

## Peer Review File

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### Reviewer A

1. General/Introduction: The authors reference the COMET taxonomy several times and it may be beneficial to describe this taxonomy in the introduction alongside the methodology (the authors give the categories in the methods, but a more general description of this construct would be helpful).

-Response: This was a very useful comment. We now explained in the introduction what the COMET taxonomy is and described it in more detail in the 'methods' section.

- Changes:

Introduction (page 1, 2<sup>nd</sup> paragraph):

**Throughout all the steps, the outcomes are classified according to a taxonomy developed by COMET, which includes five core areas: *Death, Physiological/clinical, Life impact, Resource use, and Adverse events*, and covers 38 outcome domains.”**

Methods (page 5, under data extraction subheading):

**The taxonomy covers 38 outcome domains distributed within 5 core areas. The core area “death” includes outcomes such as survival and mortality rates. “Physiological/clinical” includes signs, symptoms, and laboratory tests. “Life impact” includes outcomes assessing the impact of the disease on physical daily life activities, on social functioning, role functioning (e.g. ability to care for children or work status), emotional functioning, or cognitive functioning. “Life impact” also includes outcomes assessing the quality of life, the perceived health status, and the delivery of care (patient preferences, withdrawal from interventions, patient/care satisfaction, among others). “Resource use” includes economic outcomes, hospital use, medications and procedures, and the financial or time burden on carer or the society (e.g. need for home help or institutional care). Finally, the category “Adverse events” includes outcomes measuring unintended consequences of interventions.**

2. Methods: Study Selection and Inclusion Criteria: The authors should specify how they evaluated whether articles were appropriately focused on the final month of life. Did the article have to specifically focus on this period in its method? What about non-time limited studies on end-of-life where the subjects' average survival time was under a month?

-Response: We understand the need to further explain the inclusion criteria

regarding the time period. We have now explained this in the methods section, as follows:

- Changes:

Methods (Page 4, under Study selection and inclusion criteria):

**Studies were only included if they specifically mentioned the time frame in which the outcomes were assessed and it was equal or shorter than the last 30 days of life. If a study assessed an outcome over a longer period of time, even if the average time in which the outcome was reported for the participants was <30 days of life, it was excluded. For a study to be included, the outcome should have been assessed in all the participants within the last 30 days of life.**

3. Methods: Data Extraction: The authors categorize outcomes by their time of collection relative to death. This strikes me as challenging because in prospective studies death cannot be precisely predicted and its likely that in prospective studies, outcomes are measured at a variable time relative to death. The authors might mention how they got around this.

-Response: In both observational prospective studies and RCTs, even if the outcomes were assessed at a variable time relative to death, at least one of the outcomes should have been reported for a time frame equal or shorter than 30 days for the study to be included. For example, an observational study assessed the correlation between performance status and aggressive care near the end of life. This is a prospective study in which performance status was evaluated at baseline and then patients were followed until death. Then, they assessed what interventions the patients had received during their last week. The same for RCTs. For example, there was an RCT in which patients were randomly assigned to an individualized advanced care planning strategy vs symptom-management educational treatment. They report, among other outcomes, the amount of patients in each group that received CPR in the last month. In all prospective studies, the follow up was different for each patient because it was until death but the outcomes were reported in certain time frames before the death, and thus we were able to include them. In these cases, we only included the outcome that had been reported within that time frame.

- Changes

As mentioned in the previous comment, this was added to the methods section on page 4, under Study selection and inclusion criteria:

**Studies were only included if they specifically mentioned the time frame in which the outcomes were assessed and it was equal or shorter than the last 30 days of life. If a study assessed an outcome over a longer period of time, even if the average time in which the outcome was reported for the participants was <30 days of life, it was excluded. For a study to be included,**

**the outcome should have been assessed in all the participants within the last 30 days of life.**

4. Methods: Data Extraction: The authors mention healthcare personnel consisted of nurses, general practitioners, or other physicians. As hospice and palliative care services are often delivered by a broader interdisciplinary team including social workers, chaplains, and other health professionals, did the authors include these professions in healthcare personnel if relevant? (It may be that this is irrelevant because none of the studies had data reported by these professions in which case there is no need to address this comment).

-Response: We did focus specifically on healthcare personnel, which include, among others, social workers. However, none of the studies had data reported by any of those health professionals.

### **Reviewer B**

1. Key words

The term "end of life care" is used; however, the definition of "end of life" is not universally agreed upon among countries and researchers. Since it specifically refers to the last month of life, "terminal care" might be a better match.

-Response: We agree with the reviewer and have now replaced the key word "end of life care" by "Terminal care".

2. The specific definition and understanding of "end-of-life" may vary across cultures and healthcare systems worldwide. Please clarify the definition of "end-of-life" as used in your manuscript.

-Response: We thank the reviewer for pointing it out the confusion that can come from using vague terms such as "end-of-life". Therefore, we have now replaced throughout the entire paper the term "end-of-life" by a more specific term or concept. As an example:

#### Introduction:

In the context of ~~the care delivered in the last month of life-of-life-care~~, outcomes serve to develop (...)

#### Results:

##### Most often reported study outcomes:

In the category *Physiological/clinical*, the frequency with which the following symptoms (n=7) were present ~~the end-of-life-at any time point within the last month~~ was evaluated: (...)

3. In line 80, please explain the grounds for setting the last month of life.

-Response: We have explained the ground for the time frame definition in the line 80 of the introduction.

Change (Introduction, page 3, last paragraph):

Introduction:

Therefore, the goal of this review was to identify outcomes that have been assessed in scientific literature in the last month of life, as a first step for the development of the COS for the best care for the dying person. **We chose the last month of life, since is when the majority of the transitions to comfort care occur (7-9).**

4. The decision to set the last month of life instead of "end of life" may have resulted in limited social-psychological outcomes; hence, please discuss the definition of "end of life" in your manuscript to address this point.

-Response: Although we extracted from the studies the outcomes that were evaluated in the last month, we included terms such as "end of life" or "terminally ill" in the search strategy to capture all types of outcomes. In addition, as suggested, the specific term "last month" is now used throughout the article rather than the ambiguous "end of life".

5. In 2002, palliative care was newly defined. Regarding the passage in lines 344–345 about palliative care physicians and the "end of life" aspect, does "end of life" refer to a timeframe longer than the last month?

-Response: We understand the confusion that can be generated by the imprecision of these terms. For this reason, throughout the article, we use more specific terms or concepts instead of the ambiguous "end of life". In the specific case of lines 344-345, we changed it to:

Discussion (page 10 under clinical and scientific implications):

Clinical and scientific implications:

For example, with the outcome "antibiotic use", it is known that there are adverse effects of antibiotic use ~~at the end of life in patients whose goal of treatment is to palliate symptoms~~, such as drug interactions, antibiotic-associated diarrhea, intravenous line discomfort, and of worldwide concern, bacterial resistance (23, 24). However, there is also evidence of beneficial effects, such as symptoms' improvement, which may outweigh the potentially adverse effects (25) and that even at present, palliative care physicians prefer to use antibiotics ~~at the end of life~~ in the majority of cases ~~in which the treatment goal is to palliate symptoms (88-100%)~~ (26).

6. This manuscript specifically reviews the outcomes of terminal care among end-of-

life care, terminal care, and palliative care. I believe it would be reader-friendly to clearly define these three terms in your manuscript.

-Response: Thank you for this comment. We review the outcomes of care during the last month of life in this manuscript, which we have now made clearer as described above. For this reason, we have now replaced throughout the entire paper the term “end-of-life” by a more specific term or concept.

7. Regarding line 194 and Table 1, due to setting the last month of life, there is a possibility that cancer accounted for 77% of the cases. By modifying the timeframe, it may have been possible to introduce variations in target diseases such as worsening of chronic conditions, dementia, and frailty, thus impacting social-psychological outcomes.

-Response: Thank you for this observation. It is not that 77% of the studies included cancer patients, but rather that 77% of the studies included patients with one disease category, of which, the most commonly assessed was cancer. We understand this sentence was confusing and have now explained it better:

Results:

General characteristics of the included papers:

Most of the studies (n=476, 77%) included only patients with one disease category, ~~predominantly patients with malignancies~~. The other studies (n=143, 23%) included patients combining varying life-limiting diseases. ~~Among the 77% studies that included only patients with one disease category, the most predominantly disease category was patients with malignancies.~~

-Additionally, cancer has always been the main type of illness treated and therefore studied by palliative care. In the last 10 years, 10 times more has been published on palliative care and cancer than on palliative care and dementia, COPD or HF (Bernardis A, Gonzalez-Jaramillo V, Ebnetter AS, Eychmüller S. Palliative care and COVID-19: a bibliometric analysis. *BMJ Support Palliat Care*. 2023 Jan 26;spcare-2022-004108. doi: 10.1136/spcare-2022-004108. Epub ahead of print. PMID: 36702518.). In this systematic review, about 7.5% of the studies included patients with dementia or heart failure, and about 70% of the studies included patients with cancer, i.e., 10 times more, a proportion similar to the proportion across all palliative care studies.

However, we understand and appreciate the reviewer's remark that a different time frame could have had an impact on the socio-psychological outcomes identified, notwithstanding, this remains unknown to us, as we were focusing on the period closest to death. This is why, as outlined in the discussion section (second to last paragraph on page 9), the subsequent phases of the COS development include data collection through interviews to patients, caregivers and health professionals to identify important aspects to be taken into account in the care during the last month of life from their perspective.

