PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	EVIDENCE AVAILABLE FOR PATIENT-IDENTIFIED PRIORITIES IN DEPRESSION RESEARCH: RESULTS OF 11 RAPID RESPONSES
AUTHORS	Sebastianski, Meghan; Gates, Michelle; Gates, Allison; Nuspl, Megan; Bialy, Liza; Featherstone, Robin; Breault, Lorraine; Mason-Lai, Ping; Hartling, Lisa

VERSION 1 – REVIEW

REVIEWER	Angelo Barbato Istituto di Ricerche Farmacologiche Mario Negri-IRCCS, Milan, Italy
REVIEW RETURNED	05-Dec-2018

GENERAL COMMENTS	This is an important paper presenting an innovative way of addressing patient priorities in the are of outcome research for depressive disorders. I recommend to accept it without revisions.

REVIEWER	Michelle Banfield Australian National University, Australia
REVIEW RETURNED	12-Dec-2018

GENERAL COMMENTS	This paper represents a synthesis of a very large amount of work to examine the evidence for patient-identified priorities, which is an important but often neglected step in priority-setting. The rapid response method is well-suited to the purpose and the review is comprehensive, but in its present form is more like a summary than a considered and contextualised discussion. My main concerns are as follows: 1) The review is about about examining evidence for patient-identified priorities, but patients were not involved in the review or synthesis process, and the questions to be addressed were reframed by the reviewer when the rapid reviews were conducted. This feels like a very big step away from best practice in patient involvement as there are several degrees of reinterpretation happening, and the opportunity to examine things through a patient lens was lost. This should be acknowledged as a limitation of the study and an area for future attention. 2) Related to point 1, there is no elaboration on why the choice was made to apply design filters and only focus on evidence from systematic reviews, RCTs and observational studies, and no comment on whether this sort of filtering would be supported by the people who developed the priorities. There is increasing evidence that people who have experience of health problems, particularly chronic physical and mental health problems, support the use of experiential knowledge (e.g., qualitative data). The

	authors need to acknowledge the limitations introduced by focusing on the types of studies included and that they may not include the evidence of interest to patients. There also needs to be discussion of whether the identified limitations and research needs would be consistent with the original interest/intention of the patient priorities. For example, in Table 2, the conclusions and limitations for question 2 focus on a lack of causal link, but it is not clear whether the patient priority was about a direct cause or about an association/increased risk. 3) The discussion is very underdone. This is where I would expect more reflection on the effect of the types of studies identified by the filters, what the findings may mean for those who identified the priorities and in particular, a discussion of why patients still prioritise things that have hundreds of studies. Clearly the research is not reaching where it is needed, but the paper does not discuss this in detail. Part of the point of patient involvement is to ensure research is relevant and this is noted in the introduction, but we are left to our own speculation as to why there seems to be plenty of research aligned with patient needs and they're still the top priorities. 4) It might also be useful to contextualise the priorities with other priority-setting exercises conducted globally, to give some sense of whether these particular priorities are specific to the population. There are patient priority studies from the UK and Australia for example, including some that have also compared patient priorities with existing research. Although these studies used different methods, they identified substantial disparities between patient priorities and existing research. This difference deserves comment. 5) The paper is titled as about depression research, but the search strategies in the appendix all include terms for mood disorders more generally. Since the research presented is not broken down by different disorders, and there is significant heterogeneity noted in many places, this feels a bit misleading. Unless there was exclusion of other disorders during screening (which is not evident in the brief flow diagram) it might be more accurate to say this was a study on priorities for mood disorders. If there was screening, this needs to be better elaborated in the methods.

REVIEWER	Graham Thornicroft King's College London
REVIEW RETURNED	07-Jan-2019

GENERAL COMMENTS	Review of: EVIDENCE FOR PATIENT-IDENTIFIED PRIORITIES IN DEPRESSION RESEARCH: 2 RESULTS OF 11 RAPID RESPONSES The strengths of this paper include: • The focus on Patient priority setting projects is interesting and relatively novel • The paper attempts to forge a bridge, cross-links between more traditional systematic reviews and patient identified priorities • The paper does identify questions for which stronger or weaker evidence exists, and does summarise this evidence The paper could be improved by: • Discussion on whether patients views also support giving greater salience to systematic reviews rather than to consensus statements of evidence eg by patient groups

	• A self-critical discussion of the process to establish patient research priorities • Describing in more detail which patients/patients groups contributed towards identifying priorities, and how these were these identified and on what basis? • Giving more detail of how the research questions were themselves formulated, and how far patients were involved in the selection and phrasing of the research questions after the patient priority areas had been identified • Saying why 'patients were not directly involved in the knowledge synthesis process.'- is it not important that patients are involved at every stage of this project/study? • Why were patient interpretations/uses of the results of the knowledge syntheses not undertaken or reported? • Simplifying the appendices which are voluminous

REVIEWER	A.Schene Radboudumc, Netherlands
REVIEW RETURNED	03-Feb-2019

GENERAL COMMENTS	This is a great paper. I like the question, the method, the detailed presentaion of results, and the confrontation between patient generated questionsn and the availlebel scientific evidence. Well written.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1 Comments
Reviewer Name: Angelo Barbato

This is an important paper presenting an innovative way of addressing patient priorities in the area of outcome research for depressive disorders. I recommend to accept it without revisions.

Thank you Dr. Barbato for your supportive comments.

Reviewer 2 Comments
Reviewer Name: Michelle Banfield

This paper represents a synthesis of a very large amount of work to examine the evidence for patient-identified priorities, which is an important but often neglected step in priority-setting. The rapid response method is well-suited to the purpose and the review is comprehensive, but in its present form is more like a summary than a considered and contextualised discussion.

Thank you for your comments Dr. Banfield. We agree that detailed methodology for examination of evidence for patient priority setting projects is often overlooked and would enhance the rigour of the process.

My main concerns are as follows:
1) The review is about about examining evidence for patient-identified priorities, but patients were not involved in the review or synthesis process, and the questions to be addressed were reframed by the reviewer when the rapid reviews were conducted. This feels like a very big step away from best practice in patient involvement as there are several degrees of reinterpretation happening, and the opportunity to examine things through a patient lens was lost. This should be acknowledged as a limitation of the study and an area for future attention.

According to guidance from the JLA, patients are not involved in reframing the questions or the review and synthesis process. The JLA Guidebook identifies 'format submissions into PICO format' as a task for the Information Specialist. Moreover, based on the JLA guidance the entire

review work is to be undertaken by an Information Specialist. The JLA Guidebook acknowledges this part of the PSP process to be complex and continues to welcome feedback on this section of the Guidebook. Outside of a PSP there is a lack of guidance on how best to involve patients in reviews in general. We feel that this project is an important step forward in terms of conducting reviews within a patient priority-setting project. We have addressed the issue of limited patient involvement in the review process in the manuscript (Limitations: page 28, line 427), and made suggestions for more guidance moving forward.

2) Related to point 1, there is no elaboration on why the choice was made to apply design filters and only focus on evidence from systematic reviews, RCTs and observational studies, and no comment on whether this sort of filtering would be supported by the people who developed the priorities. There is increasing evidence that people who have experience of health problems, particularly chronic physical and mental health problems, support the use of experiential knowledge (e.g., qualitative data). The authors need to acknowledge the limitations introduced by focusing on the types of studies included and that they may not include the evidence of interest to patients. There also needs to be discussion of whether the identified limitations and research needs would be consistent with the original interest/intention of the patient priorities. For example, in Table 2, the conclusions and limitations for question 2 focus on a lack of causal link, but it is not clear whether the patient priority was about a direct cause or about an association/increased risk.

We agree with your comment that patients with lived experience support the use of experiential knowledge (e.g., qualitative data). We also support the use of qualitative data for certain research questions, especially around patient experiences, values and preferences, etc. However, the questions we were addressing related mostly to interventions to help manage depression, or association of different factors related to depression. The JLA guidance was originally focused on 'treatment uncertainties' and only recently (November 2018; after our project) have they changed this to 'evidence uncertainties'. The JLA Guidebook focuses on the use of systematic reviews as the initial source of identifying evidence uncertainty, although it recognizes that a search beyond systematic reviews may be needed depending on the topic, question, and type of uncertainty. The JLA recognizes that "a large amount of rich data and patient stories might come from the [PSP]" and that some PSPs have produced a separate report from this data, although JLA recognizes this as "extra work" and not the main purpose of the PSP.

Filtering of the available evidence in our work was based on accepted principles of evidence-based medicine and standard methods in knowledge synthesis (i.e., systematic reviews, rapid reviews, etc.) which advise to focus on the most methodologically relevant and rigorous evidence to answer the question of interest (e.g., systematic reviews of randomized trials, then randomized controlled trials are recognized as offering the highest quality of evidence for questions of treatment efficacy and effectiveness) and to begin with the highest quality and use lower quality evidence only as needed (this is also supported by extensive work done through the GRADE initiative to assess quality of evidence for different research questions). Further, some filtering and organization and selection of the studies by their methodological rigour was necessary in order to manage the large amounts of available evidence and ensure any decisions made about fulfillment of an uncertainty was also based on the highest quality of evidence. An explanation regarding the use of design filters and their potential limitations has been added to the manuscript (Search: page 6, line 120) and Limitations: page 28, line 426).

3) The discussion is very underdone. This is where I would expect more reflection on the effect of the types of studies identified by the filters, what the findings may mean for those who identified the priorities and in particular, a discussion of why patients still prioritise things that have hundreds of studies. Clearly the research is not reaching where it is needed, but the paper does not discuss this in detail. Part of the point of patient involvement is to ensure research is relevant and this is noted in the introduction, but we are left to our own speculation as to why there seems to be plenty of research aligned with patient needs and they're still the top priorities.

This is an important observation and it will help strengthen our paper. We have added an additional paragraph addressing the role of knowledge translation in addressing knowledge gaps identified in the PPSP (Discussion: page 25, line 372).

4) It might also be useful to contextualise the priorities with other priority-setting exercises conducted globally, to give some sense of whether these particular priorities are specific to the population. There

are patient priority studies from the UK and Australia for example, including some that have also compared patient priorities with existing research. Although these studies used different methods, they identified substantial disparities between patient priorities and existing research. This difference deserves comment.

The focus of our paper is specific to the knowledge syntheses that supported the PSPP rather than the PSPP process as a whole, details of which were previously published. In light of your comment we have added a few sentences comparing the results to the UK JLA Depression project, but feel any in-depth commentary is better suited to the previous paper (Limitations: page 28, line 431).

5) The paper is titled as about depression research, but the search strategies in the appendix all include terms for mood disorders more generally. Since the research presented is not broken down by different disorders, and there is significant heterogeneity noted in many places, this feels a bit misleading. Unless there was exclusion of other disorders during screening (which is not evident in the brief flow diagram) it might be more accurate to say this was a study on priorities for mood disorders. If there was screening, this needs to be better elaborated in the methods.

We developed searches that were overly sensitive, including related terms such as mood disorders to identify depression research, in order not to miss studies that report mixed mental health populations. The specific inclusion/exclusion criteria for each question are listed in Table 1 and general examples were added to the text (Study selection: page 9, line 140).

Reviewer 3 Comments
Reviewer Name: Graham Thornicroft

The strengths of this paper include:
1) The focus on Patient priority setting projects is interesting and relatively novel
2) The paper attempts to forge a bridge, cross-links between more traditional systematic reviews and patient identified priorities
3) The paper does identify questions for which stronger or weaker evidence exists, and does summarise this evidence

Thank you Dr. Thornicroft for recognizing these strengths. We appreciate your comments.

The paper could be improved by:
4) Discussion on whether patients views also support giving greater salience to systematic reviews rather than to consensus statements of evidence eg by patient groups.

This is an interesting point that could inform future PSPP processes but is outside of the intended scope of our manuscript.

5) A self-critical discussion of the process to establish patient research priorities.

We agree that a discussion of the process is important; the entirety of the PSPP process was discussed in a previous publication and referenced in the introduction. The present manuscript focuses on the knowledge synthesis methods and results. We have provided some critical reflections and limitations of the knowledge synthesis process within the PSPP (Limitations: page 27, line 420).

6) Describing in more detail which patients/patients groups contributed towards identifying priorities, and how these were these identified and on what basis?

This information was detailed in a previous publication and referenced in the introduction. In order to meet the word limit for this article we felt further explanation of the process that led to the rapid reviews was outside the scope of this manuscript.

7) Giving more detail of how the research questions were themselves formulated, and how far patients were involved in the selection and phrasing of the research questions after the patient priority areas had been identified.

As per our response to the first comment by Reviewer 2, this is a really important point and we feel that the JLA and broader community needs to better understand and guide how patients can be involved in phrasing the research questions. The JLA Guidebook acknowledges that "submissions from patients, carers and clinicians may need to be rewritten or rephrased…to clarify the precise uncertainty." They also acknowledge that this part of the process is "interpretative and subjective".

They further present PICO as a helpful framework and "to reiterate, the process of turning those themes [identified by patients, carers and clinicians] into precise research questions is something the Steering Group is encouraged to work with funders and researchers on after the final workshop." Therefore, JLA does not advise (nor provide guidance) on involving the patients in refining the questions to make them suitable for the literature review part of the process. We have added some clarification to the methods section regarding how we formulated the questions (page 5, line 104) and we have tightened up the patient involvement paragraph to make it clear that patients were not involved after the priorities were identified (Patient involvement: page 9, line 152; Limitations: page 28, line 428).

8) Saying why 'patients were not directly involved in the knowledge synthesis process.'- is it not important that patients are involved at every stage of this project/study?

The extent of patient involvement research varies greatly; we did not find any previous PSPP studies that included patients in the knowledge synthesis process and the JLA guidance does not provide specific guidance on this aspect; moreover, their guidance indicates that this should be undertaken by an Information Specialist. We strongly agree that the involvement of patients in research is important, especially in identifying research questions and priorities. To date, there is little guidance and evidence on how best to involve patients in the review part of the process, and how to ensure that involvement is meaningful.

9) Why were patient interpretations/uses of the results of the knowledge syntheses not undertaken or reported?

This is not a part of the JLA PSP process. This may be an important next step for the ongoing Knowledge Translation aspect of the larger PSPP, however we feel it is outside the scope of this manuscript.

10) Simplifying the appendices which are voluminous

We recognize there is a lot of data in the appendices, however we felt it was important to provide access to the full results of all the rapid responses for transparency and to provide researchers a solid foundation for future depression research. We look to the editor for guidance on this.

Reviewer 4 Comments
Reviewer Name: A.Schene

This is a great paper. I like the question, the method, the detailed presentation of results, and the confrontation between patient generated questions and the available scientific evidence. Well written.

Thank you for your positive feedback Dr. Schene.