Peer Review File

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Reviewer Comments

Overall, I think your work addresses an important and urgent theme. However, I also felt there were important limitations to this work, which limit its implications. I will outline my most important objections below.

In general, the aim of the review to both summarize the literature on prognosis of four very heterogeneous neurological diseases and to review best practices on communication of prognosis is too broad. As a result, to my opinion both topics are insufficiently addressed.
Reply: Thank you for this feedback. We have made substantial changes to the manuscript with more detail about literature reviewed for each of the diseases discussed and to the section on communication of prognosis. More details of these changes are below.

Comment 1:
The section on prognosis contains general information with an overall conclusion that, currently, for none of the diseases an individualized precise estimation of the prognosis can be given. To be informative and of relevance for physicians and others treating these patients, it should go more into detail. For example, more detailed information on the predictive value of certain characteristics reflected in the sensitivity/specificity or positive and negative predictive value is missing. In several paragraphs it is mentioned that certain predictive characteristics are associated with an increased mortality, but without a statement on the time frame regarding the outcome of death, this information also is nonspecific.
Reply 1: We agree that this would be more informative for readers and therefore have added details from cited literature throughout the manuscript.
Changes in the text: Numerous additions have been made throughout the text, including relevant characteristics such as area under the receiver operating curve (AUROC), hazard ratio (HR), for various prognostic models and factors included in this review.

Comment 2:
Unfortunately, also the summary of best practices on communicating prognosis with patients and their carers appears too general – some relevant topics, a more detailed link with the previous paragraphs on prognostication (and the uncertainty thereof) and practical implications are missing or remain underexposed.
Reply 2: While there are existing communication tools such as SPIKES for disclosure of prognosis, few are specific to neurologic disease, and a full review of general prognostic tools is beyond the scope of this paper. However, we agree that specific recommendations and practical tools for prognostic communication are relevant to include and have therefore added to the manuscript discussion of the application of the previously published MVP framework for serious illness conversations to neurologic disease.
Changes in the text: We have added a section discussing the MVP framework for serious illness

conversation and its application to patients with neurologic disease (see pages 10-11 of the edited manuscript.)

Comment 3:

The communication of prognosis of the different neurological diseases is highlighted in one paragraph. This while one might argue that patients who suffer from these different diseases (dementia, Parkinson's disease, MS, ALS) are in need for different strategies of communication regarding their prognosis. For example, patients with cognitive decline due to dementia or Parkinson's disease might benefit a smaller amount and more concrete information regarding their prognosis, than younger patients with MS without cognitive decline.

Reply 3: We agree that this is an important consideration. We now include mention of prognostic communication tools including SPIKES, Ariadne Labs Serious Illness Conversation Guide, and take an expanded focus on the MVP framework and its application to neurologic disease, including exploration of patient values and medical plan in context of the medical situation.

Changes in the text: As stated above we have added information on the MVP framework, including the need to ask patients and care partners how they would like information presented and consider various communication methods to address individual needs (see page 10-11, lines 426-437 specifically for recommendations on individualized approach to patients.)

Comment 4:

In this paragraph on communication regarding prognosis, some relevant information seems to be missing. For example, regarding existing literature on how to best communicate prognostic information, what tools there are to support clinicians, patients and carers during communication regarding prognosis, and what practical implications there are to consider while communicating prognostic information. Moreover, what lessons learned from other specialties, for example oncology, can be recommended to neurologists?

Reply 4: We agree that this is important to include in the manuscript, as detailed in reply 2 and 3 above. While a general review of prognostic communication tools is beyond the scope of this review paper, and would require its own dedicated review, we have discussed the previously published MVP framework and discussed its application to neurologic disease.

Changes in the text: The section on the MVP framework was added on pages 9-10.

Comment 5:

The important topic of uncertainty intertwined in the prognostic communication is mentioned. It is stated that clinicians might avoid to discuss prognostic information, without a reference (line 258-260). And in line 276 - 277 it is written that it is important to discuss this uncertainty honestly with patients and care partners, but important nuances are missing.

Overall, the paper reflects on an important theme, but to my opinion does not add enough relevance due to the superficial nature the various topics regarding diverse neurological disorders have been addressed.

Reply 5: We have added a reference where recommended. We have also added discussion of the topic of uncertainty.

Changes to the text: We have added a reference at the line recommended. We have also

expanded the sections on dementia, PD, ALS, MS, and prognostic communication to provide more detail as outlined above in replies to other comments. For topic of uncertainty, see page 10 lines 419-424.)

Alongside the major objections stated above, there are some smaller objections. I've listed them on line #:
Introduction

Comment 6:
• 59 □ you write latter, I think you mean first
Reply 6: Thank you for pointing this out.
Changes in the text: "First" was substituted for "latter" in the text on this line.

Comment 7:
• 67 □ both references are on Parkinson's disease, but this is not specified
Reply 7: Thank you for this point.
Changes in the text: We added citations regarding ALS and dementia in addition to PD.

Comment 8:
• 83 □ you don't specify what other limitations there are
Reply 8: Thank you for this point. While we cannot exhaustively list all possible limitations in patient understanding or communication that could result from neurologic disease, we agree that it may be helpful to add a few more examples here.
Changes in the text: We added "neuropsychiatric symptoms, severe dysarthria or anarthria" as other examples of neurologic symptoms that may impact patient comprehension of their prognosis and/or participation in advance care planning.

Comment 9:
• 92 □ missing reference
Reply 9: Thank you for pointing this out.
Changes in the text: Reference was added.

Methods
Comment 10:
• Table 1 □ search term Parkinson disease, might it be that you have missed articles on Parkinson's disease? Search term Alzheimer disease, might it be that you have missed articles on Alzheimer's disease? Search term ALS, might it be that you have missed articles on amyotrophic lateral sclerosis?
Reply 10: We repeated the search using these suggested terms and did not find any additional literature.
Changes in the text: We have added these search terms to Table 1 in the Methods section.

Comment 11:
• Overall: 1. you have not specified your process for identifying the literature used.

Reply 11: Thank you for this point. We have expanded the Methods section to describe our literature selection process for this narrative review.
Changes in the text: We have added text to the Methods section clarifying our literature search and selection strategy for this narrative review (see Methods section "For this narrative review...")

Comment 12:
• Overall: 2. A table showing the used literature with main determinants and prognostic outcomes would gain more insight.
Reply 12: Thank you for this feedback. We have created such a table which is submitted as a separate file.
Changes in the text: Table separately submitted for publication with the manuscript.

Comment 13:
• It is not clear why the "Current End of Life Palliative Care Guidelines" are stated here.
• Table 2; it is not clear why the "Hospice Eligibility Criteria" are stated here.
Reply 13: Thank you for this feedback. We agree that this section did not add significantly to the manuscript and have removed it in this draft. In its place we make a brief mention in the introduction section of several end of life palliative care frameworks and their limited study in patients with neurologic disease.
Changes in the text: We have removed the original "Current End of Life Palliative Care Guidelines" and original Table 2. In its place we have added brief text in the Introduction (See page 3 line 182-185 "Existing frameworks such as US Medicare Hospice guidelines...")

Comment 14:
• As of line 112 findings are reported but this is not clear from the headings.
Reply 14: Per the comments above, we have made multiple revisions to the document including more detailed findings from cited literature.

Comment 15:
• Line 175: sentence structure not correct.
Reply 15: Thank you for noting this.
Changes in the text: Text was modified to clarify this sentence.

Discussion/summary
• In my opinion, you have not discussed the limitations and or quality of the literature that you have used. For example, in line 179-181, you discuss an article that claimed different determinants associated with death in Parkinson's disease. However, you do not mention that the original study was done on PD patients living in a nursing home, and thus already have a shortened life expectancy.
Reply: We feel that systematic appraisal of individual studies is beyond the scope of this scoping review. Literature review completed for this manuscript may form the basis for future systematic review on prognosis for the diseases discussed in this manuscript.

Line 265 – typo: undue negative undue

Reply: Thank you for noting this.

Changes in the text: Text was corrected to “undue negative impact.”