

International variations in clinical practice guidelines for palliative sedation: a systematic review

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ABSTRACT

Objectives Palliative sedation is a highly debated medical practice, particularly regarding its proper use in end-of-life care. Worldwide, guidelines are used to standardise care and regulate this practice. In this review, we identify and compare national/regional clinical practice guidelines on palliative sedation against the European Association for Palliative Care (EAPC) palliative sedation Framework and assess the developmental quality of these guidelines using the Appraisal Guideline Research and Evaluation (AGREE II) instrument.

Methods Using the PRISMA criteria, we searched multiple databases (PubMed, CancerLit, CINAHL, Cochrane Library, NHS Evidence and Google Scholar) for relevant guidelines, and selected those written in English, Dutch and Italian; published between January 2000 and March 2016.

Results Of 264 hits, 13 guidelines—Belgium, Canada (3), Ireland, Italy, Japan, the Netherlands, Norway, Spain, Europe, and USA (2) were selected. 8 contained at least 9/10 recommendations published in the EAPC Framework; 9 recommended ‘pre-emptive discussion of the potential role of sedation in end-of-life care’; 9 recommended ‘nutrition/hydration while performing sedation’ and 8 acknowledged the need to ‘care for the medical team’. There were striking differences in terminologies used and in life expectancy preceding the practice. Selected guidelines were conceptually similar, comparing closely to the EAPC Framework recommendations, albeit with notable variations.

Conclusions Based on AGREE II, 3 guidelines achieved top scores and could therefore be recommended for use in this context. Also, domains ‘scope and purpose’ and ‘editorial independence’ ranked highest and lowest, respectively—underscoring the importance of good reportage at the developmental stage.

INTRODUCTION

Providing sedation in end-of-life care involves the monitored use of medications to reduce consciousness in order to relieve otherwise intractable suffering at the end of life in a manner ethically acceptable to patients, their families and healthcare providers.¹ It is a ‘last resort’ means of managing refractory symptoms, such as terminal dyspnoea and delirium.^{2–4} Research suggests a growing use for patients with cancer and non-cancer diagnoses,^{3–6} and available studies demonstrate huge variations in its prevalence and practice.^{7–12} Depending on individual need, it may be administered intermittently or continuously until death,¹ and the appropriateness of its use revolves around sound clinical judgement and decision-making.¹³

Worldwide, guidelines are used for standardising practice;^{14 15} the aim being to improve care,^{14 16} encourage prudence¹⁴ and close the gap between research and practice.¹⁷ Expectedly, the principles of evidence-based medicine dominate guideline programmes^{18 19} although in the field of palliative medicine much credit is given to the work of experts.¹ Interventions that combine evidence-based medicine²⁰ with evidence-based guidelines^{21 22} can be used to monitor this practice.^{23 24} Despite their numerical strength, institutional guidelines are often tailored to suit localised needs and themes.^{1 14} To circumvent this, the European Association of Palliative Care (EAPC) has developed a broad Framework to guide policy and facilitate the development of high-quality local procedural guidelines. It incorporates themes that are grounded in the available literature and guidelines and internally supported by



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experts from the palliative care community across Europe.^{1 25} The aim of this systematic review is to identify and compare national and regional clinical practice guidelines on palliative sedation against the EAPC's recommended Framework. We assess available evidence of selected guidelines on palliative sedation regarding content, scope and assess the developmental quality of these guidelines using standardised criteria for guideline development (Appraisal Guideline Research and Evaluation (AGREE) II).²⁶

METHODS

Search strategy and selection criteria

Using the PRISMA criteria,²⁰ we identified relevant references through multiple searches in electronic databases (PubMed, CancerLit, CINAHL, Cochrane Library, NHS Evidence Google and Google Scholar) and bibliographies of journals for national/regional guidelines on palliative sedation. Then we combined search terms 'continuous deep sedation', 'palliative', 'terminal', 'care', 'practice', 'guideline' and 'recommendation' using Boolean operators (AND, OR); and sought articles published between January 2000 and March 2016. In addition, the first author requested from individual and collective members of a palliative care association for the guidelines used in their countries.²⁷ A final list was generated based on relevance. A guideline was defined as 'systematically developed statements used to facilitate decision-making in a clinical setting'.¹⁴

We limited our search by excluding articles on procedural/intensive care sedation, sedation for weaning off the ventilator, and other emergency uses of sedation outside the context of planned end-of-life care. We removed duplicates, review papers, case studies, commentaries, position statements and frameworks.^{1 28} Next, we excluded guidelines from France, Sweden and Switzerland^{29–31} because none of the authors could adequately assess them based on the author's first language.²⁵ A summary of this selection process is presented in online supplementary table S1.

Content evaluation

Based on EAPC's conceptual Framework, the authors developed a checklist for comparing the guidelines (see online supplementary appendix 1). Section A examined general characteristics of the guideline, that is, the nomenclature and how the practice was described in a broad sense, aiming to identify similarities and differences. Section B compared guideline recommendations with the EAPC's recommended Framework.¹

- I. Recommend pre-emptive discussion of the potential role of sedation in end-of-life care and contingency planning;
- II. Describe the indications in which sedation may or should be used;
- III. Describe the necessary evaluation and consultation procedures;

- IV. Specify content requirements;
- V. Indicate the need to discuss the decision-making process with the patient's family;
- VI. Present direction for selection of the sedation method;
- VII. Present direction for dose titration, patient monitoring and care;
- VIII. Guidance for decisions regarding hydration and nutrition and concomitant medications;
- IX. The care and informational needs of the patient's family;
- X. Care for the medical professionals.

Developmental quality evaluation

Section C assessed developmental quality of guidelines using AGREE II instrument.²⁶ The latter is a validated international tool for evaluating guideline development and their quality of reporting.²⁶ It comprises 23 key items organised in six separate domains:

- I. Scope and purpose;
- II. Stakeholder involvement;
- III. Rigour of development;
- IV. Clarity and presentation;
- V. Applicability;
- VI. Editorial independence from funding sources.

According to AGREE II user manual,²⁶ 'scope and purpose' refer to the overall aim of a guideline, its target population and specific health questions (items 1–3). 'Stakeholder involvement' focuses on the extent to which a guideline is developed by appropriate stakeholders and represents views of intended users (items 4–6). 'Rigour of development' refers to processes used in gathering and synthesising evidence, and methods used in formulating recommendations (items 7–14). 'Clarity of presentation' refers to the language, structure and format of a guideline (items 15–17). 'Applicability' pertains to likely barriers and facilitators to implementation, strategies to improve uptake, and resource implications of applying the guideline (items 18–21). 'Editorial independence' refers to elimination of undue bias as a result of competing interests (items 22–23).

The 23 items were scored separately using a seven-point scale: ranging from '1' where the required information was absent (strongly disagree) to '7' where the criteria was fully satisfied (strongly agree). Next the AGREE II scores were combined into a total quality score, which led to a final question: 'whether the guideline should/should not be recommended for use'.²²

Section D examined the guidelines for written evidence of dissemination or simply, its implementation plans.

RESULTS

Selected guidelines

Our search generated 264 published and unpublished guidance documents on the subject of sedation with national or regional coverage (see online supplementary

table S2). From the hits, we selected 13 clinical practice guidelines, originating from 10 countries/regions: 1 from Belgium,³² Ireland,³³ Italy,³⁴ the Netherlands,³⁵ Norway,³⁶ Spain³⁷ and Japan,³⁸ 3 from Canada^{39–41} and 2 from USA^{42–43} and 1 European.⁴⁴

Characteristics of the guidelines

The guidelines had been published between 2003 and 2016, and were issued by associations involved in hospice/palliative care (6), general medicine (2), oncology (1) and critical care (1), health service providers (2) and a national task force (1) (see online supplementary table S3). They ranged between 2 and 78 pages, and existed in electronic and paper formats. Three of them were revised, one contained proposed review dates and two provided specific dissemination plans.^{41–44} Four were published in peer-review journals.^{37–42–44–45} Two explicitly referred to the EAPC Framework on palliative sedation.^{33–44}

Content evaluation

Terms, definition and types of palliative sedation

Palliative sedation was defined in analogous ways in all guidelines, that is, as an intervention instituted solely for the purpose of refractory symptom control (see online supplementary table S4). It could be light (or superficial) or deep (patient is asleep and unresponsive). This could be intermittent and temporary, or continuous until death. The authors applied the terms 'palliative sedation' and 'palliative sedation therapy', 8 and 4 times, respectively, although phrases like 'calming down' and 'alleviation of suffering' were also used in this context. The purposes, indications and drugs recommended for the use of palliative sedation overlapped in many respects, but this always seemed to revolve around what 'palliative sedation' was or was not. Albeit the guidelines were always clear in acknowledging that it was a deliberate, intentional and yet purposeful intervention that needed to be cautiously considered for use only within specified circumstances (ie, the process of dying had begun and refractory suffering was present). With regard to the former, most contained a position statement or declaration that emphasised the need for proportionality and adequacy (via titration) during the actual sedative process, and provided clear differences between palliative sedation and other end-of-life decisions, that is, euthanasia.

Indications and life expectancy

The guidelines all mentioned among the indications for palliative sedation that the 'suffering' should have been appropriately diagnosed, and treatments for individual symptoms sought and tried, or at least carefully considered and found to be futile. Also they mentioned the use of palliative sedation for non-physical symptom control (see online supplementary table S4). Two of them^{34–41} focused solely on continuous sedation until death, providing a more limited range of

indications and life expectancy (hours to days). In few cases, only individuals or teams specialised in palliative care undertook patient assessment prior to palliative sedation.^{34–40–44} There were obvious differences in the prescribed life expectancies: some described as 'hours-days', while others as 'days' or even 'weeks'. Again there appears to have been a relationship between the proffered life expectancy and the terminology/definition that had been adopted for the practice of palliative sedation. In general, a shorter life expectancy (hours to days) was advocated in continuous palliative sedation until death.

Assessment of recommendations based on the EAPC Framework

Regarding recommendations, 8/13 guidelines contained 9–10 recommendations in the EAPC Framework; 9/13 guidelines recommended 'pre-emptive discussion of the potential role of palliative sedation in end-of-life care'; 9/13 advised on 'nutrition/hydration while performing sedation' and 8/13 mentioned 'care of the medical team' (see online supplementary table S5). All 13 guidelines presented indications for using palliative sedation, requirements for obtaining patient consent and direction for the actual administration, including dose titration, patient monitoring and care; the commonest indicators being dyspnoea and terminal restlessness or delirium. The decision to sedate was often based on a plan or an overall medical assessment of the patient's situation involving a multidisciplinary team familiar with the patient's illness, or professionals qualified to participate in such decision-making. The items lacking in four guidelines were: pre-emptive discussion of the potential role of sedation in EOLC, that is, while care was ongoing, decisions regarding hydration and nutrition and concomitant medications, and care for the medical professionals.

Standardised scores for developmental quality using the AGREE II instrument

Standardised scores for the six domains are presented in online supplementary table S6. Domain 1 (scope and purpose) scored highest, where 6/13 guidelines scored 100%. 'Rigour of development' likewise received low scores, ranging from 16% to 71%, and the Dutch guideline recorded the highest score in this section. Domain 4 (clarity and presentation) was rated fairly high. Domain 5 (applicability) had the lowest rating, with 5/13 guidelines scoring 0%, and 0/12 guidelines scoring more than 54%. On calculating the overall scores, nine guidelines were ranked moderate-high, and three were 'recommended for use', being they scored above 60% for rigour of development.

DISCUSSION

We reviewed 13 guidelines: emerging from Europe (7), Canada (3), USA (2) and Japan (1). The guidelines were similar in content. All presented palliative sedation as a 'last resort' alternative for refractory symptom

management, in the presence of adequate treatment and optimal palliative care. Recommendations provided were mostly consistent with the EAPC recommended Framework on palliative sedation, although there were few important variations between and within countries. We noted that such revolved largely around the specific definition of 'palliative sedation' that had been adopted. According to the AGREE II instrument and scoring scheme, three guidelines were 'recommended for use' in their current form.

This is the first review paper that evaluates and compares systematically palliative sedation guidelines between countries and with the EAPC Framework. It comes at a time when variations in the actual practice of palliative sedation appear on the increase in Europe and abroad^{7-9 12 46} and builds further on the work of Schildmann and Schildmann⁴⁷ as we compared existing palliative sedation guidelines with an official and widely supported Framework. The search for guidelines was challenging, especially because many existed as grey literature.²⁵ We used a generic approach, applying widely endorsed instruments for evaluation: the EAPC Framework¹ and AGREE II instrument,¹⁸ in order to provide objective and useful insights about core common components, differences between these guidance documents and their developmental quality. However, what exactly the guidelines recommend remains unknown and differences between the EAPC Framework and the guideline cannot be excluded. For instance, the way consultation is addressed in the Dutch guideline is strikingly different from the strong recommendation to consult experts in the EAPC Framework. Another general limitation was the non-uniformity of the materials assessed, in terms of nomenclature, volume (full vs abridged versions) and language. It is possible some items 'missed' might have been present in the original document and we could not adequately assess guidelines from France, Sweden and Switzerland based on the author's first language. Also we acknowledge that the instruments used for this evaluation are not without their individual shortcomings.

Important variations were observed, and these centred on the essence of the practice itself. For instance, the term 'palliative sedation' was applied broadly to refractory symptom management in terminally ill patients in some cases, but at other times there was a specific mention of 'the last days'—meaning the patient's terminal illness and condition at the time had been thoughtfully accounted for. In the latter scenario, palliative sedation was portrayed as 'a planned and often, continuous event', with 'a physician' or an expert at hand, and its duration was 'hours to days'. Although some explicitly applied different terms to clearly demarcate these subcategories,^{32 35 38-41} this seemingly trivial difference appeared to be most fundamental to most of the differences observed, underscoring the rationality behind continued hydration,

and the need for proportionality, caution and after care. However, this point is mentioned as a theoretical construct, since we did not actually observe clinical practice per se. The truth is, although guidelines may not be able to establish with absolute clarity what 'normal practice' is, clinicians are likely to benefit from a clearer stance on how to recognise patients who may eventually require palliative sedation, and what to do in such circumstances. In the past, the emphasis of debates were on the ethics of the practice, and the EAPC and other respected bodies did address those issues quite extensively, helping practitioners clearly differentiate palliative sedation from other end-of-life decisions (ie, euthanasia, physician assisted suicide), especially from an 'intent' point of view. Going forward the focus should be on supporting clinicians (doctors and nurses) who provide the care in the different settings where people die.

According to AGREE II criteria, guidelines from Japan, the Netherlands and Spain were recommended for use in their current form being that they satisfied the criteria for quality in the developmental process. In general, the scoring was low (10 guidelines scored <50%) because many did not meet the conditions for proper documentation. Furthermore, zero could mean an item was not properly reported (eg, conflict of interest) in the document assessed. However, low scores could also be attributed to the scarcity of scientific evidence in the field of palliative medicine.³⁷ While one can argue about reasons for potential gaps between guideline quality, applicability and their impact on quality of care,⁴⁸ there are compelling reasons to advocate for improved transparency of reporting and some standardisation in nomenclature.

In terms of recommendations, this review shows pre-emptively discussing palliative sedation as a treatment option, caring for the medical team and the role of specialists were items often missed in the guideline recommendation, and understandably so. In reality, palliative sedation may not 'fit' so well in a routine discussion about advance care directives, however mentioning it as an unlikely option at a time when a patient is competent and capable of decision-making is somewhat beneficial.¹ Regarding the other two items, the practice of palliative sedation is a complex one, for the patient and practitioner. Hence, specialists should be involved in its delivery and the individuals or teams providing it should be duly supported.⁴⁹

Finally, we noted that the guidelines had been issued by organisations/associations supposedly involved in improving the quality of the practice and protecting potentially vulnerable patients and their families.¹⁴ However, we observed from the scope of the review that several countries are yet to authorise guidelines for this delicate and growing practice. In the mean time, some countries, that is, Germany and Romania have adopted or are adopting (ie, Russia) the EAPC Framework,⁵⁰ to at least provide guidance. Given that

palliative sedation is being delivered away from the domain of specialists and in non-specialised care settings, there is a need for detailed guidance tailored to settings where it is administered. Also we suggest that further research be done to compare other aspects of specialist versus generalist palliative sedation provision.

SUMMARY

In sum, the 13 selected guidelines on palliative sedation touched on similar topics with reasonable consistency, showing variations in quality and significant differences in practical utility. Their recommendations were largely comparable with the recommended EAPC Framework, suggesting the latter as a plausible standard on the subject. We observe that these guidelines relied somewhat heavily on the consensus of experts. However, it is important to yet improve the empirical and scientific base of existing guidelines, and monitor their dissemination and overall impact on practice. Hence, we recommend standardisation of terminologies and improvement of documentation where possible, to enhance the developmental quality of these guidelines and create a needed platform for international collaboration.

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Data sharing statement All data generated during the project will be made freely available via Lancaster University's Research Data Repository. DOIs to these data will be provided (as part of the DataCite programme) and cited in any published articles using these data and any generated in the review (to allow data unrelated to any published work to be found). All data used in the review will be generated directly as a result of the review, without any pre-existing data being used. Any data relevant to a published article will be made available alongside the article when published.

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Correction: *International variation in clinical practice guidelines for palliative sedation: a systematic review*

Abarshi E, Reijtens J, Robijn L, *et al.* International variation in clinical practice guidelines for palliative sedation: a systematic review. *BMJ Supportive & Palliative Care* 2017;3:223-9. doi:10.1136/bmjspcare-2016-001159.

The EUROIMPACT collaborator's name Miccinesi Guido has been corrected to Guido Miccinesi.

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