



Schofield, G., Baker, I., on behalf of the Association of Palliative Medicine UK Ethics Committee, Bullock, R., Clare, H., Clark, P., ... George, R. (2019). Palliative opioid use, palliative sedation and euthanasia: reaffirming the distinction. *Journal of Medical Ethics*. <https://doi.org/10.1136/medethics-2018-105256>

Peer reviewed version

License (if available):
CC BY-NC

Link to published version (if available):
[10.1136/medethics-2018-105256](https://doi.org/10.1136/medethics-2018-105256)

[Link to publication record in Explore Bristol Research](#)
PDF-document

This is the author accepted manuscript (AAM). The final published version (version of record) is available online via BMJ Publishing at <https://jme.bmj.com/content/early/2019/06/20/medethics-2018-105256> . Please refer to any applicable terms of use of the publisher.

University of Bristol - Explore Bristol Research

General rights

This document is made available in accordance with publisher policies. Please cite only the published version using the reference above. Full terms of use are available:
<http://www.bristol.ac.uk/pure/about/ebr-terms>

Palliative Opioid Use, Palliative Sedation and Euthanasia: Reaffirming the Distinction

G Schofield¹, I Baker², R Bullock³, H Clare⁴, P Clark⁵, D Willis⁶, C Gannon⁷, R George⁸ on behalf of the Association of Palliative Medicine UK Ethics Committee

¹ Centre for Ethics in Medicine, Population Health Sciences, Bristol Medical School, University of Bristol, Canynge Hall, 39 Whatley Road, Bristol, BS8 2PS, United Kingdom Tel: +44(0)117 33 14550. guy.schofield@bristol.ac.uk Orcid ID: 0000-0002-9055-292X [* Corresponding Author]

² Association of Palliative Medicine, Southampton, UK

³ Worcestershire Acute Hospital Trust, Worcester, UK

⁴ Northwest Deanery, UK

⁵ Rowcroft Hospice, Torquay, Torbay, UK

⁶ University of Chester Faculty of Medicine, Dentistry and Life Sciences, Chester Medical School
Chester, UK

⁷ Princess Alice Hospice, Esher, Surrey, UK

⁸ St Christopher's Hospice, Sydenham, Kent, UK

Keywords

Clinical Ethics, Palliative Care, End-of-life, Euthanasia

Abstract: 250

Current word count: 1642

Current Reference count: 10

Abstract

We read with interest the extended essay published from Dr Riisfeldt and are encouraged by an empirical ethics article which attempts to ground theory and its claims in the real-world. However, such attempts also have real world consequences. We are concerned to read the paper's conclusion that clinical evidence weakens the distinction between euthanasia and normal palliative care prescribing.

This is important. Globally the most significant barrier to adequate symptom control in people with life limiting illness is poor access to opioid analgesia. Opiophobia makes clinicians reluctant to prescribe and their patients reluctant to take opioids that might provide significant improvements in quality of life.

We argue that the evidence base for the safety of opioid prescribing is broader than that presented, restricting the search to palliative care literature produces significant bias as safety experience and literature for opioids and sedatives exists in many fields. This is not acknowledged in the synthesis presented. By considering additional evidence we reject the need for agnosticism and reaffirm that palliative opioid prescribing is safe.

Secondly, palliative sedation in a clinical context is a poorly defined concept covering multiple interventions and treatment intentions. We detail these and show that Continuous Deep Palliative Sedation (CDPS) is a specific practice that remains controversial globally and is not considered routine practice.

Rejecting agnosticism towards opioids and excluding CDPS from the definition of routine care allows the rejection of Riisfeldt's headline conclusion. On these grounds we re-affirm the important distinction between palliative care prescribing and euthanasia in practice.

We read with interest the extended essay published from Dr Riisfeldt(1) and are encouraged by an I ethics article with empirical evidence that attempts to ground theory and its claims in the real-world. This is the world we inhabit in our daily clinical practice.

However, such attempts grounded in an incomplete evidence-base also have real world consequences specifically for clinical practice. We are concerned that the paper concludes that clinical evidence supports the finding that the distinction between euthanasia and normal palliative care opioid and sedative prescribing is not as clear as people might believe. We contend, from additional evidence, that this is both factually wrong and likely to cause significant concern and fear for current and future patients, their families and healthcare professionals.

This is important. Globally the most significant barrier to adequate symptom control in people with life limiting illness is poor access to opioid analgesia. Regional variation in their availability is inequitable and justified often by the assumption that they are addictive and lethal as a matter of course.(2) 'Opiophobia' makes clinicians reluctant to prescribe and their patients reluctant to take opioids that might provide significant improvements in quality of life.(3)

In order for applied philosophy to be useful it is important that it leaves or at least gives the abstract its real-world application and engages with the context of issues under investigation. It is paramount, however, that the rigour applied to the philosophical is also applied to selection, generation and processing of the empirical. (4)

In this response we argue that the empirical aspect of Dr Riisfeldt's argument does not meet with the rigour required. This paper aims to highlight areas of the review's methodology that introduce bias in the findings and to introduce the reader to some of the wider literature on opioid safety from other clinical fields, to allow readers to form a broader opinion of the available evidence. We believe that this evidence allows for a rejection of agnosticism on the safety of opioids. We also aim to clarify the conceptual variation surrounding palliative sedation as a term within clinical practice.

We do not intend to critique in detail the author's interesting examination of the Doctrine of Double Effect. We argue that the full evidential picture demonstrates that routine prescribing does not shorten life, and therefore resorting to the Doctrine of Double Effect is irrelevant, whatever the strengths or weaknesses inherent to the doctrine.

This rejection of Riisfeldt's agnosticism allows us to clarify why routine palliative care prescribing practices and euthanasia are distinct and different. This holds irrespective of one's views on the appropriateness of physician assisted dying in any of its forms.

Clinical Definition in Context

Appropriately Titrated Administration of Opioids (ATAO)

Riisfeldt is right generally that prescribing excessive doses of any drug is reckless, likely to be harmful and potentially lethal. Insulin is the best and most widespread example. For opioids, inappropriate escalation or doses, disproportionate to individual need risk, respiratory dysfunction. However, some people require and tolerate, with no ill effect, very large doses of opioids to control their pain. A study by Estfan on the respiratory effect of opioid doses used for analgesia show a range of final doses from 72mg to 21600 mg (daily oral morphine

equivalent dose) - orders of magnitude different and yet demonstrably safe, based on irrefutable physiological parameters.(5) Another example from Edwards et al focuses on sedation in ventilation withdrawal procedures. This case series describes the paradoxical observation that sedation prolongs life when ventilatory support is withdrawn and that the time to death reflects underlying respiratory function directly and not sedative or opioid use. This study also gives a history as to why the original research in the 1950's that linked opioids and barbiturates with increased risk of mortality might have erred in the causative pathway.(6)

Given our understanding of the broader relevant literature base, we consider it inappropriate to adopt an agnostic position on the safety of routine palliative care opioid prescribing. The objective and relevant empirical literature demonstrates the safety of routine palliative care prescribing.

Palliative Sedation

Sedative prescribing is complex, and practice varies depending on the indication, setting and international context. The term 'palliative sedation' is used across the literature loosely and encompasses disparate prescribing practices, covering a broad selection of pharmaceutical agents, indications and intentions – see this recent review by Robert Twycross.(7) It is more of a concept than a specific and comparable clinical intervention.

To make sense of sedation the imperative is to distinguish between symptom control and transient 'clinically-indicated' sedation, for say a procedure, and continuing 'sedation on demand'.

The 'everyday' expert control of specific symptoms using targeted and titrated drugs as part of a comprehensive treatment plan accords with best practice. This is 'acceptably' safe as it applies equally across all disciplines of healthcare and at all points in a person's disease trajectory. When transient sedation is needed to manage time-limited crises or incidents, standard drugs will reduce or remove cognitive awareness. Managing burns, wound care or the acute distress that accompanies traumas are good examples of specific uses. This is 'acceptably' safe. Though necessary, such sedation is never desirable (i.e. it is a means but not an end).

Continuing Deep Palliative Sedation

Continuing Deep Palliative Sedation (CDPS) should not be grouped with routine palliative prescribing. It remains controversial globally. The 'atypical' electing to put a patient into an induced coma, at the patient's request, potentially weeks or months in advance of what may have been a peaceful death is not in line with acceptable practice in many health systems. In the United Kingdom (UK) 'coma on demand' is not considered best practice in any discipline of healthcare or at any point in a patient's trajectory, and it is not part of routine UK palliative care practice. The European Association of Palliative Care (EAPC) guidelines are also clear.(8) CDPS, though described in some medicolegal jurisdictions outside of the UK, imagines 'special rules' for patients with advanced illness and can indeed overlap with euthanasia, both in theory and in practice (and typically without the same level of legal safeguards even if inherently limited). Examples of this exist in jurisdictions where legalisation of various euthanasian practices exist. One explanation is that it reflects the

disorientation to which it subjects clinicians when ending life is seen as a type of treatment, rather than being separated clearly from clinical practice.

In summary the inclusion of CDPS into the analysis of 'widely accepted mainstream practices of palliative care opioid/sedative use' p6 (1) is invalid.

Literature Review Methodology

In recent years increasing emphasis has been placed on the need for literature reviews to be systematic, prospectively registered, and designed and reported with regards to agreed standards, for example the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.(9) This best practice approach is promoted to help readers identify and researchers possibly mitigate potential sources of bias within a review. This protocol standard is missing from the review and as such, the retrieved records may inadvertently contain significant bias, which cannot be identified as much of the methodology is not described.

To us, a clear and significant source of bias in the empirical review presented is the sole focus on the palliative care literature. All reviews involve choices in inclusion and exclusion criteria, however this narrow focus is not justified in the article, and this is important as much of the documented safety experience of opioids and sedation lies outside the field of palliative care. This includes both Edward's (6) and Estfan's (5) research above.

There is not space for a more detailed description of the empirical literature here, and we recommend reviewing the cited articles in this review commentary by one of the authors.(10)

In summary, we do not wish to underplay the amount of work the author has undertaken in producing the review. However, the author has excluded a significant volume of relevant literature and does not describe the methodology of the review in detail. If this review is to be used as a base to argue for a challenge to accepted thinking on the distinction between palliative care and euthanasia then it must be robust, and there are too many methodological uncertainties for this to be the case.

Conclusion

We value, welcome and encourage input into our field from all disciplines and are always prepared to consider and respond to challenges to our practice and the principles behind it. We hope that our response will allow for an updated real-world context to be considered by those academics who take this work forward.

The broader empirical evidence is clear that appropriately titrated opioid use is safe. CDPS is not part of routine practice and therefore its inclusion into the analysis is unwarranted. Excluding CDPS allows for the reaffirmation that sedative use is also safe.

The importance of reviewing the full literature is that it shows the prescribing within routine palliative care is safe and does not shorten life. As it does not shorten life, but only relieves suffering (fully or partially), there is no need to resort to the Doctrine of Double Effect to

justify prescribing practice, whatever inherent merits of challenges the doctrine may possess.

As palliative care physicians we work daily with many complex ethical challenges. We have to ground ethical debate in the real-world and we are obliged to base this on the best empirical data available that represent accurately the problems at hand in the right clinical context required. Thought experiments will not harm people, but clinical mis-information will.

Finally, we do not wish to down play the dangers of inappropriate prescribing of opioids or sedatives. We stress that training in palliative prescribing must form part of all healthcare prescribers' education and clinical governance procedures. Recurrent examples of poor prescribing and resultant lethal outcomes persist. They are as unacceptable in palliative care as any branch of modern clinical practice.

Contributors

All authors conceived the response. GS, CG and RG wrote the first draft of the manuscript. All authors contributed to subsequent drafting and critical revisions. All authors approved the final version.

Funding

No specific funding was received for this response article.

GS is supported by Wellcome Trust Research Award for Health Professionals (208129/Z/17/Z). This funder had no role in the drafting of this manuscript or in the submission decision.

Competing Interests

None declared

Patient Consent

None required

Ethics Approval

Response article – none required.

1. Riisfeldt TD. Weakening the ethical distinction between euthanasia, palliative opioid use and palliative sedation. *J Med Ethics*. 2018 Oct 23;medethics-2018-105074.
2. Cleary J, Radbruch L, Torode J, Cherny NI. Next steps in access and availability of opioids for the treatment of cancer pain: reaching the tipping point? *Ann Oncol*. 2013 Dec 1;24(suppl_11):xi60–4.
3. Bennett DS, Carr DB. Opiophobia as a Barrier to the Treatment of Pain. *J Pain Palliat Care Pharmacother*. 2002 Jan;16(1):105–9.
4. Singh I. Evidence, Epistemology and Empirical Bioethics. In: Cribb A, Ives J, Dunn M, editors. *Empirical Bioethics: Theoretical and Practical Perspectives* [Internet]. Cambridge: Cambridge University Press; 2016. p. 67–83. (Cambridge Bioethics and Law). Available from: <https://www.cambridge.org/core/books/empirical-bioethics/evidence-epistemology-and-empirical-bioethics/2E3083F12066A136974F7D48DE8328E9>
5. Estfan B, Mahmoud F, Shaheen P, Davis MP, Lasheen W, Rivera N, et al. Respiratory function during parenteral opioid titration for cancer pain. *Palliat Med*. 2007 Mar;21(2):81–6.
6. Edwards MJ. Opioids and Benzodiazepines Appear Paradoxically to Delay Inevitable Death After Ventilator Withdrawal. 2005;4.
7. Twycross R. Reflections on palliative sedation. *Palliat Care Res Treat*. 2019 Jan;12:117822421882351.
8. Cherny NI, Radbruch L, The Board of the European Association for Palliative Care. European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. *Palliat Med*. 2009 Oct;23(7):581–93.
9. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. 2009 Jul 21; Available from: <http://www.bmj.com/content/339/bmj.b2535.full?view=long&pmid=19622551>
10. George R, Regnard C. Lethal opioids or dangerous prescribers? *Palliat Med*. 2007 Mar;21(2):77–80.