⁷ brings a time element to the concept. He considers it necessary to distinguish true existential suffering from suffering caused by experiencing difficult problems that appear intractable but in reality may be solved within a definite time frame. Other authors^{76,78,80} argue that borders are blurred between

existential suffering and pathological conditions as anxiety and depression, which require therapeutic intervention instead of PS.

Schuman-Olivier et al.³⁶(p. 340) presented a useful framework to differentiate existential suffering from existential distress. They consider the latter to be a type of existential suffering that specifically develops as a result of facing one's own mortality. Existential distress in their view is a kind of existential suffering emerging at the end of life and is distinct from existential suffering arising from personality traits, socioeconomic disadvantages, traumatic situations, and others.

Thus, there is great variability in how different authors define and view existential suffering, often arising from opposing stances on mind-body dualism and views of suffering at different points and conditions in one's life.

Refractoriness. The idea of refractoriness is another concept that emerged from our analysis. When pain is refractory and unremitting, suffering follows despite efforts to palliate a patient's medical condition. This notion is integrated in the definition of PS, and the presence of refractoriness in a patient is considered by some authors to be a decisive criterion for administering PS-ES.⁷²⁻⁷⁴ PS is considered to be a proportionate intervention for physical refractory suffering, but several authors are more cautious about operationalizing and assessing refractoriness for existential symptoms.^{36,69,70,74,76,77,81} This discretion practically means that PS would mostly be deemed inappropriate for refractory existential suffering.^{69,70} Moreover, a significant degree of subjectivity in evaluating existential suffering—in the absence of adequate and standardized instruments to assess it—leads to the idea that the patient is the final judge of the refractoriness of his symptoms.^{74,76,80,81}

Terminal Condition/Imminent Death. The patient's terminal condition is also an important concept that emerged. According to Schuman-Olivier et al.,³⁶ patients having acute existential suffering who meet the imminent death condition or the two-week criterion are eligible for PS, but those having chronic existential suffering are not. Otherwise, they argue it would be a form of physician-assisted suicide. Jansen and Sulmasy^{69,70} argue that the imminent death and two-week criterion do not terminate the patient's restorative goals of psychosocial well-being. Consequently, there is no difference between terminally ill and non-terminally ill patients, and in these conditions, PS-ES should be denied. Hallenbeck⁷⁸ supports PS-ES in near-death situations but argues that it should be denied to patients who are not near to death. He reasons that non-terminally ill patients still have time and potential to find relief within themselves. According to ten Have and Welie,⁷⁴ the main reason to set the imminent death condition is that PS carries risks to the patient, such as paradoxical agitation and interruption of communication. Sandler⁸⁰ points out that the prognostic assessment is not very precise, which makes it difficult to establish the terminal condition of the patient, an essential element for ethical decision making in PS context.

Ethical Principles Used to Build Arguments Regarding PS-ES

Several ethical principles were used to justify or oppose the use of PS-ES in the included literature (Table 5). These were the principle of double effect, the proportionality principle, the principle of therapeutic responsiveness, and the four principles of biomedical ethics, which are 1) respect for autonomy, 2) beneficence, 3) nonmaleficence, and 4) justice. These seven principles will be considered in turn with regard to how they are used in the PS-ES debate.

Principle of Double Effect. The principle of double effect states the conditions for an action that has two effects: an intended good effect and an unintended bad effect. Four conditions must be met for ethical justification of the action^{80–82}: 1) the nature of the action must be either neutral or good, independently of consequences, 2) the intention of the agent must be good, 3) the bad effect must not cause the good effect, and 4) the good effect is sufficiently desirable to compensate for the bad effect. Some authors^{36,80} add a fifth condition, that is, the action must be an option of last resort. This essentially means that no less harmful option is available.

This principle has been used to provide ethical justification for PS, in general,⁸² and for refractory existential suffering, in particular.^{36,81} In the latter case, relief of existential suffering embodies the good effect, and

the bad effect is associated with hastening death (although this aspect still needs empirical evidence). Morita et al.⁸² argue that if decreased consciousness (or unconsciousness) is set as the bad effect, PS-ES cannot be justified by the principle of double effect because unconsciousness (bad effect, Condition 3, previously mentioned) would be the means of relieving existential suffering (good effect). Hence, the double effect rule can only be used to justify PS if death is considered to be the bad effect because death is not a direct means for symptom relief (good effect, Condition 1, previously mentioned).⁸²

Having said this, the double effect principle has been used to justify PS-ES, and this has been criticized. How could this be if hastening death is a bad effect? First of all, death is not always seen as untoward or adverse,^{77,82} suggesting it is not necessarily a bad effect. The principle of double effect in action always assesses the agents' intention and verifies that the action intends to provide care that will relieve the patient's suffering. With PS interventions, it is possible that the intention of relieving the patient from existential suffering coexists with the indirect or covert intention of hastening death.^{78,82} It is also possible that an agent views the person under their care as an inconvenient problem and has the surreptitious intention of getting rid of the problem in an easy and inexpensive way through PS till death.⁸³ The condition that the action must be an option of last resort (i.e., fifth condition) also appears in the included literature.^{36,80} Some authors argue that PS-ES is undesirable when viable alternatives exist,⁷⁷ or specific tailored approaches seem more reasonable.⁸³ Such reasonable alternatives include good palliative care measures,⁷⁹ supportive environment,⁷⁸ psychological and spiritual interventions,^{36,70} dignity therapy,^{75,79,84} and introspection.^{75,78}

Principle of Proportionality. The proportionality principle states that there should be a justifiable proportion between the intended good effect and the unintended bad effect. This means that the extent of harm should be offset proportionally by the proposed benefit and that the proportion allocated to each can be justified. This principle is applied in PS for physical suffering, but its suitability for existential suffering needs further discussion.⁸² According to Gamblin et al.,⁷⁶ the risk of appreciating only subjectively levels of existential suffering—which can be very dynamic and variable by nature—can be a source of bias and error. This bias may be eliminated by imposing objective criteria or using adapted evaluation tools. However, Hallenbeck⁷⁸ states that the way professionals titrate sedatives reveals either the intention of relieving the patient from suffering or the intention of hastening death in cases when they administer massive doses of sedatives without observing and monitoring the signs of distress.

Table 5
Ethical Principles in PS-ES Debate

Ethical Principles	Used in Arguments	
	Pro PS-ES	Contra PS-ES
Principle of double effect	Schuman-Olivier et al.; ³⁶ Crenshaw ⁸¹	Cherny; ⁷⁷ Hallenbeck; ⁷⁸ Morita et al.; ⁸² Davis & Ford ⁸³
Principle of proportionality	Schuman-Olivier et al. ³⁶	Jansen & Sulmasy; ⁷⁰ Wirth & Hurwitz; ⁷⁵ Gamblin et al.; ⁷⁶ Hallenbeck; ⁷⁸ Davis & Ford ⁸³
Principle of therapeutic responsiveness	Rich ^{72,73}	Jansen & Sulmasy ⁷⁰
Principle of respect for autonomy	Cassell & Rich; ⁷¹ Rich ^{72,73}	Jansen & Sulmasy; ⁷⁰ Wirth & Hurwitz; ⁷⁵ Gamblin et al.; ⁷⁶ Hallenbeck; ⁷⁸ Sadler; ⁸⁰ Crenshaw; ⁸¹ Davis & Ford; ⁸³ Materstvedt & Bosshard ⁸⁴
Principle of beneficence	Cassell & Rich; ⁷¹ Rich ^{72,73}	Jansen & Sulmasy; ⁷⁰ Wirth & Hurwitz; ⁷⁵ Hallenbeck; ⁷⁸ Materstvedt & Bosshard ⁸⁴
Principle of Nonmaleficence		Jansen; ⁶⁹ Jansen & Sulmasy; ⁷⁰ Wirth & Hurwitz; ⁷⁵ Gamblin et al.; ⁷⁶ Sadler; ⁸⁰ Davis & Ford; ⁸³ Materstvedt & Bosshard; ⁸⁴ Kirby ⁸⁵
Principle of justice	Crenshaw ⁸¹	Jansen & Sulmasy; ⁷⁰ ten Have & Welie; ⁷⁴ Wirth & Hurwitz; ⁷⁵ Gamblin et al.; ⁷⁶ Hallenbeck; ⁷⁸ Bruce & Boston; ⁷⁹ Sadler; ⁸⁰ Davis & Ford; ⁸³ Materstvedt & Bosshard ⁸⁴

PS-ES = palliative sedation for refractory existential suffering.

Davis and Ford⁸³ maintain that PS-ES cannot produce a justifiable proportion between the good effect and the bad effect. They reason that just as one could not intend to kill the physical body to remove physical pain, one cannot kill the social/existential self to remove existential/social suffering.⁸³(p. 700) Wirth and Hurwitz⁷⁵ find as well that PS is not a proportional action toward existential suffering in terminally ill patients because PS continues until death (i.e., leads to sleep without awakening). Schuman-Olivier et al.³⁶ see proportionality from a time perspective. They maintain that some of the patient's unconscious conflicts (i.e., existential suffering) cannot be treated within a limited time frame at the end of life; therefore, PS can be considered to be an appropriate intervention only for terminally ill patients (i.e., in the case of imminent and inevitable death).

Jansen and Sulmasy⁷⁰ criticize the proportionality principle as espoused by Quill et al.⁸⁶ They embrace the notion that the greater the patient's suffering, the greater risk the physician can take of potentially contributing to the patient's death, so long as the patient understands and accepts the risk.⁸⁶ Jansen and Sulmasy argue that this formulation of the proportionality principle does not take into account distinct kinds of suffering, submitting all to the same condition of proportionality.⁷⁰ In fact, according to the proportionality principle, the ethical justification for PS intervention depends on the intensity of the patient's suffering, not on the nature of suffering.

Principle of Therapeutic Responsiveness. The idea that the proportionality principle does not take into account distinct kinds of suffering pushed some authors to advance a revised formulation. Jansen and Sulmasy⁷⁰ proposed a revision of the proportionality principle to

take into account the nature of suffering rather than its intensity or refractoriness as decisive criterion for PS. Because of the shift in focus from the intensity of suffering to the nature of suffering, the revision really amounts to a new ethical principle: the *principle of therapeutic responsiveness*. It is formulated as follows:

"A physician's therapeutic response to terminal suffering is justified, even if it imposes a high risk of hastening the patient's death, if and only if 1) the measures implemented are directly proportionate to the intensity of the patient's suffering, 2) the measures implemented are appropriate for the type of suffering the patient is experiencing and, therefore, are properly responsive to the patient's restorative interests, and 3) the patient or the patient's legal surrogate understands and accepts the risks associated with the measures."⁷⁰(p. 330–331)

The second condition establishes the need to evaluate kinds of suffering, which calls for distinct interventions to respond in an appropriate way to the patient's needs. According to Jansen and Sulmasy,⁷⁰ the nature of existential suffering (agent-narrative suffering) makes PS an inappropriate intervention for this indication because psychological and spiritual care measures are adequate interventions to restore the patient to psychosocial well-being at the end of life.

Rich^{72,73} criticizes the principle of therapeutic responsiveness because it is not grounded in any authority or reference. Besides, it can lead to paradoxical situations. For example, a patient diagnosed with some type of a clinical psychic suffering (neurocognitive suffering) that is refractory to therapeutic interventions would be eligible for PS under the principle of therapeutic responsiveness, whereas a terminal patient diagnosed with a nonclinical type of suffering (agent-narrative suffering/existential suffering) would not be

eligible for PS leading to unconsciousness. Most would agree that this is an unreasonable confusing outcome. At a minimum, then, the principle of therapeutic responsiveness needs refinement to remedy this fault.

Four Principles of Biomedical Ethics

Respect for Autonomy. This principle refers to the capacity to decide and act in a free, independent, and informed way. In the decision-making context of PS, the principle of respect for autonomy advocates for the patient's right to choose what he believes is the most adequate form of therapy to manage his refractory symptoms. However, as some authors recognize,^{78,80,81} there are limits to this principle in PS decision making because the patient's autonomous desire for PS has to meet the physician's criteria (regarding indication and refractory symptoms) and the health care provider's willingness to grant it. These can be in conflict.

Jansen and Sulmasy⁷⁰ assume that every patient has an interest in the restoration of his psychosocial well-being, even at the end of life. Therefore, PS-ES is not an option to be offered to terminally ill patients, as it, in effect, cancels one's psychosocial life. However, according to Rich,^{72,73} the presumption of a self-preservation interest may be a false one. The patient may have neither a real interest in the restoration of his psychosocial health nor a desire for psychological and spiritual care support, preferring PS to lead to unconsciousness and death. In this situation, as Rich remarks, respect for the patient's autonomy is negated as he is not eligible for PS according to Jansen and Sulmasy's criteria and presuppositions.

Wirth and Hurwitz⁷⁵ argue that choosing unconsciousness is not a common strategy for autonomous people to deal with difficulties and that people have capacity for an autonomous approach to suffering by maintaining distance from it. PS permanently removes the patient's consciousness and the possibility of making autonomous choices. For Materstvedt and Bosshard⁸⁴(p. 623), "autonomously deciding to be nonautonomous" is a contradiction. In this sense, as Gamblin et al.⁷⁶ remark, there is tension between the beneficence principle and the autonomy principle because the action that intends to benefit the patient also dissolves autonomy of that patient.

Informed Consent. The patient's autonomy implies informed consent concerning the risks and benefits of PS.^{36,81,85} Informed consent means that a competent autonomous patient has the right to make a voluntary uncoerced decision to accept or reject some proposed course of action, in this case PS. In this sense, Schuman-Olivier et al.³⁶(p. 347) stated that "to consent to treatment, the patient must be capable of 1) communicating a stable choice, 2)

understanding relevant information, 3) rationally manipulating information, and 4) appreciating the seriousness of the decision." Kirby⁸⁵ argues that PS requires informed and direct consent of a capable patient, or in case of incapacity, the consent of the legitimate surrogate decision maker. In the latter situation, it can be difficult to assess whether the patient is experiencing unbearable existential suffering (in the absence of physical signs). Therefore, Sadler⁸⁰ and Schuman-Olivier et al.³⁶ maintain that PS is not appropriate for individuals lacking cognitive and decisional capacity. According to Schuman-Olivier et al.,³⁶ the only exception would be neuropsychiatric patients with advance directives indicating their wish for palliative care but without indications concerning PS. In this context, it is requisite that the families and caregivers of these patients firmly believe that the patients would have indicated PS-ES in their advance directives, if they had been aware of this possibility at the moment they were formalizing their directives.

Personhood. Personhood is another aspect of the autonomy principle. It refers to the value of being a person, a concept with a long and durable tradition in philosophy, theology, and law. It grounds autonomy and dignity claims. The intent of medicine to eliminate all suffering (existential and spiritual suffering) in terminally ill patients by proposing the application of PS leads to a separation of the individual from himself and his environment.⁸⁰ This eliminates him by means of reducing him to unconsciousness,⁷⁸ converting him into a kind of living dead,⁸⁴ and essentially making him sociologically dead.^{75,80,83,84} These are all additional reasons to withhold PS-ES.

Cassell and Rich⁷¹(p. 436) argue against a dualist anthropological view of human beings, maintaining that "a person is an embodied, purposeful, thinking, feeling, emotional, reflective, relational individual existing through time in a narrative sense." Thus, suffering that affects one of these dimensions affects the whole person, threatening his integrity. As they clearly state: Suffering is an affliction of persons, not bodies. It is this very same concept that underscores the suggestion of dignity therapy as a personalized and an adequate treatment for existential suffering.^{75,79,84} Crenshaw⁸¹(p. 105) also uses this concept, advocating for patient-centered care. He states that "clinicians must realize that patients are physical, social, emotional, and spiritual beings."

Beneficence. Beneficence involves balancing the benefits of treatment against the risks and costs involved. The beneficence principle is used to ethically justify PS, in general, because PS is meant to relieve patients from suffering and provide them comfort at the end of their life. Nevertheless, Crenshaw⁸¹(p. 104) notes

that some patients may think that “suffering during the dying process is beneficial.”

Dignity. Patients’ dignity is a very common aspect of beneficence discussed in ethics to justify positions contrary to PS-ES. Because refractory suffering undermines a patient’s dignity by way of occupying the center of his existence, Rich⁷² argues that PS can be permitted for the sake of the patient’s dignity. But this view can also be used to support the claim that PS-ES is inappropriate because doubts arise as to whether PS-ES promotes a dignified dying process.^{75(p. 314)} Several authors write that there are other means besides medical interventions to enhance a patient’s dignity, such as supportive environment,⁷⁸ psychological-spiritual interventions,⁷⁰ or dignity therapy.^{75,79,84} Hallenbeck⁷⁸ states that a cure for loss of dignity must come from within the person.

Goals of Medicine. The goals of medicine also relate to beneficence. One of the goals of medicine is to relieve patients of suffering, including existential suffering.^{72,73,81} Nevertheless, alleviating all human suffering at the end of life, especially existential suffering, some argue is beyond the legitimate scope of medicine⁷⁵ and can constitute the extreme medicalization of death.⁸⁴

According to Jansen and Sulmasy,⁷⁰ the goal of medicine is also to restore patients to a state of psychosocial well-being, not just relieve them from suffering. Thus, PS-ES is inappropriate in the view as it cannot achieve restoration; on the contrary, it puts patients to sleep until they die. Cassell and Rich^{71–73} criticize this opinion because sometimes the restorative goals of medicine do not coincide at all with the patient’s own goals. Hallenbeck⁷⁸ believes that the duty to relieve physical suffering is more compelling than the duty to relieve psychological or existential suffering. This is because in the latter situation, the patient still has the potential and the time to find the solution by himself. However, according to Schuman-Olivier et al.,³⁶ existential suffering can occasionally originate from unconscious conflicts that cannot be solved within a short lapse of time, demanding long-term interventions.

Nonmaleficence. Beneficence and nonmaleficence are closely related. Beneficence involves balancing benefits and risks and costs, whereas nonmaleficence means avoiding the causation of harm (*primum non nocere*). Many authors argue that PS-ES might be considered to be harmful and thus contrary to the nonmaleficence principle. For example, PS has potential side effects because it impairs human awareness;⁷⁵ it limits the patient’s potential growth at the end of life;⁷⁸ it hinders patients from solving an end-of-life crisis, interrupting consciousness and psychological life;^{75,76} it prevents restoring the patient to a state of

psychosocial well-being;^{69,70} it hastens premature social death by preventing interactions between the patient with others;^{80,83,84} in a patient displaying existential suffering symptoms, it can reduce life expectancy if PS is initiated when he or she is still able to receive hydration and nutrition naturally.⁸⁵

Justice. The principle of justice regulates the fair distribution of benefits and burdens. ten Have and Welie⁷⁴ pointed out that PS-ES is a cheaper form of suffering relief than a complete package of physical, psychotherapeutic, and spiritual care interventions. This leads to an acceptance of PS as a preferable choice for complex situations⁷⁹ and also leads to an extreme medicalization of the dying process.^{76,84} In this situation, Materstvedt⁸⁴ argues that institutions can be tempted to control every aspect of a patient’s life, becoming total institutions.

ten Have and Welie⁷⁴ noted that the for-profit hospice industry tries to generate income by offering less comprehensive care services, saving on human resources, and by selecting patients as a function of their potential to generate reimbursements. As they remark, PS-ES can become quite attractive to institutions as it reduces the need for comprehensive care and given that health care systems and insurance usually reimburse PS.

From families’ perspective, PS is a less time-consuming option because they do not need to accompany and support the patient through his and/or her time of dying. From health care providers’ perspective, PS-ES can be in opposition to their personal values and beliefs. But as Crenshaw^{81(p. 104)} states that if health care providers fail to meet the needs of dying patients because of personal beliefs, the principle of justice has been violated, mainly because PS is sometimes the last resort to alleviate the patient’s suffering and the way for a peaceful dying process. *Slippery Slope Arguments and Vulnerable Groups.* PS-ES can lead to abuse, having huge societal impact. In other words, because it can be an easy solution to difficult complex problems, once it is applied in one situation, it becomes a slippery slope to wider application: PS becomes an easy alternative to adequate palliative care.^{74,78,80,83} This can then lead to voluntary and involuntary euthanasia, even extending it to non-terminally ill persons with refractory existential suffering.⁷⁰ If PS-ES becomes an accepted common practice, people can claim they have the right to treat other forms of psychological harm by this means.⁷⁵

Discussion

Main Findings

Our systematic review of the argument-based bioethics literature on PS-ES revealed that the understanding and application of the concepts of

mind-body dualism, existential suffering, refractoriness, terminal condition, and imminent death in PS-ES are manifold. Although unanimity exists on using PS for controlling refractory physical suffering in end-of-life situations, using it for controlling refractory existential suffering remains controversial. Definitions and terminology for existential suffering are unclear, ambiguous, and imprecise, leading to a lack of consensus for clinical practice. Moreover, the assessment of existential suffering is still a difficult and controversial issue as subjectivity is involved in the patient's narrative of his and/or her suffering and in the physician's interpretation of it.

Our systematic review revealed many new aspects of the ethical debate on PS-ES that call for further analyses and interpretation. The ethical literature embodies some serious weaknesses of understanding and application of traditional ethical principles with regard to PS-ES. For instance, the use of the principle of double effect to justify PS-ES raises serious difficulties related to the definition of bad effect and to the assessment of clinical practitioners' intentions. In particular, reaching consensus on the correct application of the principle of double effect in PS-ES depends critically on reaching consensus on what is a good effect and what is a bad effect. Is hastening death always a bad effect? Clarifying these issues is essential to validly applying this classical rule.

The proportionality principle is equally problematic when applied to PS-ES decision making because it implies that the proportion between the intended good effect and the unintended bad effect needs to be assessed. With physical end-of-life suffering, this proportion may be more objectively assessed with available tools. However, with existential suffering, how is this proportion assessed? In the literature, evaluating the intensity and refractoriness of existential suffering symptoms is a controversial issue that largely has not reached a consensus, as this evaluation relies more on subjective criteria than on objective and reliable assessment. Moreover, there are differences also among health care professionals' ethical understanding and practices. A recent study showed that significant differences exist in the perception of PS practices between Belgian and U.K. physicians/nurses regarding the terminology, the approach to proportionality, and the different views on intentions while using PS.⁸⁷

The concept of refractoriness also emerged in our analysis, but it is unclear if it can be used in the case of existential suffering. The difficulty to establish refractoriness of existential suffering is linked to the controversial question of the nature of existential suffering and whether it is distinct from other kinds

of suffering and distress. Cassell and Rich^{39,71–73} argue that the distinction is false, whereas others like Jansen and Sulmasy^{69,70} argue that not only it is distinct but also a typology of suffering can be established, with distinct interventions for refractory symptom management at the end of life. The problem derives from the implicit anthropological conceptions that are neither challenged nor grounded by the various authors, thus calling for further discussion and analysis. A philosophical materialist conception of human nature tends to reduce suffering to its physical dimension and to interpret human physical and psychological suffering in terms of manageable physiological variables of a complex organism. However, a dualistic philosophical approach of human nature assumes a difference between body and mind, the latter being irreducible to the former, thus grounding the distinction between various types of suffering and the use of psychological and psychotherapeutic interventions for the management of psychological and existential suffering.

What This Study Contributes to the PS-ES Debate

This article provides a systematic description of the ethical concepts and arguments underpinning the debate on PS-ES, as reported in the argument-based bioethics literature up to the end of 2016. Gathering these concepts and arguments in one place can enrich the discussion of the role of anthropological models in ethical decision making. This article reveals that ethical discussions about PS-ES are grounded in anthropological and philosophical assumptions like mind-body dualism, all of which need further elucidation. It is evident that these models emerge from philosophical and existential options regarding the problem of human nature. As Jansen⁶⁹ (p. 440) states, "medical science need not affirm or deny any controversial view on the mind/body issue." However, as the ethical discussion about PS-ES lies in options of anthropological schemes, it is desirable to bring to light—using philosophical analysis tools—the unchallenged and uncriticized assumptions grounding it. These will improve the quality of the ethical decision-making process and stimulate a better understanding of each agent's perspective.

Strengths and Limitations of the Study

To the best of our knowledge, this is the first systematic review of argument-based literature concerning PS-ES. Its methodological strength derives from the use of PRESS and PRISMA protocols. Even if we considered only journal articles in our analyses, excluding, for instance, book chapters, we believe that we have captured the most important ethical arguments made for/against PS-ES. We showed that the anthropological

models used conflict. We believe a systematic literature review of guidelines and policies relating to PS use would reveal different perspectives about its application to existential suffering, even if these kinds of documents were less grounded in ethical arguments and theories.

We believe that ethical discussions concerning PS-ES ultimately lead to difficulties of unavoidable grounding questions, such as the following: What is the essence of human nature? What comprises personhood? What does dignified death mean? These questions cannot be adequately addressed from the sole perspective of medical rationality. Rather, an interdisciplinary approach is necessary, one that brings together the contributions of science, philosophy, religious studies, and ethics. Here, we appeal to a philosophically grounded discourse. This discourse, however, is still far from reaching a final consensus and conclusion about the use of PS-ES, mainly because it appeals to personal values, convictions, and worldviews. These issues are beyond the scope of this review. Indeed, further research is necessary to elucidate ethical discussions on PS-ES, as stated also by other authors doing research on this topic: “The justification of PS for existential distress will require greater uniformity and clarification regarding the definitions of existential distress, the criteria for intolerability and refractoriness to treatment, and the routine earlier referral to mental health experts for the evaluation and treatment of existential distress.”^{88(p. 50)}

Conclusions

In the recent bioethics literature, there is an ongoing discussion about PS-ES, which appeals to several ethical arguments and their underlying concepts and principles. This review underscores the need to clearly define the basic terminology used in the PS-ES debate and to ground and systematize ethical arguments for PS-ES in a more effective way. The nature of existential suffering appeals to implicit anthropological models and presuppositions underpinning the PS-ES debate, necessitating further elucidation guided by an interdisciplinary approach. This would likely have the effect of improving clinical decision making and harmonizing clinical practice regarding PS.

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