PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of Using Patient-reported Outcome Measures in Routine Clinical Care of Pediatric Patients with Chronic Conditions: A Systematic Review Protocol
AUTHORS	Bele, Sumedh; Mohamed, Bijan; Chugh, Ashton; Haverman, Lotte; Santana, Maria-Jose

VERSION 1 - REVIEW

REVIEWER	Orna Fennelly University College Dublin, Ireland.
REVIEW RETURNED	09-Nov-2018

GENERAL COMMENTS	Dear authors, I have some minor queries regarding the proposed protocol. Introduction: There is some inconsistency in describing disease-specific PROMs. Could you keep the term consistent throughout the protocol (e.g., use of condition-specific or specific)? Word ‘measures’ omitted in line 24 page 5. You discuss the use of electronic platforms for collecting PROMs on page 7 line 47 – do you plan on including electronically-collected PROMs and the feasibility in your systematic review? If not, this may not be relevant in the introduction. In your first objective, it is not clear whether only PROMs completed by the child are included or whether parent-reported PROMs are being included. Please specify. Methods: Search strategy page 9 – The use of Boolean operators isn’t fully clear. Are your inclusion criteria either a medical outcome or patient outcome, or both? If either or, perhaps putting all outcomes under one heading would be clearer. Search strategy page 9 - Use of phrase 'keywords like' makes the search strategy sound haphazard. Could this be more definitive with reference to Appendix 1. Inclusion criteria - You have mentioned on page 10 line 24 that study design limits will not be imposed on the search but in the inclusion criteria, you specify prospective trials only. Why have retrospective cohort studies been excluded? Inclusion criteria – The fourth inclusion criteria is somewhat ambiguous due to use of “at least one..” and “such as..”. Does one of the mentioned patient outcomes have to be reported or is any patient outcome relevant?

	Inclusion criteria - further information on your definition of a chronic condition is required in selecting papers. Selection process page 11 - Are the two reviewers both reviewing all the titles and abstracts, or will they do half each? This is not clear. Also, there are three authors' initials mentioned here. Further information on how the patient-partners will assess the face-validity would be interesting.

REVIEWER	Michelle M Holmes AECC University College, U.K.
REVIEW RETURNED	12-Nov-2018

GENERAL COMMENTS	This review is very interesting and relevant. From a methodological point of view, this study is sound and follows appropriate guidance. Very minor amendments needed for clarification: 1) The sixth exclusion criteria is studies published prior to the year 2000, please clarify why they have chosen this timeframe? 2) If there is not sufficient homogeneity, and meta-analysis cannot be conducted, please summarise what approach will be taken. Minor edit: 1) The word measures is missing on Page 5, line 24. Overall, this was a great study protocol for a systematic review and I am looking forward to reading the results. It was particularly great to see the details regarding involvement of the patient partner.

REVIEWER	Sarah Damery University of Birmingham, United Kingdom
REVIEW RETURNED	13-Nov-2018

GENERAL COMMENTS	This protocol outlines a systematic review focusing on identifying and consolidating the evidence on the impact of using PROMS in a number of outcomes for chronic conditions in paediatric settings. The protocol is generally well written and conforms to the PRISMA-P checklist, although there is scope for more detail to be added in places, particularly in terms of how the data will be synthesised, as this is currently a weak part of the protocol. My comments are numbered below: 1. Abstract: Add that the review has been registered in PROSPERO 2. Introduction: Paragraph 2, sentence 2: "Patient-reported Outcomes (PROMs) are the tools or instruments used to measure PROs". Correct to Patient-reported Outcome Measures. 3. Introduction: Paragraph 2: "Evidence from adult populations suggests that the integration of PROMs in clinical care enhances patient-clinician communication, reduces the use of healthcare services, and improves HRQoL". Although several references are cited here, it would be useful to provide a greater level of evidence

	in the text here, particularly as the fact that PROMs have been effective in adults is the main justification for looking to see whether they have been effective for paediatric populations. 4. Introduction: Paragraph 3: No need to state the aim of the systematic review at the end of this paragraph, as this aim is stated in the objective section at the end of the introduction. 5. Introduction: The sub-headings (impact of PROMs on…) break up the flow of the introduction. I would like to see the information from these paragraphs integrated into the introduction, especially as the interrupt the structure of the introduction. For example, what is currently in sub-sections 1, 2 and 3 is justification/background for the aims and objectives so should be integrated into the introduction properly. This will mean some reworking of the introduction's structure but will strengthen it. 6. Introduction: Sub-heading 2: Can PROMs really 'predict' adverse events? Change wording here, as although they may help to identify at-risk individuals, they are not a prediction tool. 7. Methods: The authors mention that patient-partners will be consulted throughout the review. This is a fairly innovative approach, and it would be helpful if the authors added a sentence or two about how this will work in practice (i.e. is it just consultation: e.g. commenting on paperwork developed by the researchers, or is it actual collaboration: e.g. co-creating the relevant documents? And how will assessments of face validity be undertaken by patient-partners given that (presumably) these individuals will not be directly involved in the screening and data extraction of information from included papers. Will the patient-partners receive training in systematic review methodology to ensure that their contributions are meaningful? 8. The search strategy outlines keywords to identify paediatric populations etc. But none of the keywords focus on chronic conditions – how will the search strategy capture the chronic condition aspect of the review? Following from this, will there be some chronic conditions that are excluded from the review, or some that are deemed particularly important? This has implications for how the evidence from the included papers is synthesised e.g. PROMs may be extremely effective for HRQoL for chronic renal disease, but they may be ineffective for HRQoL in paediatric heart disease. The protocol doesn't give much information about how the data from the included papers will be handled in order to ensure that the best possible information can be distilled from them. 9. There are also no keywords relating to setting – the introduction talks about 'paediatric settings' but this is not described further. Will family practice be included? Is it just hospital inpatient settings that are of interest? What about outpatient settings (home/community?). All of these may be important, but the authors say little about this other than 'clinical care' or 'paediatric chronic care' which are extremely loose terms. 10. How will generic vs. condition-specific PROMs be handled in the analysis? Will they all be analysed together, or will the effectiveness of generic and condition-specific PROMs be analysed separately?

	11. There are a number of typographical and grammatical errors throughout, and words missing from sentences. The protocol would benefit from a thorough proof-read before publication if accepted. 12. The inclusion criteria mentions 'related measures' to the main outcomes. Such as what? 13. It is not clear how many reviewers will be assessing potentially eligible articles taken through to the full-text screening stage after title and abstract screening. Please clarify. 14. The data extraction section contains a fairly comprehensive list of data to be extracted from included texts. Yet the foregoing paragraphs describe the patient-partners having a key role in developing a data extraction form. If the information to be extracted from included papers is already known, it's not clear what the patient-partners will add to the data extraction process. 15. The methods section is fairly comprehensive right up until the data synthesis section, which is very brief. Although clearly the authors do not yet know the kind of information they will be able to obtain from their included papers (and the associated level of complexity), I would like to see more evidence that they have thought through how they may handle the data they obtain. What will the outputs be? Will they be broken down by individual chronic condition and/or setting? Will generic PROMs be assessed separately from condition-specific PROMs? The level of detail provided in the data synthesis section at the moment does not really give me confidence that the authors have thought enough in advance about what they will do with the data they extract. This has implications for the conduct of the review and more information should be added about data synthesis. Meta-analysis is unlikely to be possible given the nature of most of the outcomes being assessed (e.g. quality of care may be measured using a large number of different metrics and data are unlikely to be comparable across studies). Similarly, the studies included are likely to be qualitative and quantitative – how will the authors handle these potentially very different types of write-ups in their synthesis?

VERSION 1 – AUTHOR RESPONSE

Response to comments from Reviewer 1: Orna Fennelly

Comment: There is some inconsistency in describing disease-specific PROMs. Could you keep the term consistent throughout the protocol (e.g., use of condition-specific or specific)?

Response: We would like to thank the reviewer for informing us about this inconsistency. We have made changes throughout the manuscript to keep the term consistent (condition-specific).

Comment: You discuss the use of electronic platforms for collecting PROMs on page 7 line 47 – do you plan on including electronically-collected PROMs and the feasibility in your systematic review? If not, this may not be relevant in the introduction.

Response: Yes, we plan on including electronically-collected PROMs in our review.

Comment: In your first objective, it is not clear whether only PROMs completed by the child are included or whether parent-reported PROMs are being included. Please specify.

Response: Thank you for raising this important issue. We will only include self-reported PROMs and have explicitly mentioned it in the 'objectives' section of revised version of this manuscript.

Comments: Search strategy page 9 – The use of Boolean operators isn't fully clear. Are your inclusion criteria either a medical outcome or patient outcome, or both? If either or, perhaps putting all outcomes under one heading would be clearer.

AND

Search strategy page 9 - Use of phrase 'keywords like' makes the search strategy sound haphazard. Could this be more definitive with reference to Appendix 1.

Response: Our inclusion criteria are both medical and patient outcome. To clarify it further, we have combined them under the title 'outcomes' within 'search strategy' sub-heading. We have also made search strategy more definitive by removing term 'like' and by adding specific keywords from appendix 1.

Comment: Inclusion criteria - You have mentioned on page 10 line 24 that study design limits will not be imposed on the search but in the inclusion criteria, you specify prospective trials only. Why have retrospective cohort studies been excluded?

AND

Inclusion criteria – The fourth inclusion criteria is somewhat ambiguous due to use of "at least one.." and "such as..". Does one of the mentioned patient outcomes have to be reported or is any patient outcome relevant?

AND

Inclusion criteria - further information on your definition of a chronic condition is required in selecting papers.

Response: We agree with the reviewers regarding the discrepancies in inclusion criteria. We have revised the inclusion criteria to include all the 'studies reporting primary data' which will include retrospective cohort studies as well. We also made changes to the fourth inclusion criteria to explicitly mention which outcomes must be reported. We will follow the definition of the World Health Organization for chronic condition to select papers. We have added this definition in the first paragraph of the 'introduction' section.

Comment: Selection process page 11 - Are the two reviewers both reviewing all the titles and abstracts , or will they do half each? This is not clear. Also, there are three authors' initials mentioned here.

Response: We would like to thank the reviewer for raising this query. Two reviewers will independently review all the titles and abstracts in duplicates. BM will screen all the titles and abstracts while SB and AC each will complement BM by screening half of the total retrieved abstracts.

Comment: Further information on how the patient-partners will assess the face-validity would be interesting.

Response: We have revised the anticipated role of patient-partners and additional details on their role in assessing face-validity has be included under the 'data extraction' section of revised version of the manuscript.

Response to comments from Reviewer 2 : Michelle M Holmes

Comment: The sixth exclusion criteria is studies published prior to the year 2000, please clarify why they have chosen this timeframe?

Response: We had failed to provide clarification on why we chose to exclude studies prior to the year 2000. Evidence revealed that the integration of PROMs in routine clinical care started after the year 2000, so we will apply this time limit to exclude studies before the year 2000. We have added this explanation under the 'information sources' section in this revised manuscript.

Comment: If there is not sufficient homogeneity, and meta-analysis cannot be conducted, please summarise what approach will be taken.

Response: We overlooked this information in the previous version, so thank you for pointing this issue. In this revised version, we have added additional details on data analysis under the 'Data synthesis' section.

Response to comments from Reviewer 3: Sarah Damery

Comment: Add that the review has been registered in PROSPERO

Response: Thanks to the reviewer's comments. We have added that the review has been registered on PROSPERO and have provided the registration number as well.

Comment: it would be useful to provide a greater level of evidence in the text here, particularly as the fact that PROMs have been effective in adults is the main justification for looking to see whether they have been effective for paediatric populations.

Response: We agree with reviewer's comment that although we had added references to the evidence around effectiveness of PROMs in adult population, greater level of evidence is required in the text. In this revised version, we have strengthened this part by adding more evidence demonstrating evidence around the effectiveness of integrating PROMs in routine clinical care for adults with chronic conditions.

Comment: Introduction: Paragraph 3: No need to state the aim of the systematic review at the end of this paragraph, as this aim is stated in the objective section at the end of the introduction .

AND

Introduction: The sub-headings (impact of PROMs on…) break up the flow of the introduction. I would like to see the information from these paragraphs integrated into the introduction, especially as the interrupt the structure of the introduction

Response: We would like to thank the reviewer for these suggestions. We have made structural changes to incorporate some of these suggestions in this revised manuscript.

Comment: Introduction: Sub-heading 2: Can PROMs really 'predict' adverse events? Change wording here, as although they may help to identify at-risk individuals, they are not a prediction tool.

Response: We would like to thank the reviewer for pointing out this error, we agree with reviewer that PROMs may help to identify at-risk individuals, but they are not a prediction tool. We have changed this wording and have also added a reference to support this revised wording.

Comment: Methods: The authors mention that patient-partners will be consulted throughout the review. This is a fairly innovative approach, and it would be helpful if the authors added a sentence or two about how this will work in practice…..

Response: Since submitting the first draft of this manuscript, we have revised the role of patient-partners. More details have been included about how we plan to assess the face-validity of included studies and retrieved data from our patient partners. Following information has been added in the last paragraph of the 'data extraction' section.

"Extracted data from included studies will be presented to the whole research team to ensure consistency in data extraction. At this stage, patient-partners will be consulted to verify if the extracted data is meaningful from the patient's perspective, ensuring that our study conforms to patient-oriented research. Consultation sessions will be organized with the patient-partners, where they will be briefed on the process of synthesizing evidence through systematic review. The process and extracted data will be presented to them in lay terms. Then face validity will be assessed by asking them if this systematic review measures what it purports to measure and if those findings make sense from patient's perspective."

Comment: – how will the search strategy capture the chronic condition aspect of the review? Following from this, will there be some chronic conditions that are excluded from the review, or some that are deemed particularly important?

Response: We would like to thank the reviewer for this query. It is impossible for us to list all the chronic diseases, so we did not include any keyword for chronic disease. In the process of refining the search strategy, we added keywords for chronic diseases, but it did not capture key studies, so we expanded the strategy to include studies reporting all types of diseases. While screening titles and abstracts, we will include all types of chronic diseases.

Comment: – . Will family practice be included? Is it just hospital inpatient settings that are of interest? What about outpatient settings (home/community ?).

Response: We would like to thank the reviewer for this query. We will include all types of settings and have added a sentence about at the end of third paragraph under 'introduction' section of this revised manuscript.

Comment: – How will generic vs. condition-specific PROMs be handled in the analysis? Will they all be analysed together, or will the effectiveness of generic and condition-specific PROMs be analysed separately ?

Response: We would like to thank the reviewer for this query. Effectiveness of generic and condition-specific PROMs will be analysed together. Additional sentence in this regard has been added under the 'data synthesis' section of this revised manuscript.

Comment: – The inclusion criteria mention 'related measures' to the main outcomes. Such as what?

Response: We would like to thank the reviewer for pointing this issue. It was an error, so 'related measures' has been removed.

Comment: – It is not clear how many reviewers will be assessing potentially eligible articles taken through to the full-text screening stage after title and abstract screening. Please clarify.

Response: We would like to thank reviewer for raising this query. Two reviewers will independently review all the titles and abstracts in duplicates. BM will screen all the titles and abstracts while SB and AC will complement BM by screening half of the total retrieved abstracts each.

Comment: – what the patient-partners will add to the data extraction process.

Response: We have revised the role of patient-partners and additional details on their role in assessing face-validity has be included under the 'data extraction' section of this revised version of the manuscript.

Comment: – I would like to see more evidence that they have thought through how they may handle the data they obtain. What will the outputs be? Will they be broken down by individual chronic condition and/or setting? Will generic PROMs be assessed separately from condition-specific PROMs?

AND

the studies included are likely to be qualitative and quantitative – how will the authors handle these potentially very different types of write-ups in their synthesis?

Response: We agree with reviewer's comment that the data synthesis section in previous version did not include details around data synthesis, so we have made significant changes in the 'data synthesis' section to include the anticipated outputs of this review.

Additional response:

The word 'measures' was missing on Page 5, line 24 and was pointed out by all the reviewers. We have corrected that error and have proof read this revised version to eliminate typographical and grammatical errors.

VERSION 2 – REVIEW

REVIEWER	Orna Fennelly University College Dublin, Ireland.
REVIEW RETURNED	22-Jan-2019

GENERAL COMMENTS	Dear authors, I look forward to reading the completed version of this systematic review. I have only minor comments to make regarding the updated protocol. Data synthesis: Change disease-specific to condition-specific as this is the chosen term throughout. Data synthesis: You have added that you will use the COSMIN risk of bias guide to assess individual studies but I am unsure if you will be identifying studies which evaluated the psychometric properties of the identified PROMs. From my understanding, once you identify the papers which used PROMs, you would then need to identify the papers which validated the PROM in that population if you plan on using COSMIN. If this is the case then this is great that COSMIN will be used but I also understand this may not be feasible and I wanted to clarify your use of COSMIN. will be assessed independently by two Also, insert a full stop after 'PROMs[36] Discrepancies'. The use of the COSMIN checklist may only be possible if the authors plan on identifying the papers which evaluated the PROM initially. Strengths and limitations: change patient's to patients' perspective.

	Data extraction: patients' perspective. Good luck with the very worthwhile piece of work.

REVIEWER	Sarah Damery University of Birmingham, United Kingdom
REVIEW RETURNED	18-Jan-2019

GENERAL COMMENTS	The authors have done a good job of addressing the reviewers' comments, and the paper is much improved and more focused as a result. I have no further issue with the paper.

VERSION 2 – AUTHOR RESPONSE

Response to comments from Reviewer 1: Orna Fennelly

Comment: Data synthesis: Change disease-specific to condition-specific as this is the chosen term throughout.

Response: We would like to thank the reviewer for informing us about this inconsistency. We have made changes in data synthesis and throughout the manuscript to keep the term consistent (condition-specific).

Comment: Data synthesis: You have added that you will use the COSMIN risk of bias guide to assess individual studies, but I am unsure if you will be identifying studies which evaluated the psychometric properties of the identified PROMs. From my understanding, once you identify the papers which used PROMs, you would then need to identify the papers which validated the PROM in that population if you plan on using COSMIN. If this is the case, then this is great that COSMIN will be used but I also understand this may not be feasible and I wanted to clarify your use of COSMIN.

will be assessed independently by two

Response: Thank you for raising this important issue. We anticipate using COSMIN guideline, but it might change when we reach the risk of assessment phase of this systematic review. We also would like to reiterate that the risk of bias assessment will be done independently by two.

Comment: Also, insert a full stop after 'PROMs (Discrepancies).

Comment: Strengths and limitations: change patient's to patients' perspective.

Data extraction: patients' perspective.

Response: Thank you for bringing these discrepancies to our notice. We have already made the changes.