

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

## ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Burden of disease and barriers to comprehensive care for rheumatic heart disease in South Africa: an updated systematic review protocol
<b>AUTHORS</b>	Murugasen, Serini; Abdullahi, Leyla; Moloi, Hlengiwe; Wyber, Rosemary; Abrams, Jessica; Watkins, DA; Engel, Mark E, ZUHLKE, LIESL

## VERSION 1 – REVIEW

<b>REVIEWER</b>	Boyarchuk, Oksana I Horbachevsky Ternopil National Medical University
<b>REVIEW RETURNED</b>	19-Mar-2023

<b>GENERAL COMMENTS</b>	Dear author, The study protocol "Burden of disease and barriers to comprehensive care for rheumatic heart disease in South Africa: an updated systematic review protocol" is well written, the research has a clear goal and task. The topic is relevant for South Africa, where rheumatic heart disease remains one of the most frequent causes of cardiovascular diseases and is the cause of mortality in a significant number of cases. It is important to determine the impact of the COVID-19 pandemic on the prevalence and burden of the disease. I have no additional comments.
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<b>REVIEWER</b>	Vervoort, Dominique Johns Hopkins University Bloomberg School of Public Health
<b>REVIEW RETURNED</b>	22-Mar-2023

<b>GENERAL COMMENTS</b>	The authors present a protocol for an updated systematic review on the burden of disease and barriers to care for patients living with rheumatic heart disease (RHD) in South Africa. I thank the authors for their work and have some comments to improve their manuscript:  Major Comments: 1. The authors are encouraged to replace "developing countries" with "low- and middle-income countries," as the former is a subjective (i.e., what is the threshold of development?) and harmful term (i.e., developing suggests "not developed"). The authors may wish to refer to doi: 10.1136/bmjgh-2022-009704 for more information. 2. Based on the scope of the question, one may argue that Objective Two lends itself more to a scoping review (whereas a systematic review is appropriate for Objective One). Can the authors comment on this?
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	<p>3. Search strategy: the authors state that they will use “pre-defined search terms.” Can the authors clarify whether these terms are consistent with the previous systematic review or were newly developed or updated? Was a medical librarian consulted for the development and/or appropriateness of the search strategy?</p> <p>4. Search strategy/Limitations: the authors will identify unpublished works through their networks. Reproducibility and transparency are important pillars of literature reviews; however, these may conflict with anecdotal evidence and/or unpublished works. Can the authors comment on this or reflect on this in the limitations?</p> <p>5. Data synthesis and analysis: the authors state that “We intend to investigate for potential publication bias, should the number of studies allow.” Can the authors elaborate on the methods that will be applied for this?</p> <p>6. Discussion/Limitations: a brief discussion of the (anticipated) limitations of the study would be appropriate.</p> <p>Minor Comments:</p> <p>1. Abstract: the abbreviation “RHD” should be introduced in the first line.</p> <p>2. Introduction: “World Health Organisation” should be “World Health Organization.”</p> <p>3. The authors should be consistent in focusing on observational studies only (e.g., 2.1 Objective One) versus also including randomized controlled trials (e.g., 3.1 Objective One). Can the authors correct as appropriate?</p> <p>4. The authors are encouraged to use the more recent 2020 PRISMA guidelines as opposed to the older 2015 ones.</p> <p>5. References: some research article references are cited as websites (i.e., “Available from...”), whereas website references are missing access dates, which should be corrected.</p>
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<b>REVIEWER</b>	Vaughan, Geraldine University of Technology Sydney Faculty of Health, Australian Centre for Public and Population Health Research
<b>REVIEW RETURNED</b>	02-Apr-2023

<b>GENERAL COMMENTS</b>	<p>An important proposed study building on previous work on the burden of RHD in South Africa.</p> <p>See below comments.</p> <p>I was unclear on aspects of the methodology described in the manuscript. ‘Mixed methods’ is referred to under Strengths/Limitations but no other detail given on how the two studies integrate methodologically.</p> <p>Are you using a qualitative synthesis with (inductive?) content analysis for Objective 2? Can this be made clearer and more consistent.</p> <p>“3. This review only captures information from the last 8 years, ...”</p> <p>The proposed study continues and extends the Zuhlke et al work published in 2015 so I am unsure if this is a limitation.</p> <p>(Strengths &amp; Limitations) 3 and 4 – specify which Objective is being referred to</p> <p>“...identification and development of public figures as ‘RHD champions’,”</p> <p>Fostering or promoting rather than development?</p> <p>Vaccine development – specify GAS. Would the 5 strategic targets be better placed in a table to highlight</p> <p>... ‘past decades’ Change to recent decades or specify which past decades</p>
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	<p>Clarify this sentence – sub-Saharan Africa is a hotspot for RHD, but it is also endemic across the continent?</p> <p>Specify that you are referring to RHD prevalence</p> <p>Are those aged 13+ in adult category</p> <p>“Postoperative mortality at...” specify – cardiac valve surgery postoperatively?</p> <p>(justification for study) ... and identify barriers to care for patients with RHD? / challenges to challenges faced by SA in responding to the 2018 WHA RHD resolution?</p> <p>Include advocacy?</p> <p>Omit or replace ‘redundant’</p> <p>Include strategy on exporting search results to Endnote here? (currently under Objective 2 methods)</p> <p>“A standardised data extraction form will be utilised to extract information...” using which tool – Rayyan? Specify</p> <p>Would the more recent 2018 TIPS Handbook be a more useful reference for mapping against framework, needs assessment tool, other...</p> <p>Should ‘qualitative assessment’ be ‘quantitative? If that is correct, can you give more detail</p> <p>How will the five main strategic areas listed here align to the 3 categories described above?</p> <p>Conclusion –last sentence - include reference to early diagnosis. Also improved continuity of care?</p>
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### VERSION 1 – AUTHOR RESPONSE

<p><b>Reviewer 1</b></p> <p>No revisions suggested</p>	<p>No action required</p>
<p><b>Reviewer 2</b></p> <p><b>Major Comments:</b></p> <ol style="list-style-type: none"> <li>The authors are encouraged to replace “developing countries” with “low- and middle-income countries,” as the former is a subjective (i.e., what is the threshold of development?) and harmful term (i.e., developing suggests “not developed”). The authors may wish to refer to doi: 10.1136/bmjgh-2022-009704 for more information.</li> <li>Based on the scope of the question, one may argue that Objective Two lends itself more to a scoping review (whereas a systematic review is appropriate for Objective One). Can the authors</li> </ol>	<p><b>Major Comments:</b></p> <ol style="list-style-type: none"> <li>Amended throughout document to ‘low- and middle-income countries’ with acronym ‘LMIC’ also employed</li> <li>As we are using a systematic approach, with a pre-defined protocol and employing similar methods across both objectives, with the intention to perform</li> </ol>

<p>comment on this?</p> <p>3. Search strategy: the authors state that they will use “pre-defined search terms.” Can the authors clarify whether these terms are consistent with the previous systematic review or were newly developed or updated? Was a medical librarian consulted for the development and/or appropriateness of the search strategy?</p> <p>4. Search strategy/Limitations: the authors will identify unpublished works through their networks. Reproducibility and transparency are important pillars of literature reviews; however, these may</p>	<p>meta-analyses/synthesis where robust data is found, we felt that drafting the protocol for a systematic review would be appropriate at this stage. Current members of the review team have previously been involved in similar reviews elsewhere in Africa, and are drawing on these experiences (please see publications by Moloi et al 2016, 2017 and 2022 referenced within the protocol for further details). We will be careful to frame the results appropriately according to its strengths and limitations prior to dissemination.</p> <p>3. Expanded to provide clarity as to which aspects are consistent and which have been adapted from other relevant sources.</p> <p>4. Addressed under new section entitled “4.1 Strengths and limitations of proposed review”</p> <p>5. Amended to include further detail on the method to be employed to investigate for publication bias (i.e., funnel plots)</p> <p>6. Added: “4.1 Strengths and limitations of proposed review”. However, the BMJ Open guidelines for authors for protocols does not ask for a specific section dealing these other than under the “Strengths and limitations” box immediately</p>
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<p>conflict with anecdotal evidence and/or unpublished works. Can the authors comment on this or reflect on this in the limitations?</p> <p>5. Data synthesis and analysis: the authors state that “We intend to investigate for potential publication bias, should the number of studies allow.” Can the authors elaborate on the methods that will be applied for this?</p> <p>6. Discussion/Limitations: a brief discussion of the (anticipated) limitations of the study would be appropriate.</p> <p><b>Minor Comments:</b></p> <p>1. Abstract: the abbreviation “RHD” should be introduced in the first line.</p> <p>2. Introduction: “World Health Organisation” should be “World Health Organization.”</p> <p>3. The authors should be consistent in focusing on observational studies only (e.g., 2.1 Objective One) versus also including randomized controlled trials (e.g., 3.1 Objective One). Can the authors correct as appropriate?</p> <p>4. The authors are encouraged to use the more recent 2020 PRISMA guidelines as opposed to the</p>	<p>following the abstract and so it may be removed by the journal.</p> <p><b>Minor Comments:</b></p> <p>1. Amended</p> <p>2. Amended</p> <p>3. Corrected to be consistent – interventional and observational studies will be included.</p> <p>4. Text and reference updated to reflect 2020 PRISMA guidelines</p> <p>5. Amended</p>
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<p>older 2015 ones.</p> <p>5. References: some research article references are cited as websites (i.e., "Available from..."), whereas website references are missing access dates, which should be corrected.</p>	
<p><b>Reviewer 3</b></p> <p>1. I was unclear on aspects of the methodology described in the manuscript. 'Mixed methods' is referred to under Strengths/Limitations but no other detail given on how the two studies integrate methodologically. Are you using a qualitative synthesis with (inductive?) content analysis for Objective 2? Can this be made clearer and more consistent. (P3, P16 L5, P17 L48)</p> <p>2. "3. This review only captures information from the last 8 years, ..." The proposed study continues and extends the Zuhlke et al work published in 2015 so I am unsure if this is a limitation. (P4)</p> <p>3. (Strengths &amp; Limitations) 3 and 4 – specify which Objective is being referred to. (P4)</p> <p>4. "...identification and development of public figures as 'RHD champions'," Fostering or promoting rather than development? (P5)</p> <p>5. Vaccine development – specify GAS. Would the 5 strategic targets be better placed in a table to highlight? (P5 L43-48)</p> <p>6. ... 'past decades' Change to recent decades or specify which past decades. (P6 L4)</p> <p>7. Clarify this sentence – sub-Saharan Africa is a hotspot for RHD, but it is also endemic across the continent? (P6 L16-20)</p>	<p>1. Methods for analysis for objective two are listed under 3.2.2 "The qualitative data will then undergo inductive analysis for overarching themes and inconsistencies, and reported under the five main strategic areas listed in section 2.2. If any numerical estimates are provided, they will be assessed to see if a formal quantitative meta-analysis is feasible, employing similar methods to objective one." Methods for objective one are described under section 3.1.5.</p> <p>2. Amended</p> <p>3. Amended</p> <p>4. This wording is taken directly from the original position statement of the World Heart Federation as referenced.</p>

<p>8. Specify that you are referring to RHD prevalence (P6 L29)</p> <p>9. Are those aged 13+ in adult category? (P6 L38)</p> <p>10. "Postoperative mortality at..." specify – cardiac valve surgery postoperatively? (P6 L45)</p> <p>11. (justification for study) ... and identify barriers to care for patients with RHD?/ challenges to challenges faced by SA in responding to the 2018 WHA RHD resolution? (P7 L7-11)</p> <p>12. Include advocacy? (P8 L45-51)</p> <p>13. Omit or replace 'redundant' (P12 L25)</p> <p>14. Include strategy on exporting search results to Endnote here? (currently under Objective 2 methods) [P12 L36]</p> <p>15. "A standardised data extraction form will be utilised to extract information..." using which tool – Rayyan? Specify (P13 L22)</p> <p>16. Would the more recent 2018 TIPS Handbook be a more useful reference for mapping against framework, needs assessment tool, other... (P14 L26)</p>	<p>5. Amended to include GAS – the wording is again taken directly from the same position statement as referenced.</p> <p>6. Amended</p> <p>7. Amended to provide clarity</p> <p>8. Amended</p> <p>9. Yes – as stated in text. In the cited study, patients aged &gt;13 years were defined as adults.</p> <p>10. Amended to "all-cause"</p> <p>11. Amended</p> <p>12. Adapted from the reference. The framework allows programme evaluation which may serve as an advocacy tool – this is mentioned elsewhere in the paper (e.g., under "dissemination and anticipated impact")</p> <p>13. Omitted</p> <p>14. Amended</p>
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<p>17. Should 'qualitative assessment' be 'quantitative? If that is correct, can you give more detail (P17 L34)</p> <p>18. How will the five main strategic areas listed here align to the 3 categories described above? (P17 L47)</p> <p>19. Conclusion –last sentence - include reference to early diagnosis. Also improved continuity of care? (P19)</p>	<p>15. Amended to provide clarity</p> <p>16. The data extraction and analysis methods are informed by the work done by Wyber and Moloi et al, who are members of the current team undertaking the review. Previous studies using this framework are reported in the references and our team would like to remain consistent in our analytical methods.</p> <p>17. Amended</p> <p>18. Please see note clarifying under section 3.2.1</p> <p>19. Conclusion has been removed as per editor's note</p>
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## VERSION 2 – REVIEW

<b>REVIEWER</b>	Vervoort, Dominique Johns Hopkins University Bloomberg School of Public Health
<b>REVIEW RETURNED</b>	03-May-2023
<b>GENERAL COMMENTS</b>	The authors have extensively responded to and incorporated previous reviewer comments. I thank the authors and have no further comments.
<b>REVIEWER</b>	Vaughan, Geraldine University of Technology Sydney Faculty of Health, Australian Centre for Public and Population Health Research
<b>REVIEW RETURNED</b>	22-May-2023
<b>GENERAL COMMENTS</b>	No other comments; reads well.



