Peer Review File

Article information: https://dx.doi.org/10.21037/apm-23-364

Reviewer Comments

Reviewer A

The authors have produced a well written, easy to read paper. I've enjoyed reading it. I have one very minor point of feedback. Under 2.1, line 63, by-proxy completion is discussed and reported on as being of variable reliability. By-proxy completion is generally viewed as 'not reliable', especially for non-observatory subjects such as distress or depression. Additionally, caregiver burden and distress has a significant influence on the already poor reliability of proxy completion. Some studies even show that proxy assistance for completion can negatively influence reliability. As this is such an important subject, I would suggest to elaborate on this a bit more and/or add some additional references for this subject.

Reply: Thank you for your review and suggestion. The emphasis of the editorial has since shifted from measuring PROMs to selecting PROMs. As a result, what was Section 2 was omitted to align with this new emphasis. Nevertheless, we incorporated your concerns regarding the reliability of by-proxy completion of PROMs in the introduction. We also added supplementary references, as far as the constrained reference count allows (Introduction, page 3).

Reviewer B

Dear authors,

thank you for the opportunity to review this paper. This manuscript did not include a reporting checklist. It is marked as "Editorial".

General questions and remarks

The manuscript addresses an important topic, it aims to discuss the methodological challenges of collecting and measuring PROMs in palliative care and their "effect" on the evaluation of (cost) effectiveness.
The authors report on problems and challenges in using PROMs, conducting studies in palliative care, and challenges in economic evaluation in PC. The topics included are relevant to the aim of the manuscript; however, some are not specific to PROMs. Unfortunately, the content of the manuscript does not reflect the international state of research on all relevant topics included.
The language in the manuscript is sometimes imprecise, definitions are not always clear to the reader, professional terms are not always used unambiguously. Despite an extensive bibliography, current reviews and studies on the economic evaluation of palliative care are hardly included.

I cannot recommend the manuscript for publication with the current focus. However, perhaps a narrative review / scoping review with a more focused topic (e.g. how to identify QALYs in palliative care) and a broader literature base could provide an opportunity for publication using parts of the current manuscript.

1. Introduction

The introduction points out the role of PROMs in studies and the need for economic evaluation of palliative care.

The reader does not receive background information on e.g. (a) - the current role, importance and research status of PROMs in health economics in general and palliative care in particular, (b) considerations on the specific value of PROMs compared to alternative methods for determining QALYs in economic evaluation or the (c) meaning of quality of life and length of life in palliative care and economic evaluation. However these informations would facilitate the understanding of the following chapters.

Reply: Notwithstanding the constraints of the editorial format and the reference limit, we extended the Introduction with background information (Introduction, page 3). The QALY concept had already been introduced, as referenced in Section 2, page 4.

Line 33/34: In the objective of the manuscript, the authors should define what a "PC setting" is. Are both general medical and specialised palliative care settings included? Early and timely integration of palliative care – or only end-of-life care? Inpatient and outpatient? Only complex or also specific interventions (e.g. ACP)? This is important because, for example, some of the "key methodological factors" do not apply in the same way to all possible settings/patient groups/studies/interventions.

Reply: We added a definition of palliative care and clarified that our discussion focuses on the measurement of PROMs and economic evaluations of patients receiving palliative or end-of-life care that is not limited to a specific setting such as hospitals or nursing homes (Introduction, page 4). We also removed the word ‘settings’ for for clarity.

2. Challenges for measuring clinical effectiveness of PC interventions using PROMs

Overall, the challenges mentioned are relevant for palliative care research. However, the descriptions are often imprecise and/or incomplete in terms of the current state of research. They almost completely disregard the existing approaches to solving these problems in palliative care research as well as the examples of studies that have successfully solved the problems.

Furthermore, the challenges mentioned often do not apply to all settings/studies/patient populations. Some of the challenges described are not / only indirectly related to the use of PROM.

Examples:

Line 38/39: The sentence mixes two issues (1) identification of PC patients (definition of inclusion and exclusion criteria/definition of palliative care etc.) and (2) 'patients not addressed' (selection bias, gate keeping etc). The literature cited does not reflect the current state of research on either methodological challenge.

Line 39/41: Example of unclear sentence: In relation to which characteristics are the patients "highly diverse"? In relation to which aspects are there "definitional ambiguities". What is "comfort terminal care" (not an internationally used and defined term in palliative care) and why should it be distinguished from "symptom-relieving measures at an earlier stage"?

Not all studies/settings in palliative care have a "diverse" study population (line 40, lines 69/70), problems with recruitment (e.g. line 49) or include patients based on their prognosis (line 69). Studies and concepts that contribute to solving the problems and reflect the goals of palliative care are not included in the description.

Reply: Thank you for these detailed comments. While we acknowledge the validity of your points, due to the constraints of the editorial format, it was not feasible to delve into every single aspect and include definitions for all of the terms used.
During the revision process, we updated the discussion to concentrate solely on methodological facets associated with economic evaluations in palliative care. This modification aligns with the preferences of the editors, who opted to retain the editorial discussion format as originally planned, rather than converting it into a systematic review on the subject.
Furthermore, in our pursuit of enhancing clarity and readability, the revised manuscript underwent professional language editing.

3. Challenges for measuring cost-effectiveness of PC interventions using PROMs

Chapter 3.1.1 describes relevant aspects of the problems with generic instruments from the curative field in palliative care; chapter 3.1.2 describes some aspects of PROMs specifically developed for palliative care. Overall, these descriptions are informative and easy for the reader to understand. This part could be written in a good format for an editorial – but for an real overview on the topic it would also need more in-depth discussion based on the literature on the topic.

Chapter 3.1.3 discusses different approaches to comparing the economic value between palliative and curative interventions. Palliative care practitioners without

training in health economics will not understand the chapter sufficiently, as the descriptions are too superficial and assume prior knowledge. For experts in health economics, the information is not sufficient to learn about the specific requirements in palliative care. Nevertheless, this topic should be interesting for readers on both sides and the topics are the most interesting ones to consider for a publication.

Reply: As already mentioned, we agreed to prioritize the above aspects in the editorial. We are currently working on a systematic review in which we separately analyze the quality of conducting and reporting on applied economic evaluations in the palliative and end-of-life care field. This ongoing analysis confirms the lack of awareness of many necessary methodological considerations and/or their potential impact by researchers in the field.
In alignment with the editors' decision, we have maintained the editorial format, which precludes a comprehensive literature review but focuses on discussion (as detailed in our response to RB.3). Even though our co-author is a palliative care practitioner without expertise in health economics, we focused more strongly on ensuring the comprehensibility of the content for palliative care practitioners, for example by expending explanations of economic concepts (Introduction page 3, page 4).

4. Conclusions

In the conclusions, suggestions are made for future research focusing on understanding PROMs in the context of EE in PC. However, the discussion should also take a broader perspective, as is the case in chapters 1-3: If dying people cannot fill in questionnaires (by themselves) - what other ways of evaluation could be applied to quality of life? What challenges and solutions are discussed by experts who already use QALYs in their studies in palliative care and conduct economic evaluations? What are the solutions in different settings, patient groups, etc.?

Reply: While we acknowledge the significance of the points you raised, we need to stick to the editorial format (restricted references and word count). Furthermore, the scope of the manuscript has since evolved; the editorial now focuses exclusively on facets closely tied to economic evaluations within this domain (see also responses to RB3 & RB4). Accordingly, the discussion relates only to the repercussions for practice, policy and research within this specific realm, encompassing a spectrum of solutions and potential ways forward discussed in the literature. These include simultaneously using generic and context-specific measures to enable mapping studies and further psychometric validation studies, personalizing evaluation frameworks, incorporating discrete choice experiments and utilizing best-worst scaling techniques to increase understanding in the valuation of health state utilities (Discussion page 7/8).