CSD Continuous Sedation until Death; A Response to Changing Practices in the Use of Continuous Sedation at the End of Life: A Systematic Review of the Literature (Heijltjes et al., 2020)

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To the Editor, *JPSM*

CSD Continuous Sedation until Death; A Response to Changing Practices in the Use of Continuous Sedation at the End of Life: A Systematic Review of the Literature (Heijltjes et al., 2020)

We write to express our concerns about this Review.[1] First and foremost: the data included do not substantiate the claims made that, over time, the frequency of Continuous Sedation until Death has increased (in Results) or "seems to increase" (in Discussion and Conclusion). This is the case for only three of the seven European countries for which data from nationwide studies are included: The Netherlands, Switzerland, and Belgium. For the other four countries (Denmark, Italy, Sweden, and the United Kingdom), data were available for only one study, making it impossible to make any claims about trends. This is not readily apparent from Figure 2, which includes nationwide studies from all seven countries. This Figure would have been more accessible had it only included studies for those countries for which the Review included more than one study. As it is, with all nationwide studies included, we found that some of the colours were difficult to distinguish, and the variation in the sizes of the coloured balls unhelpful.

Our second concern relates to inconsistent terminology. The Review title refers to Continuous Sedation at the End of Life, and the paper repeatedly uses the abbreviation CSD (Continuous Sedation until Death). However, the title for Table 1 uses the term "Continuous *Deep* Sedation" (CDS) (our italics). Table 1 entries under Definition of Sedation for those nationwide studies included do indeed all relate to CDS. However, for the subpopulation studies included, the listed Definitions are roughly 60/40 for CSD and CDS. These two terms are distinct, and *not* synonymous: CSD embraces all levels of sedation, including light, responsive to stimuli, and rousable, whereas, by definition, CDS is limited to unresponsive and unrousable.[2]

It is vital to understand and be clear about the distinction between CSD and CDS when discussing or interpreting reports about the use of sedation at the end of life. We welcome the recent shift in the literature from the often imprecise "palliative sedation" to these more precise terms. However, this shift needs to be accompanied with an associated concern not to conflate the two terms, particularly as the abbreviations use the same letters, and are therefore easy to confuse.[2] Indeed, the comment in Table 1 that a Canadian subpopulation study included light levels of sedation raises doubts about how many other subpopulation studies were inappropriately included in a Table which includes the term "Continuous Deep Sedation" in its title. It would have been helpful - resolving this issue with the title, and also making Table 1 more accessible - if the nationwide and subpopulation studies had been presented separately, rather than in a single table.

Being from the UK, we were particularly interested in the UK studies included. The UK data presented under nationwide studies in Table 1 are from Seale 2009.[3] The column "Patients who Received CSD, No. (%)" gives "n/a" for the number who received sedation, followed by 16.5%. This does not make sense. A subsequent analysis of the same dataset gives the number as 519, and revises the percentage to 18.7%.[4] Yet, surprisingly, despite citing this second paper, the Review did not include these data. Both 16.5% and 18.7% are considerably higher than the roughly contemporaneous figures for the Netherlands (8.2% in 2005) or Belgium (8.3% in 2001). However, as Seale observes, without a better understanding of the context in which decisions about sedation are taken, it is difficult to evaluate the significance of the UK data.[3]

The other UK paper included in the Review, listed under subpopulation studies (Table 1), describes the evolution of a protocol to monitor the use of sedation at the end of life at a 14-bed UK hospice.[5] This paper records the results of three clinical audits conducted for 12, 3, and 3 months at intervals during 2010-14. The numbers included were small: 147, 47, and 40, with sedation rates of 80, 62, and 73% respectively (Table 1). These remarkably high rates are probably at least partly explained by the fact that patients were counted as receiving sedation if they received midazolam ≥10mg or levomepromazine ≥25mg in the last 24 hours before death. It is impossible to say how many of these patients were only lightly sedated and how many deeply sedated, because "staff rarely used the scale provided to record the level of sedation, preferring a more narrative approach… using terms such as 'settled and 'comfortable'". [5] The use of these expressions strongly suggest that, in these cases, the primary intention was patient comfort, not the reduction of the patient's level of consciousness – 'intention' being an essential element of the definitions of both CSD and CDS. In this respect, this paper reflects the findings of several other UK studies published within the Review's timeframe (2000–2020) but not included in the Review, on one of which one of us was the lead author.[6]

The Discussion offers several hypotheses as possible explanations for the increase in CSD in those few countries for which consecutive national data exist. Surprisingly, no mention is made of the possible impact on medical practice of the availability of euthanasia in Belgium and The Netherlands. This situation, together with the high use of CDS, could perhaps contribute to a culture in which all struggle is seen as suffering, and unresponsiveness or unconsciousness equated with peace. One Dutch source has commented: 'The advantage of palliative sedation is that it provides an easy resolution of severe discomfort and refractory symptoms'.[7] However, easy for whom? It is certainly much easier for a physician to increase the dose of midazolam than to support a patient with existential distress, or seek to engage with their underlying issues.

The Strengths and Limitations do not include any mention of the difficulties with making meaningful comparisons between studies from different countries, nor possible methodological issues. For example, the nationwide surveys from The Netherlands, the UK, and Italy were all retrospective, all elicited information about the respondent's last patient death in the previous 12 months, and all included the question, "Was the patient kept continuously in deep sedation or coma until death?" However, sampling methods differed, and the answers relied totally on memory. The Limitations do not address the selection bias associated with this kind of study – the tendency to report the last "problematic" death, instead of the last patient who died.[8]

The Conclusion suggests that CSD might have lost its status as a treatment of last resort. That may well be so, at least in some countries. However, ethically, because it permanently ends a patient's 'biographical' (social) life, CDS can never be anything other than last resort.[2] The question which needs to be asked is: given good palliative care, what percentage of patients need this? The incidence of CDS reported from specialist palliative care services ranges up to 15%, and CSD up to 55%.[2] In contrast, at one palliative care unit in Belgium, the incidence of CDS fell over six years from 7% to 2.5%, associated with an improved standard of care and a team approach to decision-making.[9] Comparable findings from palliative care services in both Colombia and Japan have been reported, namely, 2% and 1.4% respectively.[10,11]

In summary, we were disappointed at the unsubstantiated claims in both the main text and the Abstract of this Systematic Review, which potentially mislead readers as to its more tenuous findings. We would hope that future published Systematic Reviews will ensure that they exclude unsubstantiated claims, and that their Figures and Tables are as accessible as possible.

Kind regards

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References

1. Heijltjes MT, van Thiel GJMW, Rietjens JAC, et al. Changing practices in the use of continuous sedation at the end of life: a systematic review of the literature. J Pain Symptom Manage 2020:60:828-846.
2. Twycross R. Reflections on palliative sedation. Palliat Care Res Treat 2019;12:1-16.
3. Seale C. End-of-life decisions in the UK involving medical practiitioners. Palliat Med 2009;23:198-204
4. Seale C. Continuous deep sedation in medical practice: a descriptive study. J Pain Symptom Manage 2010;39:44-53.
5. Dean A, Miller B, Woodwark C. Sedation at the end of life: a hospice's decision-making practices in the UK. Int J Pall Nurs 2014; 20:74-481.
6. Vivat B, Bemand-Qureshi L, Harrington J, et al. Palliative care specialists in hospice and hospital/community teams predominsantly use low doses of sedative medication at the end of life for patient comfort rather than sedation: findings from focus groups and patient records for I-CAN-CARE. Palliat Med 2019;33:578-588.
7. Hasselaar JG, Verhagen SC, Wolff AP, et al. Changed patterns in Dutch palliative sedation practices after the introduction of a national guideline. Arch Intern Med. 2009;169:430-437.
8. Miccinesi G, Caraceni A, Raho JA, et al. Careful monitoring of the use of sedative drugs at the end of life: the role of epidemiology. The ITAELD STUDY. Minerva Anestesiol 2015;81:568-579.
9. Claessens P, Genbrugge E, Vannuffelen R, et al. Palliative sedation and nursing: the place of palliative sedation within palliative nursing care. J Hosp Palliat Nurs 2007;9:100-106.
10. Palacio SP, Hoyos CEG, Rodriguez CA, et al. Palliative sedation in advanced cancer patients hospitalized in a specialized palliative care unit. Support Care Cancer 2018;26:3173-3180.
11. Koike K, Terui T, Takahashi, Y, et al. Effectiveness of multidisciplinary team conference on decision-making surrounding the application of continuous deep sedation for terminally ill cancer patients. Palliat Support Care. 2015;13:157-164.