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Revised European Association for Palliative Care (EAPC) recommended framework on palliative sedation: An international Delphi study

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Abstract

Background: The European Association for Palliative Care (EAPC) acknowledges palliative sedation as an important, broadly accepted intervention for patients with life-limiting disease experiencing refractory symptoms. The EAPC therefore developed 2009 a framework on palliative sedation. A revision was needed due to new evidence from literature, ongoing debate and criticism of methodology, terminology and applicability.

Aim: To provide evidence- and consensus-based guidance on palliative sedation for healthcare professionals involved in end-of-life care, for medical associations and health policy decision-makers.

Design: Revision between June 2020 and September 2022 of the 2009 framework using a literature update and a Delphi procedure.

Setting: European.

Participants: International experts on palliative sedation (identified through literature search and nomination by national palliative care associations) and a European patient organisation.

Results: A framework with 42 statements for which high or very high level of consensus was reached. Terminology is defined more precisely with the terms *suffering* used to encompass distressing physical and psychological symptoms as well as existential suffering and *refractory* to describe the untreatable (healthcare professionals) and intolerable (patient) nature of the suffering. The principle of proportionality is introduced in the definition of palliative sedation. No specific period of remaining life expectancy is defined, based on the principles of refractoriness of suffering, proportionality and independent decision-making for hydration. Patient autonomy is emphasised. A stepwise pharmacological approach and a guidance on hydration decision-making are provided.

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Conclusions: This is the first framework on palliative sedation using a strict consensus methodology. It should serve as comprehensive and soundly developed information for healthcare professionals.

Keywords
Palliative sedation (as the MeSH Terms refers only to one type of sedation), Delphi consensus (as the MeSH term consensus is not further defined)

MeSH terms
Deep sedation, suffering, palliative care, end-of-life, terminal care, practice guideline, consensus, Europe

What is already known about the topic?

- The European Association for Palliative Care (EAPC) developed a framework on palliative sedation in 2009, acknowledging it as an important and ethically acceptable last resort intervention for terminally ill patients experiencing refractory symptoms.
- Over the last two decades, a number of guidelines on palliative sedation have been developed in Europe and beyond.
- The general weakness of their methodological development has been criticised and their lack of consensus on terminology and concepts make their applicability difficult.
- Some issues, such as the complexity of assessing refractory symptoms or the differentiation between somatic, psychological and existential suffering, remain under debate.

What this paper adds?

- This paper provides the first consensus-based guidance on palliative sedation structured in 42 statements and explanatory texts, for which a high or very high level of consensus has been reached among experts from 28 different countries with a broad range of professions, and a European patient organisation.
- The importance of patient autonomy is emphasised in all phases of the process (timely discussion of patient preferences, shared decision-making process, informed consent by patient/legal representative).
- The term *suffering* defined as to encompass distressing physical and psychological symptoms as well as existential suffering is used to reflect the shift towards a broader recognition of existential suffering as indication for palliative sedation.
- No specific period of remaining life expectancy has been defined for the use of palliative sedation based on the three key principles of (1) refractoriness of suffering, (2) proportionality, which has been explicitly introduced in the definition of palliative sedation and (3) independent decision-making for hydration.
- A step-by-step pharmacological approach with a detailed description of the recommended medications as well as a more detailed guidance on decision-making regarding hydration based on recent literature are provided.

Implications for practice, theory or policy

- This paper provides evidence- and consensus-based guidance for healthcare professionals involved in the care of adult patients with life-limiting disease in all settings, as well as for medical associations and health policy decision-makers.

Introduction

Even with comprehensive palliative care some patients with life-limiting diseases suffer from severe physical, psychological or existential distress at the end of life, for which conventional treatment options fail. In these cases of refractory suffering, the intentional reduction of consciousness (palliative sedation) may be indicated. It is estimated that palliative sedation precedes 10%–18% of deaths of palliative care patients in Europe, although its use is known to vary considerably across cultures and countries, and even between institutions.[1–10] In 2009, the European Association for Palliative Care (EAPC) developed a framework on palliative sedation[11] to inform the development of local procedural guidelines. Over the last two decades, a number of national or regional guidelines on palliative sedation have been issued.[12–14]

An update to the EAPC framework was deemed necessary as the general weakness of the methodological development and applicability of existing guidelines on palliative sedation[13] and the variations in the terminology used[2,13–16] have been criticised. More recently, a new

terminology has been suggested, introducing the term 'intentional sedation', focussing on the causal role (intention to sedate) of the clinical action (sedation).[17] Even though new research on palliative sedation has been published,[2,17,18] issues such as the complexity of assessing refractory symptoms[14,19] or the differentiation between somatic, psychological and existential suffering[14] remain under discussion. In addition, a recent systematic review showed an underlying need to emphasise the principle of proportionality in palliative sedation practice with regard to the patient's individual situation, considering the continuum from light to deep and from intermittent to continuous sedation.[2]

Based on these issues, the Palliative Sedation (PalSed) project,[1] funded by the European Union (Horizon 2020 grant no. 825700), included the remit to update and revise the EAPC framework on palliative sedation using a rigorous Delphi consensus procedure with international experts and the European Cancer Patient Coalition (ECPC). The aim was to provide evidence and consensus-based guidance on palliative sedation for healthcare professionals involved in the care of adult patients with life-limiting disease in all patient care settings, as well as for medical associations and health policy decision-makers.

Methods

In light of the considerable differences in clinical practice of palliative sedation between cultures and countries a consensus methodology was performed in addition to the evaluation of the evidence in the literature. The four-step consensus procedure was based on the widely used Delphi methodology[20] and the reporting on the standards for Conducting and Reporting Delphi Studies (CREDES), which include clear criteria for consensus projects.[21] The development of the statements also considered all relevant methodological and content aspects of the Appraisal Guideline Research and Evaluation II (AGREE II),[22] an international tool to assess the quality and reporting of practice guidelines.

The study was approved by the Ethics Commission, University of Bonn, Germany, No. 268/20 (19 June 2020).

Literature update

The references of the 2009 framework were updated with scoping reviews in PubMed for key words of each framework section for the period 2009–2021 (articles published in English). In addition, experts were invited at each stage of the consensus procedure to propose additional references. As additional outcomes of the PalSed project two systematic reviews of prospective studies,[2,] 17 a review on monitoring[18] and a review of European guidelines on palliative sedation[12] were published. However, due to the workflow of the PalSed project the literature identified in these reviews was only available during step 2 and 3 of the Delphi process and were then implemented in the document.

Delphi procedure

Preparatory phase (step 1). The consensus process was managed by two researchers (HB and SMS) and supervised by a Steering Group including palliative care experts and a patient representative from the European Cancer Patient Coalition (AC, EG, JH, BJ, SP and LR; see Figure 1).

An Expert Group (Table 1) was recruited, including the Steering Group, work package leaders from the EU-funded PalSed project consortium, the advisory board members of the PalSed project and experts on this topic identified through a literature search (criteria: collaboration on palliative sedation guidelines and peer-reviewed publications on palliative sedation).

In June 2020, the original EAPC 2009 framework was broken down by the study team under the supervision of the Steering Group into 38 statements, some with explanatory text, two assessment tools for monitoring and the list of medications was formatted in the form of a table. They were presented in an online survey (July–November 2020) to the members of the Expert Group, who were asked for each component whether they thought it was still applicable or needed to be revised, and if so, to provide suggestions for revisions or additions including new and relevant literature references. They were also given the opportunity to suggest new statements.

Delphi rounds (steps 2 and 3). A Delphi Panel of experts was recruited including the Expert Group and additional experts. The latter were identified from a broader literature search, from representatives of the national palliative care associations affiliated with the EAPC or nominated by other panelists. A balance was sought to cover the European regions as far as possible, including also experts from outside Europe, a large range of professional backgrounds (physicians, nurses, psychologists, social workers, ethicists, health researchers and legal experts) and an equal gender distribution. The invitation to take part in the different steps was made by e-mail, and the consensus consultation used an online survey tool (SoSci Survey).

The number of Delphi rounds was set at a maximum of two before the process began.

The level of consensus was rated on a five-point Likert scale either as

- low: level of agreement $<$60%, median $<$4 and interquartile range (IQR) $>$ 2;
- moderate: level of agreement 60%–79% and median $<$4, IQR $>$ 1;
- high: level of agreement $\geqslant$80%–89% and median 5, IQR = 1 and

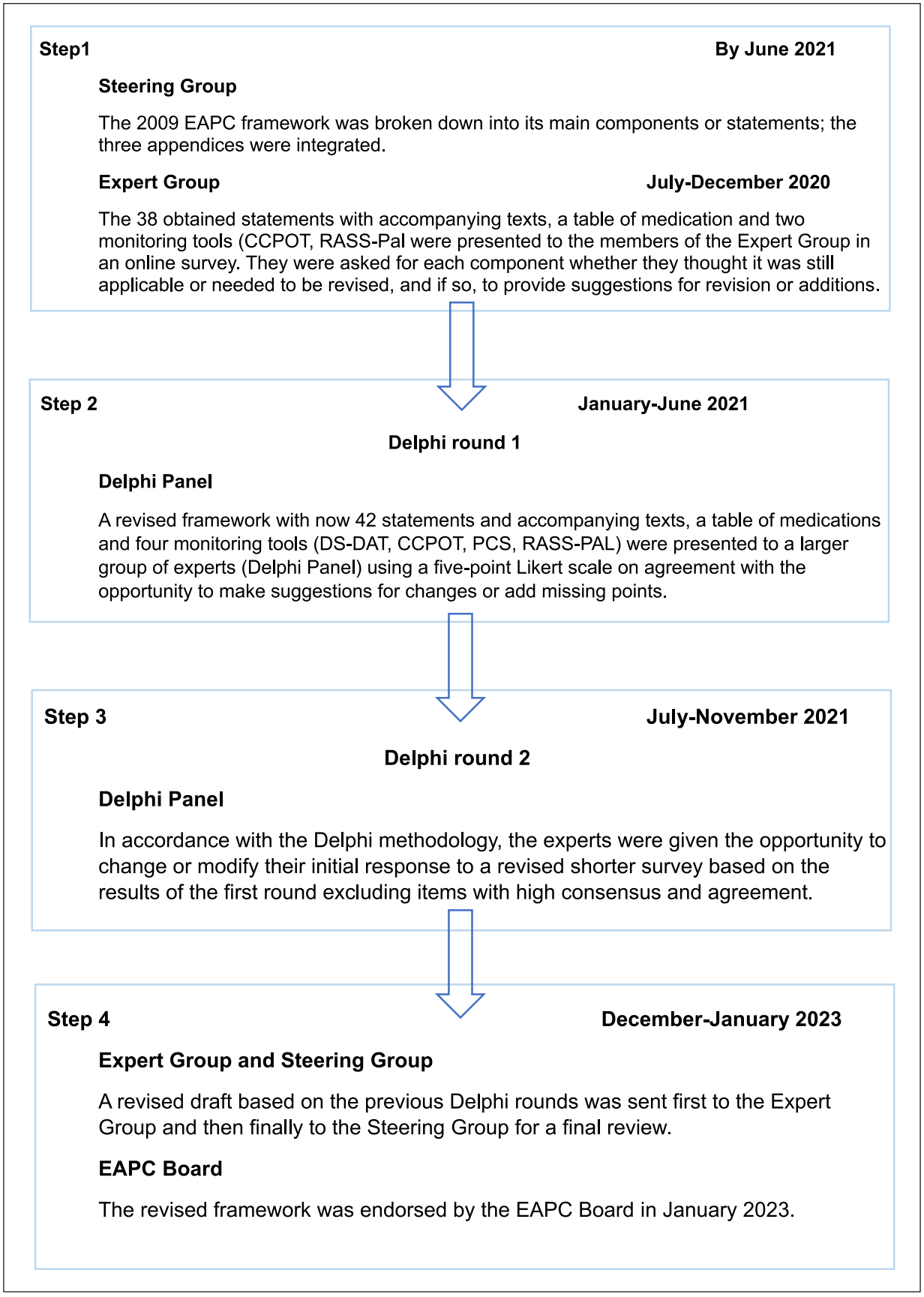

Figure 1. Steps of the Delphi procedure.

Table 1. Expert group (including steering group).

Name	Gender	Country	Profession	Institution
Apostolidis, K.	F	GR	Patient representative	European Cancer Patient Coalition, Brussels, Belgium
Aubry, R.	M	FR	Physician	Centre Hospitalier Universitaire de Besançon, Besançon, France
Broeckaert, B.	M	BE	Theologist	Interdisciplinary Centre for the Study of Religion and Worldview, KU Leuven, Leuven, Belgium
Caraceni, A.	M	IT	Physician	Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, Italy
Cardone, A.[a]	F	BE	Patient representative	European Cancer Patient Coalition, Brussels, Belgium[b]
Centeno, C.	M	ES	Physician	ATLANTES Global Palliative Care Observatory, Institute for Culture and Society, University of Navarra, Pamplona; IdiSNA, Instituto de Investigación Sanitaria de Navarra, Pamplona, Spain
Cherny, N.	M	IL	Physician	Department of Medical Oncology, Shaare Zedek Medical Center, Jerusalem, Israel
Csikós, Á.	F	HU	Physician	Department of Primary Health Care, Department of Hospice-Palliative Care, University of Pecs Medical School, Pecs, Hungary
Eychmüller, S.	M	CH	Physician	University Center for Palliative Care, Inselspital University Hospital Bern, University of Bern, Bern, Switzerland
Fainsinger, R.	M	CA	Physician	University of Alberta, Edmonton, Canada
Garralda, E.[a]	M	ES	Researcher	ATLANTES Global Palliative Care Observatory, Institute for Culture and Society, University of Navarra, Pamplona; IdiSNA, Instituto de Investigación Sanitaria de Navarra, Pamplona, Spain
Hasselaar, J.[a]	M	NL	Researcher	Department of Anaesthesiology, Pain and Palliative Medicine, Radboud University Medical Centre, Nijmegen, Netherlands
Jaspers, B.[a]	F	GE	Researcher	Department of Palliative Medicine, University Hospital Bonn, Bonn; Department of Palliative Medicine, University Medicine Goettingen, Goettingen, Germany
Leget, C.	M	NL	Ethicist	University of Humanistic studies, Utrecht, Netherlands
Ling, J.	F	BE	Nurse	European Association for Palliative Care, Vilvoorde, Belgium
Lombard, J.	M	IE	Lawyer	School of Law, University of Limerick, Limerick, Ireland
Menten, J.	M	BE	Physician	Laboratory of Experimental Radiotherapy, KU Leuven, Leuven, Belgium
Mercadante, S.	M	IT	Physician	Main Regional Centre for Pain Relief and Palliative/Supportive Care, La Maddalena Cancer Centre, Palermo, Italy
Morita, T.	M	JP	Physician	Department of Palliative and Supportive Care, Palliative Care Team, Seirei, Mikatahara General Hospital, Hamamatsu, Shizuoka, Japan
Mosoiu, D.	F	RO	Physician	Medical Faculty, Transilvania University, Brasov; Education and National Development Department, Hospice Casa Sperantei, Brasov, Romania
Payne, S.[a]	F	UK	Researcher	International Observatory on End-of-Life Care, Faculty of Health and Medicine, Lancaster University, Lancaster, United Kingdom
Preston, N.	F	UK	Researcher	International Observatory on End-of-Life Care, Faculty of Health and Medicine, Lancaster University, Lancaster, United Kingdom
Radbruch, L.[a]	M	GE	Physician	Department of Palliative Medicine, University Hospital Bonn, Bonn, Germany
Schildmann, E.	F	DE	Physician	Department of Palliative Medicine, University Hospital, Ludwig-Maximilians-University Munich, Munich, Germany
Van den Block, L.	F	BE	Psychologist	Free University of Brussels, Brussels; Ghent University, Ghent, Belgium
Vissers, K.	M	NL	Physician	Department of Anaesthesiology, Pain and Palliative Medicine, Radboud University Medical Centre, Nijmegen, Netherlands
Weixler, D.	M	AT	Physician	Department of Anaesthesiology, Horn Hospital, Horn, Austria
NN	F	AL	Nurse	NN
NN	F	NL	Health Scientist	NN
NN	M	UK	Physician	NN
NN	M	USA	Physician	NN

[a]Steering Group.
[b]Invited as member of the ECPC, new affiliation: Smoke Free Partnership, Brussels, Belgium.

- very high: level of agreement ⩾90% and median 5, IQR = 0.

Statements that did not reach a high or very high level of agreement in the first Delphi-round, as well as statements that, despite reaching a high level of agreement, were the subject of comments and/or constructive suggestions, were to be revised and submitted to the second Delphi-round. If a statement should fail in the second Delphi-round (step 3) to reach the necessary level of consensus, it was decided to mention the statement and the lack of consensus on it and to describe the underlying reasons for the lack of consensus in the discussion.

Step 2: Based on the Expert Group's feedback, a revised online questionnaire (Supplemental File 1) with 42 statements and explanatory text, a table of medications and four assessment tools for monitoring was presented to the Delphi Panel. In addition to the Likert scale assessment, the opportunity was given to provide comments and literature for each statement and explanatory text (April–June 2021).

Step 3: Statements requiring revision were presented in the second round to the Delphi Panel (Supplemental File 2), again with additional free-text entry fields for comments and literature (November–December 2021).

Final phase (step 4). The revised draft based on the Delphi rounds and a short glossary (Supplemental Material Data 3) were sent to the Expert Group for a final review.

The final version approved by the Steering Group was presented to the EAPC board of directors for approval in September 2022.

Data management. The data was collected in excel sheets and the quantitative and qualitative analysis were carried out using SPSS Statistics 27.0 and NVivo R 1.61, respectively (HB and SMS). Each proposed amendment was reviewed by HB and SMS, discussed in the working group with BJ and LR and approved by the Steering Group.

Results of the Delphi procedure

In addition to the Steering Group (n = 6), the work package leaders (n = 8) and advisory board members (n = 4) 15 experts were invited to join the Expert Group. Thirteen responded positively, resulting in an Expert Group of 31 members (Table 1). Twenty-five of them completed the online survey (step 1). All in all, a total of 193 experts (including Steering Group and Expert Group) were invited to participate to the Delphi Panel, and 91 agreed. The first and second Delphi rounds (steps 2 amd 3) were completed by 66 and 59 of these experts (response rate 73% and 65%), respectively (Table 2, Figure 2).

After the first Delphi round, 4 of the 42 statements reached a moderate, 32 a high and 6 a very high level of consensus. Feedback from participants led to significant revisions in 12 statements including explanatory text with high consensus. These statements as well as the four revised statements with moderate consensus concerning the domains *indication* (statement 4) and *selection of method* (statements 22–24) were presented to the Delphi Panel in the second round. Following the second Delphi round, 32 statements reached a high and 10 a very high level of consensus (Table 3). These 42 statements with their

Table 2. Sociodemographic data of the Delphi panelists.

Delphi round	1 (n = 66)	2 (n = 59)
Gender		
Female	26	22
Male	40	37
Age range (years)		
31–40	6	5
41–50	12	8
51–60	25	22
61–70	21	22
>71	2	1
No answer	0	1
Profession		
Ethicist	6	6
Health caregiver	9	6
Legal expert	1	1
Physician	41	38
Psychologist/psychotherapist	2	1
Researcher	4	4
Social worker	1	1
Other	2	2
Faith		
Christian		
Greece Orthodox	3	3
Protestant	19	16
Roman Catholic	21	19
Jewish	2	1
Muslim	0	0
Not belonging to a religion	18	18
No answer	3	2
Countries		
Northern Europe: Denmark, Finland, Iceland, Norway and Sweden	9	9
Western Europe: Belgium, France, Ireland, Netherlands and United Kingdom	18	17
Central Europe: Austria, Czech Republic, Germany, Hungary, Poland and Switzerland	22	20
Eastern Europe: Romania and Ukraine	2	1
Southern Europe: Albania, Cyprus, Greece, Italy and Spain	10	10
Outside Europe: Japan, Canada and Israel	4	2
No answer	1	0

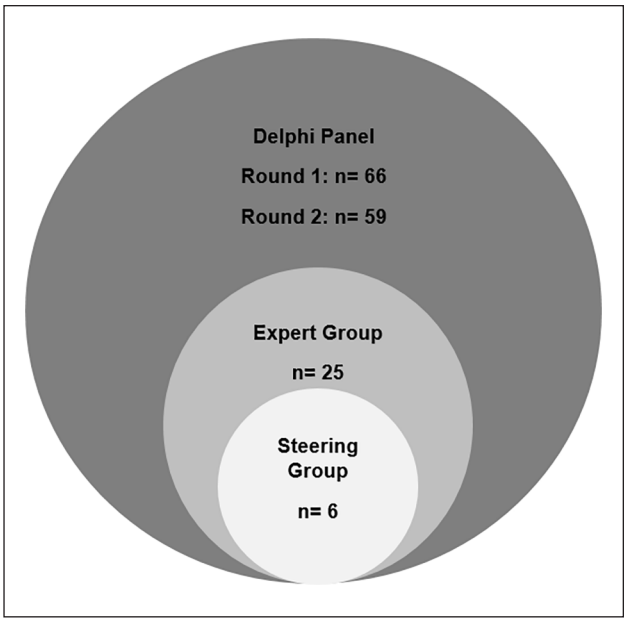

Figure 2. Delphi Panel.

explanatory text are organised into 12 distinct domains (Table 4) and include a table of medications (Table 5) and four assessment tools for monitoring (the Discomfort Scale – Dementia of Alzheimer Type (DS-DAT),[23,24] the Critical-Care Pain Observation Tool (CCPOT),[25] the Patient Comfort Score (PCS)[26,27] and the Richmond Agitation Sedation Scale – Palliative Version (RASS-PAL).[26,28–31]

The amended version included an introduction, method and discussion section and was reviewed by 21 members of the Expert Group (response rate 70%) before being approved by the Steering Group and then by the EAPC Board of Directors, after minor modifications in January 2023.

Discussion

Main findings

More than a decade after the publication of the EAPC framework on palliative sedation this paper presents an update, using a rigorous consensus methodology. A range of experts were involved, with great commitment in the consensus process providing detailed comments and recommending literature, leading to a number of revisions with considerable impact on the framework and resulting in 42 statements in 12 distinct domains. After the two Delphi rounds, a high or very high consensus level was achieved for all statements.

What this study adds?

The main criticisms of the 2009 framework were due partly to the lack of a precise definition of the term refractoriness, the vaguely defined role of the patient (or their representative) in the determination of refractoriness, and the lack of clarity regarding the status of existential suffering as a possible indication for palliative sedation[14,19]. In the revised framework, the terminology has been more precisely defined. The term *suffering* (stat. 1) is used to encompass distressing physical and psychological symptoms as well as states of existential suffering to reflect a shift towards a broader recognition of refractory existential suffering as indication for palliative sedation. The term *refractory* (stats. 2 and 3) described the untreatable (healthcare professionals) and intolerable (patient) nature of the suffering. The consultation of palliative care experts and/or other healthcare experts to determine the untreatable nature of the suffering is strongly recommended before applying palliative sedation (stat. 13).

The literature search revealed that most of the existing publications deal with deep and continuous sedation, probably because this form of sedation is easier to compare between different settings. A broad consensus emerged among the experts on the importance of stressing the principle of proportionality in palliative sedation practice. This principle encompasses proportionality along two main dimensions. First in terms of depth of sedation, with the administration of sedative medications being titrated to the lowest dosage that will provide adequate relief of suffering and maintain interactive function as far as possible, instead of aiming straight at unconsciousness (stats. 1 and 5). Secondly, it also encompasses proportionality in terms of timing, as intermittent sedation will be more appropriate than continuous sedation earlier in the course of the illness to provide temporary relief whilst waiting for treatment benefit from other therapeutic approaches (transient sedation) or to give the patient a break from the current burdensome situation (respite sedation) before regaining consciousness (stat. 1). The physician will therefore first discuss with the patient the form of sedation which is appropriate to their individual situation. Apart from emergency situations at the end of life, a planned interruption of the sedation is recommended, whenever possible, to reassess the situation with the patient. This principle of proportionality has been explicitly introduced into the definition of palliative sedation. Consequently, a sedation that does not meet this principle – for example, deep sedation for moderate symptoms – should not be considered as palliative sedation.

Consideration of remaining life expectancy varied considerably from one guideline to another.[12–14] The revised framework clearly states (stat. 1) that no specific period of remaining life expectancy is defined for the use of palliative sedation based on the three key principles (1) refractoriness of suffering, (2) proportionality and (3) independent decision making for hydration,

Table 3. Consensus data of the two Delphi rounds.

Statement	Percentage of agreement	Median	Inter-quartile range	Level of consensus	Percentage of agreement	Median	Inter-quartile range	Level of consensus
	First Delphi round				Second Delphi round			
1	84.6	5	1	High				
2	84.8	5	1	High				
3	83.3	4	1	High				
4	78.5	5	1	Moderate	84.2	5	1	High
5	90.9	5	1	High	88.2	5	1	High
6	86.4	5	1	High				
7	90.9	5	1	High				
8	86.1	5	1	High				
9	89.3	5	1	High	96.6	5	0	Very high
10	93.9	5	1	High				
11	94	5	1	High				
12	90.9	5	1	High	88.1	5	1	High
13	92.3	5	0.5	High				
14	90.7	5	1	High	95	5	0	Very high
15	86.4	5	1	High				
16	86.1	5	1	High				
17	96.9	5	0	Very high				
18	86.3	5	1	High	91.5	5	1	High
19	81.5	5	1	High	89.8	5	1	High
20	84.4	5	1	High				High
21	90.8	5	1	High	91.5	5	1	High
22	79.7	5	1	Moderate	89.7	5	1	High
23	76.5	4	1	Moderate	86.2	5	1	High
24	77	4	1	Moderate	83	5	1	High
25	80	5	1	High	93.3	5	0	Very high
26	80.3	5	1	High	86.5	5	1	High
27	85	5	1	High				
28	91.5	5	1	High				
29	93.6	5	1	High				
30	85.5	4.5	1	High				
31	84.4	4	1	High				
32	91.9	5	1	High				
33	96.9	5	0	Very high				
34	90.8	5	0	Very high				
35	80.3	4	1	High	84.5	4	1	High
36	92	5	1	High				
37	93.8	5	0	Very high				
38	95.4	5	0	Very high				
39	93.9	5	0	Very high				
40	93.8	5	1	High				
41	89.2	5	1	High	94.9	5	0	Very high
42	98.4	5	1	High				

Level of consensus	Level of agreement	Median	Interquartile range
Low	$<$60%	$<$4	$>$2
Moderate	60%–79%	4–5	$\geqslant$1
High	80%–89%	4–5	1
Very high	$>$90%	5	0

Table 4. Domains and statements through the Delphi consensus procedure.

Domain	Expert group	Delphi 1	Delphi 2	Final statements
1. Definition	Palliative sedation in the context of palliative medicine is defined 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 health-care providers	1. Palliative sedation aims to relieve refractory suffering through the monitored proportional use of medications intended to reduce consciousness in terminally ill patients. Palliative sedation has major social and ethical implications requiring specific considerations by patients, significant others and care providers.		1. Palliative sedation aims to relieve refractory suffering through the monitored proportional use of medications intended to reduce consciousness in patients with **life-limiting disease**. Palliative sedation has major social and ethical implications requiring specific considerations by patients, significant others and care providers.
	Symptoms are considered to be refractory, when there is a lack of other methods for palliation within an acceptable time frame and without unacceptable adverse effects (refractoriness).	2. Symptoms or a state of existential distress are considered to be refractory, when there is a lack of methods likely to provide appropriate relief within an acceptable time frame and without unacceptable adverse effects.		2. Symptoms or a state of existential distress are considered to be refractory when there is a lack of methods likely to provide appropriate relief within an acceptable time frame and without unacceptable adverse effects.
		3. The notion of refractoriness can be applied to a single symptom/state, or to a cluster of symptoms/states whose combination leads to a condition which the patient feels is intolerable. Determining refractoriness is a joint decision between the physician (and/or the multi-professional team) and the patient.		3. The notion of refractoriness can be applied to a single symptom/state or to a cluster of symptoms/states whose combination leads to a condition which the patient feels is intolerable. Determining refractoriness is a joint decision between the physician (and/or the multi-professional team) and the patient **or their legal representative/significant others**.
2. Indication	Palliative Sedation is used in palliative care in several settings: 1. Sedation in the management of refractory symptoms at the end of life 2. Emergency sedation 3. Respite sedation 4. Sedation for psychological or existential suffering 5. Sedation used in end-of-life weaning from ventilator support	4. Palliative Sedation can be used 1. For the management of refractory suffering 2. For emergency situations in case of imminent death 3. For a temporary respite 4. For the use in end-of-life weaning from ventilator support	Palliative Sedation is used 1. for the management of refractory suffering; 2. In emergency situations in case of imminent death or in end-of-life weaning from ventilator support*, when the occurrence of refractory suffering is foreseeable 3. As temporary respite when treatment cannot achieve sufficient relief in an acceptable timeframe.	4. Palliative sedation is used 1. For the management of refractory suffering; 2. In emergency situations in case of imminent death; 3. In end-of-life weaning from **life sustaining** support, when the occurrence of refractory suffering is foreseeable; 4. As temporary respite when treatment cannot achieve sufficient relief in an acceptable timeframe.
		5. The aim of continuous deep palliative sedation is not to shorten life, but to relieve refractory symptoms.	The aim of palliative sedation is to relieve refractory suffering, not to shorten life.	5. The aim of palliative sedation is to relieve refractory suffering, not to shorten life.
	Palliative Sedation in the management of refractory psychological symptoms and existential distress is different from other situations for four major reasons: 1. By virtue of the nature of the symptoms being addressed, it is much more difficult to establish that they are refractory; 2. The severity of distress of some of these symptoms may be very dynamic and idiosyncratic, and psychological adaptation and coping may occur; 3. The standard treatment approaches have low intrinsic morbidity; and 4. The presence of these symptoms does not necessarily indicate a far advanced state of physiological deterioration.	6. Palliative Sedation in the management of refractory psychological symptoms and existential distress is different from other situations for some major reasons: 1. The severity of the distress may be very dynamic and idiosyncratic, and psychological adaptation and coping may occur. Therefore, it is much more difficult to establish refractoriness. 2. The pharmacological and non-pharmacological approaches have low intrinsic morbidity; and 3. The presence of this distress does not necessarily indicate a far advanced state of physiological deterioration.		6. Palliative sedation in the management of refractory psychological symptoms and existential distress is different from other situations for some major reasons: (1) The severity of the distress may be very dynamic and idiosyncratic, and psychological adaptation and coping may occur. Therefore, it is much more difficult to establish refractoriness; (2) The pharmacological and non-pharmacological approaches have low **adverse effects**; (3) The presence of this distress does not necessarily indicate a far advanced state of physiological deterioration.
3. Adverse outcomes and risks	Palliative sedation should be a treatment of last resort because of its potential risks and anticipated adverse outcomes.	7. Palliative sedation should be a treatment undertaken with due care and competence because of anticipated adverse outcomes and potential risks.		7. Palliative sedation should be **carefully considered because of the probable loss of the patient's ability to interact** and of potential risks.
	Palliative sedation should not be used in an abusive, injudicious or in a substandard way.	8. Palliative sedation should not be used in an injudicious or in a substandard way.		8. Palliative sedation should not be used in an injudicious or in a substandard way **nor withheld injudiciously**.
4. Advance Care Planning	The potential role of palliative sedation in end-of-life care and contingency planning should be discussed pre-emptively.	9. The potential role of palliative sedation in end-of-life care and contingency planning should be discussed pre-emptively.	The potential role of palliative sedation in end-of-life care and contingency planning should be discussed pre-emptively.	9. The potential role of palliative sedation in end-of-life care and contingency planning should be discussed pre-emptively.
	When the potential for catastrophic events such as bleeding or extreme distress is foreseen, contingency plans for the management of these events should be discussed with the patient, family members (with the patient's consent)/legal representative and the involved caregivers.	10. When the potential for catastrophic events such as bleeding or extreme distress is foreseen, contingency plans for the management of these events should be discussed with the patient, significant others (with the patient's consent)/legal representative and the involved professional caregivers.		10. When the potential for **emergency situations** such as **massive** bleeding or extreme distress is foreseen, contingency plans for the management of these events should be discussed with the patient, significant others (with the patient's consent)/ legal representative and the involved professional caregivers.
	The outcomes of these discussions should be documented and stored in a readily accessible format.	11. The outcomes of these discussions should be documented and, together with the advance directive, stored in a readily accessible format.		11. The outcomes of these discussions should be documented and, together with the advance directive **(if available)**, stored in a readily accessible format **to all involved caregivers**.

(Continued)

Table 4. (Continued)

Domain	Expert group	Delphi 1	Delphi 2	Final statements
5. Decision making	Extreme distress requiring palliative sedation is a medical emergency and patient evaluation must be performed by a physician with sufficient experience and expertise in palliative care with due urgency. Wherever possible this evaluation should be interdisciplinary.	12. When a patient has refractory symptoms, an assessment should be performed with due urgency by a physician with sufficient palliative care expertise. Wherever possible this evaluation should be interdisciplinary and multi-professional.	When a patient has refractory symptoms, an assessment should be performed with due urgency by a physician with sufficient palliative care expertise. Wherever possible this evaluation should be interdisciplinary and multi-professional.	12. When a patient **seems to have** refractory symptoms, an assessment should be performed with due urgency by a physician with sufficient palliative care expertise. Wherever possible this evaluation should be interdisciplinary and multi-professional.
		13. If there is uncertainty concerning the patient evaluation, especially with regard to whether all options to relieve distress have been considered, consultation with a specialist palliative care team and/or with other healthcare experts (e.g. psychologists, psychiatrists, anaesthetists, pain specialists, oncologists and specialist nurses) should be sought.		13. If there is uncertainty concerning the patient evaluation, especially with regard to whether all options to relieve distress have been considered, consultation with a specialist palliative care team and/or with other healthcare experts (e.g. psychologists, psychiatrists, anaesthetists, pain specialists, oncologists and specialist nurses) **is strongly recommended**.
	The designation of psychological symptoms and existential distress as refractory should only be done following a period of repeated assessment by clinicians skilled in psychological care who have established a relationship with the patient (and their family) along with therapeutic trials of standard interventions for anxiety, depression and existential distress.	14. The designation of psychological symptoms and existential distress as refractory should only be done following a period of repeated assessment by experts skilled in psychological, social or spiritual care who have established a relationship with the patient (and their significant others) along with standard approaches for treatment of anxiety, depression and existential distress.	The designation of psychological symptoms and existential distress as refractory should only be done following a period of comprehensive assessment by experts in palliative care, considering the psychological, social and spiritual components of suffering, with, if necessary, consultation with other professionals competent in one of these areas.	14. The designation of psychological symptoms and existential distress as refractory should only be done following comprehensive assessment by experts in palliative care, considering the psychological, social and spiritual components of suffering, with, if necessary, consultation with other professionals competent in one of these areas.
	Whenever possible, the medical rationale for palliative sedation as well as the decision-making process should be based on input from the multi-professional palliative care team, rather than by the treating physician alone. Case discussion and team conferences may be suitable platforms to facilitate this process.	15. Whenever possible, the medical rationale for palliative sedation should be based on input from the multi-professional palliative care team, rather than by the treating physician alone. Case discussion and team conferences may be suitable platforms to facilitate this process.		15. Whenever possible, the medical rationale for palliative sedation should be based on input from a multi-professional palliative care team, rather than by the treating physician alone. Case discussion and team conferences may be suitable platforms to facilitate this process.
		16. The patient and, with their consent, their significant others should be, whenever possible, involved in the decision-making process.		16. The patient and, with their consent, their significant others should be, whenever possible, involved in the decision-making process.
	The medical rationale for recommending palliative sedation, the decision-making process, the aims of palliative sedation and the planned depth and duration of palliative sedation must be recorded, in any easily retrieved document (e. g. the patient's medical record).	17. The medical rationale for recommending palliative sedation, the decision-making process, the aims of palliative sedation and, in case of intermittent sedation, the planned duration of palliative sedation must be recorded in any easily accessible document (e. g. the patient's medical record), regardless of the patient's care setting.		17. The medical rationale for recommending palliative sedation, the decision-making process, the aims of palliative sedation and, in case of intermittent sedation, the planned duration of palliative sedation must be recorded in any easily accessible document (e. g. the patient's medical record), regardless of the patient's care setting.
	Apart from emergency situations the aims, methods, benefits and risks of the proposed palliative sedation should be discussed with patients capable of making decisions.	18. Apart from unanticipated emergency situations the aims, methods, benefits and risks of the proposed palliative sedation must be discussed with and approved by patients capable of making decisions by means of an informed consent.	Apart from unanticipated emergency situations the aims, methods, benefits and risks of the proposed palliative sedation should be discussed with and approved by patients capable of making decisions by means of an informed consent. The physician should nevertheless adapt the content of this discussion to the extent that the patient wishes to be informed.	18. Apart from unanticipated emergency situations the aims, methods, benefits and risks of the proposed palliative sedation should be discussed with and approved by patients capable of making decisions by means of an informed consent. The physician should nevertheless adapt the content of this discussion to the extent that the patient wishes to be informed.
	If the patient lacks decisional capacity and there is no advance directive, proxy consent should be obtained from a legal representative.	19. If the patient lacks decisional capacity, advance directives must be respected. In the absence of advance directives, their presumed treatment preferences should be, whenever possible, sought from a legal representative.	If the patient lacks decisional capacity, advance directives must be considered. In the absence of advance directives, their previously expressed preferences should be considered or presumed treatment preferences should be elicited, whenever possible, from a legal representative and/or significant others.	19. If the patient lacks decisional capacity, advance directives**/ advance care planning** must be considered. In the absence of advance directives, their previously expressed preferences should be considered or presumed treatment preferences should be elicited, whenever possible, from a legal representative and/or significant others.
	In the absence of advanced directive and health-care proxy, provision of comfort measures in the best interest of the patient (including, if necessary, the use of palliative sedation) should be the default strategy for clinician treatment decisions.	20. In the absence of an advance directive and legal representative, provision of comfort measures in the best interest of the patient (including, if necessary, the use of palliative sedation) should be the default strategy for treatment decisions.		20. In the absence of an advance directive **or similar documentation of the patient's preferences and if there is no** legal representative, provision of comfort measures in the best interest of the patient (including, if necessary, the use of palliative sedation) should be the default strategy for treatment decisions.

(Continued)

Table 4. (Continued)

Domain	Expert group	Delphi 1	Delphi 2	Final statements
	The decision-making process should be discussed with the patient's family provided the patient's consent.			
	In some cultures, family assent may be deemed necessary or desirable.	21. In a culturally-sensitive approach, it is important to acknowledge that in some cultures, family assent may be deemed necessary or desirable.	It is important to opt for a culturally-sensitive approach and to take the influence of culture, religion and worldview into account.	21. It is important to opt for a culturally sensitive approach and to take the influence of culture, religion and worldview into account.
6. Selection of method	Other than in emergency situations at the end of life, intermittent or mild sedation should generally be attempted first.	22. Other than in emergency situations at the end of life, intermittent or light sedation should generally be attempted first	Other than in emergency situations at the end of life, light sedation should generally be attempted first	22. Other than in emergency situations at the end of life, light sedation should generally be attempted first.
	Transient or respite palliative sedation could be indicated earlier in the patient's trajectory to provide temporary relief whilst waiting for treatment benefit from other therapeutic approaches.	23. Intermittent palliative sedation can be indicated early in the patient's disease trajectory to provide temporary relief whilst waiting for treatment benefit from other therapeutic approaches (transient sedation) or to give the patient a break from the current burdensome situation (respite sedation) before regaining consciousness.	Intermittent palliative sedation can be indicated early in the patient's disease trajectory to provide temporary relief whilst waiting for treatment benefit from other therapeutic approaches (transient sedation) or to give the patient a break from the current burdensome situation (respite sedation) before regaining consciousness.	23. Intermittent palliative sedation can be indicated early in the patient's disease trajectory to provide temporary relief whilst waiting for treatment benefit from other therapeutic approaches (transient sedation) or to give the patient a break from the current burdensome situation (respite sedation) before regaining consciousness.
	Palliative sedation in the management of refractory psychological symptom s and existential distress should be reserved for patients in advanced stages of a life limiting illness. In the case of psychological symptoms or existential distress where palliative sedation is indeed appropriate and proportionate to the situation, it should be initiated on a respite basis for 6–24 h with planned downward titration after a pre-agreed interval.	24. In the case of psychological symptoms or existential distress as the sole indication for palliative sedation, when palliative sedation is appropriate to the situation, it should be initiated on a respite basis for 24–48 h with planned downward titration after a pre-agreed interval.	In the case of psychological symptoms or existential distress as the primary indication for palliative sedation, when palliative sedation is appropriate to the situation, intermittent sedation should be attempted first with planned downward titration after a pre-agreed interval	24. In the case of psychological symptoms or existential distress as the primary indication for palliative sedation, when palliative sedation is appropriate to the situation, intermittent sedation should be attempted first with planned downward titration after a pre-agreed interval.
	Deeper palliative sedation should be adopted when mild sedation has been ineffective.	25. Deeper palliative sedation should be considered when light sedation has been ineffective.	Deeper palliative sedation should be considered when light sedation has been ineffective, or when it is clear that light sedation cannot provide adequate relief in time or in an emergency situation (e. g. massive haemorrhage or asphyxia).	25. Deeper palliative sedation should be considered when light sedation has been ineffective, or when it is clear that light sedation **will not** provide adequate relief in time or in an emergency situation (e. g. massive haemorrhage or asphyxia).
	Continuous deep sedation could be selected first if: (1) the suffering is intense; definitely refractory; death is anticipated within hours or a few days; the patient's wish is explicit or (2) in emergency situation at the end-of-life (e. g. massive haemorrhage or asphyxia).	26. Continuous deep sedation should be considered: 1. When intermittent or continuous light sedation has been ineffective and the patient's wish has been explicit or 2. in emergency situation at the end-of-life (e. g. massive haemorrhage or asphyxia).	The option of continuous deep sedation should be considered when intermittent sedation or continuous light sedation have been insufficient to relieve suffering adequately.	26. The option of continuous deep sedation should be considered when intermittent sedation or continuous light sedation have been insufficient to relieve suffering adequately.
7. Pharmacological measures for palliative sedation		27. A well-controllable benzodiazepine such as midazolam should be used as first line approach. Lorazepam can be used as an alternative. A low potency neuroleptic can be used in combination with the benzodiazepine if needed. Levomepromazine or chlorpromazine may be used. Propofol can be used as a third step but should be administered by an anaesthetist or a person with sufficient experience in its use. 28. Opioids and haloperidol should not be used as sedatives.		27. A well-controllable benzodiazepine such as midazolam should be used as first-line approach. Lorazepam can be used as an alternative. **As a second step,** a low potency neuroleptic can be used in combination with the benzodiazepine if needed. Levomepromazine or chlorpromazine may be used. Propofol can be used as a third step but should be administered by an anaesthetist or a person with sufficient experience in its use. 28. Opioids and haloperidol should not be used to sedate a patient.
8. Monitoring	Palliative sedation should be started by a physician and a nurse together.	29. Palliative sedation should be, whenever possible, started and supervised by a physician and a nurse together until the desired level of comfort is achieved.		29. Palliative sedation should be, whenever possible, started and supervised by a physician and a nurse together until the desired level of comfort is achieved.
	The patient should be initially assessed at least once every 20 min until adequate sedation is achieved, and subsequently at least three times per day after adequate sedation has been achieved.	30. The patient should be initially assessed at least once every 20 min until adequate sedation is achieved, and subsequently at least three times per day in case of continuous sedation.		30. The patient should be initially assessed at least once every 20 min until adequate sedation is achieved, and subsequently at least three times per day in case of continuous sedation.
	When palliative sedation is intended to be intermittent or light, efforts should be made to preserve physiological stability within the pre-agreed treatment constraints.	31. When palliative sedation is intended to be light, or for intermittent sedation, efforts should be made to preserve physiological stability within the therapeutic limits pre-agreed with the patient.		31. When palliative sedation is intended to be light, or for intermittent sedation, efforts should be made to preserve physiological stability within the therapeutic limits pre-agreed with the patient.

(Continued)

Table 4. (Continued)

Domain	Expert group	Delphi 1	Delphi 2	Final statements
	When the goal of care is to ensure comfort until death for an imminently dying patient, the only critical parameters for ongoing observation should be those pertaining to comfort.	32. For palliative sedation in the final stage of life, the goal of care is to ensure comfort until death and the only critical parameters for ongoing observation should be those pertaining to comfort.		32. For palliative sedation in the final stage of life, the goal of care is to ensure comfort until death and the only critical parameters for ongoing observation should be those pertaining to comfort.
	In all cases, the care team must maintain the same level of humane dignified treatment as before palliative sedation.	33. In all cases, the care team must maintain the same level of personalised care as before palliative sedation.		33. In all cases, the care team must maintain the same level of personalised care as before palliative sedation.
		34. In case of recurrent or complex problems with palliative sedation consultation with a palliative care team should be sought.		34. In case of recurrent or complex problems with palliative sedation consultation with a palliative care team should be sought.
9. Hydration/ Nutrition	The decision about artificial hydration/nutrition therapy should be independent of the decision about palliative sedation itself.	35. The decision about artificial hydration/nutrition therapy should be independent of the decision about continuous palliative sedation itself.	The decision about artificial hydration/nutrition therapy should be independent of the decision about continuous palliative sedation itself.	35. The decision about artificial hydration/nutrition therapy should be independent of the decision about continuous palliative sedation itself.
10. Pharmacological and non-pharmacological measures	Medications for symptom palliation used before palliative sedation should be continued, unless they are ineffective or have distressing side effects.	36. Pharmacological and non-pharmacological measures for symptom relief already in use before onset of palliative sedation should be continued unless they are ineffective or have distressing side effects.		36. Pharmacological and non-pharmacological **(e. g. mouth care)** measures for symptom relief already in use before onset of palliative sedation should be continued unless they are ineffective or have distressing side effects.
	Medications and measures that are either inconsistent with or, irrelevant to the goal of patient comfort should be withdrawn generally.	37. Pharmacological and non-pharmacological measures that are either inconsistent with or irrelevant to the goal of patient comfort should be withdrawn generally.		37. Pharmacological and non-pharmacological measures that are either inconsistent with or irrelevant to the goal of patient comfort should be generally withdrawn.
11. Significant others care	Families should be allowed and encouraged to be with the patient and, in many situations, an opportunity to say goodbye may be of critical importance.	38. The opportunity to be with the patient and to say goodbye should be given to the significant others.		38. The opportunity to be with the patient and to say goodbye should be given to the significant others.
	The care team should provide supportive care to the members of the patient's family.	39. The care team should provide information and support to the patient's significant others.		39. The care team should provide information and support to the patient's significant others.
	After the death of the patient, the family should be offered the opportunity to meet with the care providers.	40. After the death of the patient, the significant others should be offered the opportunity to meet with the care providers, including spiritual or grief counsellors.		40. After the death of the patient, the significant others should be offered the opportunity to meet with the care providers, including spiritual **caregivers** or grief counsellors.
		41. Significant others should be offered the opportunity of bereavement support.	Significant others should be informed about the opportunity of bereavement support.	41. Significant others should be informed about the opportunity of bereavement support.
12. Staff care	The care team should recognise the potential for staff distress.	42. The care team should recognise the potential for staff distress.		42. The care team should recognise the potential for staff distress.

Terms in bold in the final version correspond to editorial changes made based on the expert comments during the Delphi rounds.
New statements Statements with moderate agreement

Table 5. Table of medications.

	Medication	Initial bolus	Maintenance dose
Step 1	Midazolam	Light palliative sedation 2.5 mg SC 1.25 mg IV Deep palliative sedation 5–10 mg SC 2.5–5 mg IV Bolus with half of the starting bolus dosage may be repeated after 20 min SC or 5 min IV if necessary. It is not uncommon to give two to three additional boli during the first hrs of palliative sedation.	Use 1 mg/h (SC and IV) and then adjust as needed. Dosage has to be titrated according to effect. It can be adjusted every 1–2 h as required in conjunction with another bolus. If risk factors are present (age >60 years, weight <60 kg, severe kidney or liver function disorder, very low serum albumin and/or co-medication that could exacerbate the effect of sedation): Half the initial dose, and Longer interval (6–8 h) before increasing maintenance dose. In the case of doses higher than 10 mg/h, consider adding or changing medication.
Alternative to midazolam	Lorazepam	1–3 mg SC or IV	When administered by intermittent bolus: 1–3 mg SC or IV every 2–4 h Or 1–5 mg/h SC or IV by continuous infusion
Step 2 in combination with midazolam	Levomepromazine	12.5–25 mg SC or IV	When administered by intermittent bolus: 12.5–25 mg SC or IV every 6–8 h Or 0.5–8 mg/h SC/IV by continuous infusion. After 3 days, reduce the dose of levomepromazine by half to avoid accumulation of the sedative medication. If the desired effect is not obtained, the administration of midazolam and levomepromazine should be changed to an alternative medication.
Alternative to levomepromazine	Chlorpromazine	12.5 mg in slow IV infusion over 0.5–1 h or 12.5 mg IM every 4–12 h or 3–5 mg/h IV or 25–100 mg PR every 4–12 h	Usual effective dose: Parenteral 37.5–150 mg/day, PR 75–300 mg/day.
Step 3	Propofol		Starting dose: 1 mg/kg/h IV, increase by 0.5 mg/kg/h every 30 min. Administration under the supervision of an anaesthesiologist is advisable.
Intermittent sedation	Benzodiazepines are appropriate for intermittent sedation. Midazolam should be stopped 30 min (if IV) or 2 h (if SC) before the expected awakening of the patient. To restart palliative sedation, the starting bolus and maintenance dose are those that were optimal last time.		

although deep and continuous sedation is generally indicated in the final stages of life. However, it was not possible to reach consensus in the Delphi process on a precise definition of the final stages of life.

The new statements emphasise the need of timely discussion of patient preferences (stats. 9 and 10) and shared decision-making between patient (and with their consent, their significant others/legal representative) and healthcare professionals (stats. 16, 18 and 19).

The applicability of the framework has been improved by the development of a step-by-step pharmacological approach (stats. 27 and 28) with a detailed description of the recommended medications (Table 5) and more detailed guidance on hydration decision-making based on recent literature (stat. 35).

Nevertheless, even with this high level of agreement, some aspects were debated until the final stage of the consensus process. The comments in question could not always be integrated into the respective statements as they sometimes presented opposing views. The different positions seem to be related to heterogeneous concepts of palliative sedation. Some participants seemed to understand palliative sedation as a merely medical intervention, requiring clear indications and concise definitions and checklists, others highlighted also the social and ethical challenges related to palliative sedation and advocated for a team-based approach with more ethical safety guards, and enough flexibility in the statements for adaptation for the specific patient or cultural context. As an example, several experts expressed concerns about discussing advance care planning (ACP) and in particular palliative sedation with patients at an early stage of the disease. This might reflect reluctance to discuss a medical intervention that is not yet indicated, even though these

concerns are at odds with recent studies[32,33] showing the benefit of ACP discussion for patient and significant others as a process that occurs in a continuum.[34]

In addition, the discussion highlighted the differences in the legal, healthcare and social security systems between European countries. As an example, the role of the legal representative seems to be perceived differently. In some countries, their role is seen predominantly to communicate the patient's preferences and thus participate in the decision-making process. Within this perspective, they seem to be somewhat protected from the weight of the decision. In other countries their role is to make the final decision after receiving all necessary medical information. Similarly, some expert feedback called for mandatory consultation with palliative care experts before initiation of palliative sedation, whereas others rejected this as it would disadvantage patients based on territorial disparity in access to specialist palliative care.[35]

Strengths and limitations

In consequence of the above-mentioned differences, as with all European standards this framework might need adaptation by clinicians and health policy decision-makers to the specific national or local context with high quality procedural guidelines related to their specific legislation, regulations and culture.

Nevertheless, this is the first framework on palliative sedation using a strict consensus methodology involving experts from all over Europe and beyond (28 countries) with a broad range of professions, as well as a European patient organisation. All European regions (North, South, Central, East and West Europe; Table 2) were involved. Unfortunately, even though a gender balance in our invitations was sought, in the Delphi panel male participants predominated. The online Delphi survey was conducted in English after participants confirmed that the offer of translation into French, Spanish and Russian was not necessary. Literature search for the scoping reviews was limited to publications in English, resulting in a potential language bias. However, the analysis of existing guidelines on palliative sedation in the eight participating European countries[11,12,36–43] and the experts' recommended literature informed the framework with a number of references in other languages than English. The updated literature shows that there is still a lack of clinical trials and prospective studies.[2] The EAPC task force on palliative sedation will therefore, five years after publication of the framework, evaluate the need for an update on the basis of new evidence and changing thinking patterns. They will also audit the use of the new framework in Europe.

The full framework with explanatory texts and references will be available on the EAPC website in English (Supplemental File 4), and also other languages. It will be also disseminated through an educational programme (MOOC; https://www.futurelearn.com/courses/dying-well-the-role-of-palliative-care) and an e-book.

Conclusion

The revised framework including proposed assessment tools for monitoring, a comprehensive table of medications, dosages and administration forms, serves as comprehensive and soundly developed information for healthcare professionals on the use of palliative sedation as well as for medical associations and health policy decision-makers. Since its development considered all relevant methodological and content aspects of AGREE II,[23] an international tool to assess the quality and reporting of practice guidelines, it may be used as a guideline or serve as a basis for cultural adaptation of guidelines on palliative sedation.

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Author contributions

Conception and design of the study: HB, BJ, LR and SMS. Steering Group: AC, EG, JH, BJ, SP and LR. Data analysis: HB, BJ, LR and SMS. HB and SMS led the writing of the script. All authors (KA, HB, AC, ÀC, CC, NC, RF, EG, JH, BJ, JL, JM, SM, DM, SP, NP, LR, SMS and LVdB) provided feedback on one or more versions of the draft and contributed to the development of the paper. All authors revised and approved the final manuscript.

Declaration of conflicting interest

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The authors declare that there is no conflict of interest. The authors (apart from HB and SMS) participated in the Delphi process. However, the two researchers coordinating the consensus process and the evaluation (HB and SMS) did not participate, thus preventing any bias in the evaluation.

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Research ethics and patient consent

The study was approved by the Ethics Commission, University of Bonn, Germany, No. 268/20 (19 June 2020).

Data management and sharing

More detailed information on the consensus process results will be published separately.

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Supplemental material

Supplemental material for this article is available online.

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