Author’s response to reviews

Title: Patients’ perspectives can be integrated in health technology assessments: an exploratory analysis of CADTH Common Drug Review

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Author’s response to reviews:

Thank you for the detailed and specific feedback offered by the three reviewers. Their comments have been most valuable in helping us improve our manuscript. In response to the comments, we’ve re-structured our manuscript to create separate Results and Discussion sections, and provided greater detail to address each of the reviewers’ comments. For ease of reading, all revisions are shown in blue font in the manuscript. We also detail below the revisions made for each of the reviewers’ comments.

Reviewer #1:

OVERARCHING COMMENT

There are very few evaluations of how patient input has been used in HTA, so this research by a highly regarded HTA agency will be an important contribution to the field of HTA. The paper is well written and introduces the complex world of this specific HTA process well.

However, there is a fundamental issue of interpretation in this research - the issues extracted from the patient input are not all "outcomes" and it would be more helpful if the broad potential for use of this input was more clearly delineated.

RESPONSE: We thank the reviewer for the comment, and agree with the suggestion to be broader in our description of our analysis of how this information is used. We now explain
explicit references to patient perspectives and describe 4 different ways these are used in assessments and by the expert committees – framing an assessment, consideration of real-world applicability of clinical data, highlighting value for a specific scenario or subpopulation, and reminding all of the people and stories behind the numbers. Predominantly, we explore how implicit use of ‘patient insights’ can and do contribute to the real-world interpretation of clinical evidence.

ABSTRACT: Will need to be rewritten given comments below.

RESPONSE: Re-written to reflect new structure of manuscript.

PLAIN LANGUAGE SUMMARY:

Second sentence - this seems to imply that patients only provide input on benefits the treatment should achieve. However, the submission template covers their experience of living with the disease and of using current treatments. So this is much broader and actually is important when you see the results later, many of the items relate to issues of living with the disease. Bullet 2 may be better as the first bullet Bullet 3 could be made shorter to make it clearer.

The final sentences do not flow clearly. Would a more valuable final sentence be about the value of patient input to decision makers.

RESPONSE: Re-written to reflect new structure of manuscript, and to account for several helpful comments by the reviewers, in particular to broaden the scope and our discussion of the use of patient input.

BACKGROUND: Paragraph 2 - it would be helpful to provide a link to the patient group submission form.

RESPONSE: Added reference [10]

Page 5- line 9 - "peek" is an odd word to use in this context, provide a more professional term
RESPONSE: Replaced sentence, to expand on idea as suggested by reviewer #2.

Page 5 - line 27 - The sentence "within the stakeholder principle" does not make sense. If you are referring to principles for HTA you need to be clearer about this and reference them, and I assume that you are referring to stakeholder INVOLVEMENT.

RESPONSE: To clarify this confusion, we have removed the sentence and reworked this section.

Page5 - line 37 - unique is an odd word to use in this context - do you mean different - do you mean covering different medical conditions?

RESPONSE: Removed ‘unique’; now ‘114 patient groups…..’

Page 6 - top sentence - what about the role of clinical opinion?

RESPONSE: Agree. We added ‘insight provided by clinical specialists’.

Page 6 - lines 11-18 - This doesn't seem to be a full and accurate reflection of the impact of patients perspectives in HTA. Patients perspectives can provide more information than just a specific treatment need and clinical and economic evaluations do not merely seek to show whether a new treatment meets that need. This section really needs to be "unpacked" and should influence all the later work.

RESPONSE: We agree with this reviewer, but had previously limited our discussion of the use of patient input as a means to focus our manuscript. To better reflect how patient perspectives are used in HTA, we have added 6 new sentences to the introduction describing the difference between patients perspectives been presented, and those perspectives integrated into the assessment. Also, we added 3 new sentences to unpack the difference between ‘explicit’ references to patient input and implicit references to the insights that patient groups contribute.
METHODS: This section needs to be formalised. Methods should start by saying what the sampling frame was - as described in the paragraph on page 8, lines 14-29.

RESPONSE: We have restructured as suggested to be more in line with a formal methods section.

The section about the documents is long and not really about methods. It's setting context, so perhaps move it to background or make a table.

RESPONSE: We agree, and feel this information is better described in a table, now Table 2.

Section 2 - it states that the protocol should reflect outcomes of importance identified in the summary of patient input, but there is a need to explain how these outcomes are elicited as the patient group submission form does not explicitly ask for outcomes - does the reviewer determine the outcomes from the submission forms - how are forms from different groups handled?

RESPONSE: Added 6 new sentences to explain in greater detail how ‘patient insights’ were identified, and now include examples in Methods.

Explain whether the form of patient input and the process of HTA remained the same over the period and if not, in discussion describe what impact this may have had.

RESPONSE: Addressed within the last paragraph of the Discussion, under Implications for HTA.

Page 7, from line38, needs to be clearer about actual process. "through iterative readings" is too vague - who did the "reading", how was information extracted?
RESPONSE: Explained in greater detail with examples, in 6 new sentences in Methods (as described above).

Page 8, last paragraph - please describe how patients were involved in this research (advising on design, helping with interpretation of results, etc)

RESPONSE: Two sentences of the role of the CADTH Patient Community Liaison Forum in this research added.

Page 9 - needs some text to explain that there are a wide range of conditions that were included, so you may expect that different issues would be important.

RESPONSE: We agree this is an interesting area to explore, which we were unable to do within our data set. We have added a new within the Discussion section to explore this idea.

Give further justification as to why you chose to categorise using Porter's hierarchy given the patient group submission template has different sections. In particular discuss whether it is appropriate for terminal illnesses given the second category is about recovery.

RESPONSE: Added 2 new sentences providing further justification, which is to reconcile the short term outcomes assessed in trials and long term outcomes sought by patients. An example is used to explain how Porter’s hierarchy can accommodate progressive illness.

More explanation is needed about how you put issues in the hierarchy. In table 2, it's not entirely clear why some of the issues are in tier 2 and not tier 1 - eg why is avoiding hospitalization about progress of recovery and not about health status achieved or retained. In addition, some items seem to be squeezed into a tier - eg cost.

RESPONSE: New paragraph added to Methods explaining the rationale behind patient insights groupings. Further context is provided to explain cost.
RESULTS: 1st sentence specify tiers from the Porter's... hierarchy. The table is a little difficult to read, so it could help to describe one row. For example - In the 30 assessments, 25 of the patient summaries mentioned symptom relief as outlined in the description column. These issues were mentioned in 21 of the protocols, 22 of the drug trials and 17 of the CDEC discussions.

RESPONSE: We appreciate that there is a lot going on in this table and have tried to make it easier for the reader to follow. We have explained the difference between our analyses of outcomes within assessments separately from our grouping of outcomes within the hierarchy. We have also added two sentences providing instruction on how to read the table, both down and across for different information. Finally, we have removed the percentages to help readability.

WHAT IS IMPORTANT TO PATIENTS? Presumably this is part of the results section, but that's not obvious - it reads more as a discussion, with a wider interpretation of the results. This would be better moved to a discussion section.

RESPONSE: We have structured the overall paper to a more traditional academic format, and as such have moved this to the 4th paragraph of the Discussion.

CAPTURED WITHIN CDR ASSESSMENT PROTOCOLS? - GENERAL COMMENTS FOR ALL THESE SECTIONS This sequence of sub-titles is not very clear. As explained above the results need to be written in a different way.

RESPONSE: Thank you. As described above, we have reformatted the manuscript and created a Discussion section. Also, the results section has been edited to describe findings at patient insight level, then at assessment level, for each of the 3 CDR process stages.

Patient group submission forms do not specifically talk about outcomes as you imply and neither to appraisal committees - they consider a wide range of issues to determine the value of a treatment - the most valuable input from patients may be about context not about specific outcomes. This is exemplified in lines 24-31 on page 15.
RESPONSE: This is a good point and we have clarified our description of the assessment process in response. In the Methods section we now describe how we identified a set of issues, insights, desired treatment outcomes, and other ideas raised by patient groups. For simplicity, we now consistently refer to these as ‘patient insights’ throughout the manuscript.

There is an implication that we need to add a range of outcomes that patients consider to be important into trials and assessments, but no discussion of the fact that a confirmatory trial has one primary outcome, several secondary outcomes and perhaps some other outcomes. They must be tested carefully to avoid biases due to multiplicity and trials are designed to have power for the primary outcome only. Furthermore, for many of the issues raised, there are no outcomes and so they would need to be developed.

RESPONSE: This is an important discussion, but one we cannot adequately explore in this manuscript. We, however, have in response added five new sentences to the Discussion to explore the idea of real-world applicability of clinical trial data and the remit of clinical trials.

SPECIFIC COMMENTS ON THESE SECTIONS

Page 14 - top full sentence. This is a rather odd statement about safety, which should be evaluated by regulators and data should not be lacking about safety of comparators, otherwise treatments would not be recommended for marketing.

RESPONSE: We agree and have deleted this sentence, and instead explained this idea in greater detail within the paragraph on real-world applicability of clinical trial data in the Discussion.

Page 15 - lines 29-38 - what evidence do you have that this is the case? There may be a range factors that influence CDEC members, such as clinical experience, personally knowing a patient, general categories of consideration (e.g. end of life, unmet need etc).

RESPONSE: New sentence added to Results, after the statement to explore the factors that may have been involved.
IMPLICATIONS FOR HTA AGENCIES

1st paragraph - Many HTA agencies don't use assessment protocols, so can the implications for HTA agencies be made more general?

RESPONSE: Two sentences added on how agencies without assessment protocol can use specific research questions or deliberative framework to explore specific patient insights.

Somewhat surprising that this section doesn't discuss the potential value of patient input and the need to measure its impact and consider how it’s used by appraisal committees.

RESPONSE: Implications for HTA within Discussion restructured and further developed to explain how patient insights are used by both assessment teams and expert committees. Four key ways that patient insights are used are discussed within this restructured section.

DISCUSSION (suggested section)

Section 1 in methods explains that CADTH reviewers summarize patient input. CADTH is the only agency to do this. Other agencies make the full input available. Discuss the impact of this on your research and implications for others.

RESPONSE: We have redeveloped our methods section and outlined how we verified patient insights identified within Patient Input summaries created by CADTH reviewers with CDEC discussant reports. In our newly restructured Implications for HTA section we have explained how reviewer synthesis of patient group input feeds into use of patient insights by reviewers during an assessment.

Did you consider looking at any sub-groups?

RESPONSE: The analysis of subgroups was outside the scope of our analysis, and not possible with our sample of 30 assessments. We have added 3 sentences in paragraph 5 of Discussion explaining consideration sub-group analysis.
CONCLUSIONS: 3rd paragraph - Patient input isn't necessarily qualitative, it may present a well organised survey or other quantitative research.

RESPONSE: We feel that the narrative quality of patient input summaries is qualitative in nature, and CADTH reviewers use qualitative methods to summarize patient input. We have, however, restructured our Conclusions to focus on two activities of the analysis - integration of patient insights into CDR and need for HTA to explore long-term impacts of treatment.

Reviewer #2

This is an important subject area.

There have not been many studies relating to this topic so it is important that the research team focus on the key area with respect to ascertaining the literature.

I warmly suggest the research team highlight more examples of where patient examples can be integrated with health technology assessments, for example patient records access, summary care records and personal health records. This is otherwise a welcomed piece of research and very informative.

RESPONSE: We are pleased this reviewer feels our analysis is important and will add to the literature. In response to the suggestion, we have further developed the Discussion to explain how patient insights are used by both HTA teams and expert committees. Four key ways that patient insights are used are discussed - framing an assessment, consideration of real-world applicability of clinical data, highlighting value for a specific scenario or subpopulation, and reminding all of the people and stories behind the numbers.

Reviewer #3

1. I liked the article a lot as it shows a clear understanding of the patient experience and the value of the patient input

2. Plain English Summary: This was very good, although the third bullet point was much less clear and understandable than the previous two bullet points.

RESPONSE: We have revised wording of bullet points.
3. In the background: I liked this section very much, although where the unique knowledge of the patient is mentioned, this needs to be made clearer, ie how does the patient have this unique knowledge, what is it that makes him/her an expert in their own condition and why there can be a chasm between what the patients feels they need and what the healthcare professional thinks the patient needs?

RESPONSE: Thank you for the suggestions. We have added two new sentences to the Background explaining the difference between trials and ‘lifeworld’.

4. The information in the tables was very clear and concise as well as the summing up of the finding that followed.

RESPONSE: We are glad this reviewer found the table concise, however in response to another reviewer we have removed the % for greater readability.

5. The conclusions drawn were very interesting and I enjoyed reading this piece of research.

RESPONSE: Thank you.