Author’s response to reviews

Title: A systematic literature review of the assessment of treatment burden experienced by patients and their caregivers

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Author’s response to reviews:

Response to reviewer’s comments:

Many thanks to both reviewers for taking the time to review our manuscript. We appreciate the opportunity to address the comments below.

Please note: All line numbers refer to the tracked document.

Reviewer reports:

Reviewer 1: Thank you for the opportunity to review this manuscript. It is an important and comprehensive review regarding the measurement of treatment burden. Overall, I found the manuscript to be of high quality and worthy of publication.

Two minor concerns that should be addressed prior to publication are
1) There is a recently released multimorbidity treatment burden measure that may warrant updating the search strategy to ensure complete reporting;
Response: Thank you. We agree that this article is relevant and warrants inclusion. We have updated the search strategy to cover the period up to and including March 2019 which identified a thirteen additional articles including this one. All text, figures and tables have been updated to reflect the extended search period and additional results.

2) The introduction to could be edited to more clearly indicate the focus of this review on identifying all treatment burden measures as a way of moving towards something clinically useful. It was initially unclear to me if the authors were intending to identify measures for research or clinical practice, but the discussion nicely indicates the focus on clinical practice.

Response: We appreciate this suggestion and have edited the introduction to frame the focus of our review more clearly in the last paragraph of the introduction lines 129-132.

Detailed edits are included below.

Background

Line 103 - Should be "Treatment burden usually adds to the symptoms and physical and psychological difficulties imposed by the condition itself."

Response: This edit has been made, thank you (now line 103).

Line 115 - can "failure" be changed to "difficulties" as it sounds more patient-friendly?

Response: Yes, we agree, difficulties is a better choice and have made this change (now line 115).

Line 117 - Minimally Disruptive Medicine should be named (in replacement or addition to person-centered care) since this definition is specifically taken from the paper that names this concept.

Response: This phrase has been added in lines 119-120.

Lines 122 - 125 - Do you meant that have not been regularly implemented in clinical practice? I feel a bit unclear on the lead up rationale to the study, but they seem related to clinical practice implementation of treatment burden assessment.

Response: Thank you, we appreciate this observation and have addressed it in lines 121 and 124 – 126 to clarify that although many tools have been developed to assess treatment burden there is no consensus on which tool to use and no tools have been routinely deployed for use in clinical practice.

Results

Lines 253 - 257 The ICAN Discussion Aid may be better described in the qualitative assessments of Treatment Burden since there is no scoring of the tool - it relies on conversation between patient and clinician (qualitative) to assess the treatment burden.

Response: Thank you for this observation. We considered this a lot as the checklists completed by patients in this aid provide quantitative data. Upon reflection we agree with you that the purpose of the tool is to promote a guided discussion and therefore is more qualitative than quantitative and have updated the manuscript and tables to reflect this.

Line 267 - There is a new multimorbidity treatment burden quantitative measure out called the Multimorbidity Treatment Burden Questionnaire (MTBQ). It can be found here. While I realize this was released after the search strategy limits, I think it is worth updating your search strategy dates to include this measure since it is directly related to your research questions. It can be found here: https://bmjopen.bmj.com/content/8/4/e019413

Response: We agree that this article would enhance our review and have extended our search to include
it. It is discussed in lines 278-282 and 354-355 and also added to table 2 and supplementary table 1.

Line 271 - Please indicate what HCTD stands for, as I don't see the full naming prior to its use.
Response: Thank you. The Health Care Task Difficulty (HCTD) scale is defined in line 292-293.

Lines 280 - 281: Is the statement related to financial burden true of non-US settings? The original TBQ needed to be modified to include this aspect of burden when it was trialed in the US population compared to its French origins. I think it would be helpful to include a statement about whether this is restricted mostly to US populations or if it is seen in specific countries, or internationally as a whole, including citations supporting whichever is the case.
Response: Thank you. We agree that financial burden often contributes substantially to treatment burden and are happy to describe further the settings of reported financial burden. The Sav et al. article referred to in your comment which reports financial burden as the most widely discussed burden in their study is in fact an Australian study set in a system with federally funded universal health care. We agree that the financial pressures in a fee for service model such as in the U.S. are likely even greater. When we updated our search we found a number of additional articles referencing financial burden including that experienced in the US (Rosbach). We have added to the text (lines 313-314 and 318-320) and highlighted that financial burden may in fact be more significant in countries without free access to care such as in the U.S.

Lines 287-289 Having an unpaid caregiver increased patient treatment burden is an interesting statement. It is paradoxical to what most expect (i.e., someone else to share the load would seem to reduce the patient's individual treatment burden). If this is the correct interpretation, I think it deserves calling out as paradoxical.
Response: Yes we agree that the concept that persons with caregivers reported increased treatment burden is open to many interpretations and that one could expect that having someone to share the load would logically reduce treatment burden. We wonder, however, if the individuals who rely on caregivers to help manage their health are perhaps less able to cope and are more burdened hence their need to involve others to relieve some of the burden. Another possibility is that these individuals have a greater treatment burden to manage and although having a caregiver relieves some of the burden they still experience some treatment burden. We have taken your advice and now call out this effect as paradoxical in the manuscript (line 327).

Discussion

Line 299 - methods should be "method."
Response: This has been corrected, thank you (now line 341).

Lines 296 - 299 - this reads clearer than your lead up to the methods in your introduction section, and your aims could be tightened to more clearly match the statements here.
Response: Thank you, we appreciate this observation and have edited the introduction (lines 129-132) to address this.

Line 321 - can compliance be replaced with adherence, which is more patient-friendly, and to match the usage of adherence in the rest of the document?
Response: We are happy to make this change and agree that adherence is more patient-friendly (now line 364).
Line 327 - It may be worth mentioning that the ICAN Discussion Aid is designed to take no more than 3 minutes and could be followed-up by more intensive questionnaires.
Response: We appreciate this observation and agree that the ICAN Discussion Aid would also be a valuable screening tool. We have added this suggestion to the manuscript in lines 370-371.

Line 336 - replace compliance with adherence
Response: We have made this change in line 381, thank you.

Reviewer 2:

GENERAL COMMENTS: The literature review addresses very important topic that is going to be even more important as population aging with a lot of chronic diseases. It looks like the authors gave a lot of thinking to the review's design.
Response: Thank you for your kind observation.

REQUESTED REVISIONS:
1. Abstract - Background section lines 49-53: there is no references according to caregivers' treatment burden although the review deals both care-receivers and caregivers.
Response: Thank you for noticing this oversight on our part. We have edited the abstract to include caregivers (now line 51)

2. Method - in line 139 the authors are using a definition for treatment burden but it is unclear if it is taken from the literature (if yes - a reference is needed) or the authors composed it.
Response: Thank you, we are happy to clarify the origins of our definition. We aimed to create a simple definition that incorporated both the work that a person has to do to manage their condition and the impact that the work has on their lives. We drew from the work of Eton and colleagues which referred to “the workload of health care and its impact on patient functioning and well-being” and the work of our co-author Dr. Boyd and defined treatment burden as “the effort required by the patient or caregiver to manage the medical conditions of the patient and the impact that this has on their lives”. We have expanded our explanation in the text in line 144.

3. Search strategy - Line 147 - PRISMA guidelines - a short explanation is needed regarding what are those guidelines and why they are the best choice for this review.
Response: We are happy to provide this and have added the following text to the manuscript: “The search was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (14)…. PRISMA provides an evidence-based minimum set of items for reporting to allow a transparent and complete reporting of systematic reviews”. (lines 152-156)

4. Line 148 - Please rephrase the sentence. Instead of "described elsewhere" please give some details (shortly if you want) about the review's design and where it is mentioned in details.
Response: We are happy to rephrase this. We have changed “described elsewhere” to “using similar methodology to other systematic reviews performed by our group” and added additional details to the methodology presented (lines 155-156).

5. Line 150 - Please describe what is MESH.
Response: MESH (Medical Subject Headlines) is the National Library of Medicine controlled vocabulary thesaurus used for indexing articles in PubMed. We have updated the manuscript in line 155 to reflect this (now lines 158-159).

6. Line 157 - The reviewed articles are from 1997-2017. Maybe there is a place for explaining why the authors choose this range and not others.  
Response: We chose a 20 year window for 2 reasons:  
(i) To reflect the relatively new emergence of the concept of treatment burden and  
(ii) Our long term goal to inform the development of a quality indicator to measure treatment burden in home based medical care and the need to base the measure on literature reflective of current practice and disease burden.

ADDITIONAL REQUESTS/SUGGESTIONS:  
7. Line 195 third word from the end: I think it should be "nor" instead of "not".  
Response: Thank you for this observation. We agree that the phrasing of this sentence could be improved and have edited the manuscript lines 205-207 and removed the end of the sentence.