

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Multimorbidity in South Africa: A systematic review of prevalence studies
AUTHORS	Roomaney, Rifqah; van Wyk, Brian; Turawa, Eunice; Pillay-van Wyk, Victoria

VERSION 1 – REVIEW

REVIEWER	Letamo, Gobopamang University of Botswana, Population Studies
REVIEW RETURNED	16-Feb-2021

GENERAL COMMENTS	<p>Although there is mention that there were disagreements that were discussed and resolved, the number of times these disagreements were encountered is not stated. The number of disagreements encountered provides a rough idea of the reliability of the results. Line 141</p> <p>GENERAL COMMENTS In this study, the authors aim to review prevalence studies of multimorbidity in South Africa to identify prevalence estimates, common disease clusters and factors associated with multimorbidity. The study is topical, relevant and crucial given the increasing burden of the coexistence of two or more health conditions in low and middle-income countries and multimorbidity's implication as a risk factor for COVID-19 mortality which is ravaging most countries. I will provide specific comments below.</p> <p>Specific Comments The abstract clearly stated the review objective, the study design, the search strategies performed for the systematic review, data sources, the results obtained and the conclusion. This section clearly demonstrates the existing research gaps and the need to undertake this type of study. The search strategy and database search are clearly stated, including the eligibility criteria which shows it is well thought through and documented. Although there is mention that there were disagreements that were discussed and resolved, the number of times these disagreements were encountered is not stated. The number of disagreements encountered provides a rough idea of the reliability of the results. Quality assessment has been described and it appears that there is no potential reporting bias.</p>
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	<p>The data extraction and analysis are appropriate. The authors stated valid reasons for not performing meta-analysis which is commendable. The discussion section is detailed enough and adequately integrated the study results with previous studies. Limitations of the study are also highlighted, including those of the included studies.</p> <p>Overall, the systematic review adequately and successfully addressed the three objectives it set out to achieve: prevalence estimates, common disease clusters, and factors associated with multimorbidity.</p>
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REVIEWER	Sakhuja, Swati University of Alabama at Birmingham, Epidemiology
REVIEW RETURNED	07-Apr-2021

GENERAL COMMENTS	<p>Roomaney et al conducted a systematic review of studies on prevalence of multimorbidity in South Africa.</p> <ul style="list-style-type: none"> - The authors may want to consider discussing heterogeneity observed in the studies included in more detail and how was it accounted for in the analysis. - Authors should consider discussing policy implications of this review in South Africa and how it compares to other LMIC.
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REVIEWER	Nicholson, Kathryn Western University
REVIEW RETURNED	12-Aug-2021

GENERAL COMMENTS	<p>Thank you for the opportunity to review the manuscript entitled "Multimorbidity in South Africa: A systematic review of prevalence studies" -- the authors have done an excellent job and this will be an important contribution to the multimorbidity literature. I have included a few final minor revisions below:</p> <p>Abstract: -please change "of which and" to either "of which" or "and"</p> <p>Introduction: -please change "diseases cluster" to "disease clusters"</p> <p>Methods: -please change "epidemiology data" to "epidemiological data"</p> <p>Results: -please correct the final numbers of articles included / excluded in "Search results" -please change "decrease in the prevalence in multimorbidity" to "decrease in the prevalence of multimorbidity" -please change "age 69+ years" to "age group 69+ years" -I am not sure whether the sentence "This systematic review was limited to the information reported in the included studies." is accurate as I believe that the authors made great efforts to supplement information reported in the included studies, such as data by age and sex breakdowns.</p> <p>Conclusions: -please change "They may also" to "These findings may also"</p>
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	<p>-based on the expertise of the authors, it perhaps would be interesting to add more specific details about what types of studies (settings, samples, outcomes) would be most pertinent to best understand the burden of multimorbidity in South Africa (in addition to age and sex recommendations)</p> <p>Strengths and Limitations of Study: -as noted above, perhaps another limitation could be highlighted in the fourth bullet point</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1: Prof. Gobopamang Letamo, University of Botswana		
<p>GENERAL COMMENTS</p> <p>In this study, the authors aim to review prevalence studies of multimorbidity in South Africa to identify prevalence estimates, common disease clusters and factors associated with multimorbidity.</p> <p>The study is topical, relevant and crucial given the increasing burden of the co-existence of two or more health conditions in low and middle-income countries and multimorbidity's implication as a risk factor for COVID-19 mortality which is ravaging most countries. I will provide specific comments below.</p> <p>SPECIFIC COMMENTS</p> <p>The abstract clearly stated the review objective, the study design, the search strategies performed for the systematic review, data sources, the results obtained and the conclusion.</p> <p>This section clearly demonstrates the existing research gaps and the need to undertake this type of study.</p> <p>The search strategy and database search are clearly stated, including the eligibility criteria which shows it is well thought through and documented.</p> <p>Quality assessment has been described and it appears that there is no potential reporting bias. The data extraction and analysis are appropriate.</p>	<p>We thank Prof Letamo for the thorough review and feedback.</p>	

<p>The authors stated valid reasons for not performing meta-analysis which is commendable. The discussion section is detailed enough and adequately integrated the study results with previous studies.</p> <p>Limitations of the study are also highlighted, including those of the included studies.</p> <p>Overall, the systematic review adequately and successfully addressed the three objectives it set out to achieve: prevalence estimates, common disease clusters, and factors associated with multimorbidity.</p>		
<p>Although there is mention that there were disagreements that were discussed and resolved, the number of times these disagreements were encountered is not stated. The number of disagreements encountered provides a rough idea of the reliability of the results. Line 141</p>	<p>At the abstract and title screening phase, the two reviewers had a conflict in 2.9% of the articles. At the full-text article phase, the two reviewers had conflicts in 2 of the 41 articles.</p> <p>This has been added to the text:</p> <p><i>In the title and abstract screening phase, reviewers conflicted on 2.9% of the articles. In the full-text phase, the reviewers had conflicts in 2 of the 41 articles.</i></p>	<p>Page 7, Line 181 – 183.</p>
<p>Reviewer 2: Dr. Swati Sakhuja, University of Alabama at Birmingham</p>		
<p>Comments to the Author: Roomaney et al conducted a systematic review of studies on prevalence of multimorbidity in South Africa.</p>	<p>We thank Dr Sakhuja for the comments and helpful suggestions.</p>	
<p>The authors may want to consider discussing heterogeneity observed in the studies included in more detail and how was it accounted for in the analysis.</p>	<p>We only had three studies that reported on the multimorbidity prevalence in people over the age of 50 years. We attempted a meta-analysis but did not include it in the article. The I^2 statistic was 99.3%; indicating that heterogeneity was high which is a common finding in meta-analyses of prevalence studies. We also consulted with a biostatistician and they advised us against the inclusion of the meta-analysis results. We agreed that a narrative description of the results would be more</p>	

	<p>appropriate and thus reported the results narratively.</p> <p>In addition, Page 13, Lines 266 – 270 reports on differences in the way studies were reported which also made comparison difficult.</p> <p>Lastly, heterogeneity may have also been increased due to: a) the different diseases included in each study's definition of multimorbidity, b) the number of diseases included in conceptualisations of multimorbidity, c) differences in the way disease information was collected (e.g. self-reported, medical records, tests), d) differences in underlying demographics, and e) differences in locations (urban vs. rural) and periods of study.</p>	
<p>Authors should consider discussing policy implications of this review in South Africa and how it compares to other LMIC.</p>	<p>Thank you for the suggestion.</p> <p>We added:</p> <p><i>Prevalence estimates from systematic reviews can provide an important source of information that is used for evidence-based health decision making - especially in LMICs that have constrained health information systems. A multimorbidity prevalence systematic review conducted for South Asia highlighted the insufficient work conducted in the area of multimorbidity and called for greater methodological rigour to better build scientific evidence in this domain.[50] In a similar vein, we also advocate for more studies to be conducted and with rigorous study designs. A recent report by the Academy of Science of South Africa,[51] highlighted the problematic nature of multimorbidity research in sub-Saharan Africa as: funding provided for only specific diseases; lack of health system</i></p>	<p>Page 18, Lines 393 – 404.</p>

	<p><i>preparedness; and low prioritisation of multimorbidity due to a lack of political commitment to implement concomitant health reforms. Research into multimorbidity is crucial for better understanding of the nature of the problem in the sub-Saharan African region, and to identify ways to introduce comprehensive health service delivery.[51]</i></p>	
Reviewer 3: Dr. Kathryn Nicholson, Western University		
<p>Comments to the Author: Thank you for the opportunity to review the manuscript entitled "Multimorbidity in South Africa: A systematic review of prevalence studies" -- the authors have done an excellent job and this will be an important contribution to the multimorbidity literature. I have included a few final minor revisions below:</p>	<p>We thank Dr Nicholson for the positive feedback and comments.</p>	
<p>Abstract: – please change "of which and" to either "of which" or "and"</p>	<p>Done.</p> <p>The word "and" was removed from the sentence.</p>	<p>Page 2, Line 53.</p>
<p>Introduction: – please change "diseases cluster" to "disease clusters"</p>	<p>Done.</p>	<p>Page 5, Line 111.</p>
<p>Methods: – please change "epidemiology data" to "epidemiological data"</p>	<p>Done.</p>	<p>Page 6, Line 129.</p>
<p>Results: – please correct the final numbers of articles included / excluded in "Search results"</p>	<p>Thank you for picking up the error.</p> <p>The sentence and Figure 1 was corrected to reflect that 1040 articles were excluded:</p> <p><i>In total, 1407 titles were retrieved, and 1081 records were screened after de-duplication (Figure 1). By screening titles and abstracts, 1040 articles were excluded.</i></p>	<p>Page 7, Line 180.</p> <p>Figure 1.</p>

<p>– please change "decrease in the prevalence in multimorbidity" to "decrease in the prevalence of multimorbidity" breakdowns.</p>	<p>Done.</p>	<p>Page 15, Line 308.</p>
<p>– please change "age 69+ years" to "age group 69+ years"</p>	<p>Done.</p>	<p>Page 15, Line 309.</p>
<p>– I am not sure whether the sentence "This systematic review was limited to the information reported in the included studies." is accurate as I believe that the authors made great efforts to supplement information reported in the included studies, such as data by age and sex</p>	<p>Thank you.</p> <p>We removed the sentence.</p>	<p>Page 19, Line 406.</p>
<p>Conclusions: – please change "They may also" to "These findings may also"</p>	<p>Done.</p>	<p>Page 19, Line 420.</p>
<p>– based on the expertise of the authors, it perhaps would be interesting to add more specific details about what types of studies (settings, samples, outcomes) would be most pertinent to best understand the burden of multimorbidity in South Africa (in addition to age and sex recommendations)</p>	<p>Thank you for the suggestion.</p> <p>We added:</p> <p><i>More studies are needed in the general population to determine which disease clusters are most prevalent and could potentially be targeted for intervention. Sources of secondary data could be further explored to answer this question. Studies at health facilities would help to provide information regarding multimorbidity's effect on quality of life indicators, to assess whether people are receiving optimal treatment; and to identify the ways that multimorbidity might be impacting healthcare utilisation.</i></p>	<p>Page 19, Line 429 – 435.</p>
<p>Strengths and Limitations of Study: – as noted above, perhaps another limitation could be highlighted in the fourth bullet point</p>	<p>Two limitations were added to the Strengths and Limitations section.</p> <ul style="list-style-type: none"> • <i>A limitation of this study was that it excludes studies conducted in sub-populations with one specific disease (e.g. multimorbidity in cancer patients).</i> • <i>Grey literature (non-academic literature) was excluded.</i> 	<p>Page 4, Line 79 – 83.</p>

VERSION 2 – REVIEW

REVIEWER	Nicholson, Kathryn Western University
REVIEW RETURNED	12-Sep-2021
GENERAL COMMENTS	Thanks very much to the authors for making the final revisions to the manuscript based on the reviewers' comments. I believe that this manuscript is ready for publication.