

BMJ Open Prevalence of multimorbidity in South Africa: a systematic review protocol

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ABSTRACT

Introduction Multimorbidity has increased globally over the past two decades, due to ageing populations and increased burden of non-communicable diseases (NCDs). In a country like South Africa, with a growing burden of NCDs and a high prevalence of HIV, information on multimorbidity can improve planning for healthcare delivery and utilisation, and reduce costs in the context of constrained health resources. This review aims to synthesise prevalence studies on multimorbidity, and identify dominant clusters and trends of multimorbidity in South Africa.

Methods and analysis We will search electronic bibliographic databases (PubMed, Scopus, JSTOR, POPLINE, PsycINFO, ScienceDirect, Web of Science and CINAHL), and the reference lists of included articles. Two researchers will independently screen title and abstracts, and then full text to identify studies published before and in 2020 that report on prevalence of multimorbidity in South Africa. Risk of bias assessments will be done for each study. Information on the prevalence of multimorbidity and disease clusters will be extracted from each study. Where possible, prevalence of specific clusters of multimorbidity will be pooled using a random effects meta-analysis to account for variability between studies. The I^2 statistic will be used to establish the extent of heterogeneity due to variation in prevalence estimates rather than due to chance. The systematic review will be reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses.

Ethics and dissemination Only published journal articles will be included in the systematic review. This review received ethics approval as part of a larger project by the University of the Western Cape Biomedical Science Research Ethics Committee (BM20/5/8). The findings from this research will be used to estimate the prevalence of multimorbidity in South Africa and will contribute to the design of future research projects. The findings will be disseminated in a peer-reviewed journal article.

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INTRODUCTION

Multimorbidity, defined as the coexistence of two or more chronic conditions, has increased globally in the past two decades.^{1,2} Although a gold standard definition of multimorbidity has not been established, it has been recommended that the operationalisation of multimorbidity can include a combination of

Strengths and limitations of this study

- To our knowledge, this will be the first systematic review to estimate the prevalence of multimorbidity in South Africa.
- This systematic review will include articles conducted in community/general and health-facility settings.
- This protocol follows the Preferred Reporting Items for Systematic reviews and Meta-Analyses Protocols 2015³⁵ guidelines.
- The findings will be used to inform future research projects and can guide health policy and planning for service delivery in South Africa.
- The study may be limited by the way in which source articles define multimorbidity.

non-communicable diseases (NCDs), mental health conditions and infectious diseases.¹ The increase in multimorbidity is attributed to ageing populations³ and the growing burden of NCDs.¹ Whereas the increase in NCDs was initially predominantly observed in high-income countries; recently this increase was also reported in low and middle-income countries (LMICs).⁴

The prevalence of multimorbidity places additional stress on already severely strained health systems in LMICs⁵ by driving up healthcare utilisation and costs.⁶⁻⁹ Furthermore, multimorbidity alters the patterns of individual health behaviours and access of health services; which in turn, has further implications for health systems responsiveness and pressing the urgency for further health reforms away from a programmatic approach to comprehensive, integrated services delivery. The need for reforms to integrate the treatment of various chronic conditions has been acknowledged.^{10,11} Researchers have since highlighted the need to incorporate elements specific to people living with multimorbidity. These include the need for: multimorbid patients to have access to coordinated and multidisciplinary teams of health professionals; support for patients to self-manage their workload, and evidence-based guidelines applicable to multimorbid

conditions.¹²⁻¹⁵ It is essential to grasp the magnitude and clustering of multimorbidity to inform health policy and regulations at a national level.

South Africa has a quadruple burden of disease of HIV/AIDS, NCDs, injuries and other communicable diseases with perinatal conditions, maternal causes and nutritional deficiencies.¹⁶⁻¹⁷ As HIV treatment has improved, people living with HIV in South Africa can expect a near-normal life expectancy.¹⁸ However, ageing adults living with HIV are at a higher risk of developing chronic conditions such as NCDs compared with those not infected, and at an earlier age.¹⁹ An emerging pattern of HIV and NCD multimorbidity was described in the country.¹³ The burden of mental health conditions in people living with HIV has also been recognised²⁰⁻²³; with an estimated 40% of people living with HIV also afflicted by a diagnosable mental disorder.²⁴⁻²⁵ This demonstrates the complex burden of disease in the country.

Systematic reviews on multimorbidity that were conducted to date were mostly on older adults and in high-income countries.²⁶⁻³⁰ These reviews reported pooled prevalences of multimorbidity between 38% and 66%.²⁶⁻²⁸⁻³¹ In contrast, only two reviews included or were conducted on multimorbidity in LMICs.³² The 'global' systematic review included LMICs but limited the included studies to community settings; and did not include healthcare settings.³¹ Although the systematic review of multimorbidity in India and Bangladesh included primary healthcare settings, none were selected.³³ The authors acknowledged that this was due to a gap in the multimorbidity literature in primary healthcare settings.

While community-based studies on multimorbidity are important, it is also essential for reviews on multimorbidity to include studies conducted in healthcare settings, because these studies can give a good indication of the number of people accessing healthcare for chronic conditions.²⁹ Both community-based and health facility-based studies provide insight into the scale of the problem. To our knowledge, no study has been done to assess the prevalence of multimorbidity in South Africa that included studies in primary care settings. There is a need for research into multimorbidity in LMICs on the African continent as their disease burden differs from high income countries; that is, overlapping burdens of NCDs and infectious diseases which lead to new multimorbidity disease combinations.¹⁹ The proposed systematic review aims to synthesise existing literature on the prevalence of multimorbidity in South Africa, and identify common disease clusters and trends in the country.

Research questions

This systematic review aims to address the following review questions:

1. What is the prevalence of multimorbidity in persons over the age of 18 years in South Africa in studies reported up to and including 2020?

Table 1 Summary of eligibility criteria

Condition	Context	Population
Primary studies reporting the prevalence of multimorbidity in South Africa, using acceptable case definitions.	South African observational studies up to and including 2020.	Males and females, aged 18 years and above that reside in South Africa.
Studies focused on 'multiple chronic diseases', 'coexisting conditions' and 'multiple diseases' will also be assessed to determine if they fit the definition of multimorbidity.	Study types include population-based studies and cross-sectional studies.	
	Study settings include ambulatory, community-based, general practice, primary healthcare and other healthcare settings.	

2. What is the prevalence of multimorbidity in adult males and females stratified by age group in South Africa in studies reported up to and including 2020?
3. What are common multimorbidity disease clusters in South Africa in studies reported up to and including 2020?
4. What are the trends in the prevalence of multimorbidity disease clusters in South Africa over time?

METHODS AND ANALYSIS

Protocol and registration

The methods for this systematic review was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)³⁴ and the PRISMA Protocols statement (online supplemental appendix 1).³⁵ The systematic review is registered with the International Prospective Register of Systematic Reviews.

Eligibility criteria

The Condition, Context and Population (CoCoPop) mnemonic for prevalence systematic reviews³⁶ will be used to define the inclusion criteria (table 1).

Condition

Articles about the prevalence of multimorbidity in South Africa will be included. Case definitions for multimorbidity may be defined in various ways. Ideally, articles will need to provide a clear description and definition of how they have conceptualised multimorbidity. For articles where multimorbidity has not been clearly defined, this article will adopt an operational definition of multimorbidity, similar to Pati, Swain.³³ Their operational definition states 'studies documenting two or more chronic

conditions, even though not mentioning the term multimorbidity'.³⁴[p.4] The article will also need to be explicit about which diseases have been included in their definition of multimorbidity.

The way in which multimorbidity was measured will need to be clearly defined. For example, whether a count of conditions was done. Also, the way in which diseases were diagnosed must be clear (eg, self-report, clinical assessment, laboratory test).

Context

Articles must report on studies conducted in South Africa. The setting of the study can be community-based, or health facility-based (eg, inpatient and outpatient).

Population/types of participants

This systematic review will be restricted to people who reside in South Africa and are over the age of 18 years old. Ideally, articles should report on the prevalence of multimorbidity by age group and sex.

Outcomes

The primary outcome will be the prevalence of multimorbidity in South Africa.

Types of studies

Observational, cross-sectional study designs are the most appropriate for determining the prevalence of a health condition, particularly common conditions of long duration.³⁶ Thus, included articles will be cross-sectional or population-based study designs.

Articles must document the prevalence of multimorbidities, or their data must allow for the calculation of multimorbidity prevalence. Articles will need to define multimorbidity as the coexistence of at least two disease conditions or an operational definition will be applied. Articles with a sample size of less than 100 participants will be excluded as these studies may be susceptible to the influence of extreme observations.³⁷ All articles before and including 2020 will be included. Additionally, in order to be included in this study, articles must be original and peer reviewed.

Inclusion and exclusion criteria are described in [table 2](#). The following types of documents or studies will be excluded:

- ▶ Reviews, opinion pieces, conference presentations, letters, editorials, dissertations, abstracts, grey literature.
- ▶ Studies not conducted in South Africa.
- ▶ Studies that do not allow for the calculation of multimorbidity prevalence.
- ▶ Experimental studies.
- ▶ Studies not published in English.

Search strategy

A comprehensive search strategy was formulated by reviewing search terms used in other systematic reviews of multimorbidity.^{26–31 33 38–41} The search strategy will be modified, where necessary, according to the database or

Table 2 Summary of inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Peer-reviewed articles.	Non peer-reviewed articles and grey literature.
Articles with more than 100 participants.	Articles with smaller sample sizes (<100 participants).
Articles about multimorbidity in adults in South Africa.	Articles not about multimorbidity, not about adults or not conducted in South Africa.
Observational studies.	Experimental studies.
Articles where it is possible to calculate the prevalence of multimorbidity.	Articles where it is not possible to calculate the prevalence of multimorbidity or to only calculate multimorbidity in a subset of people with a disease.

search engine used ([table 3](#)). Reference lists of included articles will be screened for relevant articles. The following electronic databases will be searched: PubMed, Scopus, JSTOR, POPLINE, PsycINFO, ScienceDirect, Web of Science and CINAHL.

Search terms will include 'multimorbidity' and linguistic variations such as 'multi-morbidity', 'multimorbidities', 'multi-morbidities', 'multi morbidity', 'multi morbidities', 'multiple morbidities', 'multiple-morbidities'. Terms such as 'multiple conditions', 'multiple diseases', 'multiple chronic diseases', 'multiple chronic conditions', 'multiple illnesses', 'multiple diagnoses', 'multipathology', 'chronic condition', 'chronic diseases'³³ will also be included. These terms will be further restricted by location 'South Africa' and by method and study design 'prevalence, epidemiology, pattern'. This will be done by using the 'AND' and 'OR' Boolean operators where appropriate.

The term 'comorbidity' is now accepted to be distinct from multimorbidity.⁴⁰ This study will exclude the search term 'comorbidity' as was done by another multimorbidity systematic review.³¹ However, if the search results include comorbidity studies that examine the prevalence of multimorbidity, the eligibility of these studies will be considered.

Study selection and eligibility criteria

One reviewer will conduct the literature search. Once the search is run, citations will be downloaded into a reference management system such as EndNote (EndNote X8, Thomson Reuters). Duplicates will be excluded using the EndNote deduplication function. Citations will be exported from EndNote into Rayyan.⁴²

Selection process

Two reviewers (RAR and EBT) will independently screen the titles and abstracts of the search output to select potentially eligible studies using prespecified eligibility criteria. The web-based system, Rayyan, will be used to manage the screening process. Rayyan was designed by the Qatar

**Table 3** Example search strategy for PubMed

Search	Query
#4	Search ((#3 NOT (animals(mh) NOT humans(mh))))
#3	Search (#1 AND #2)
#2	Search (South Africa(mh) OR South Africa*(tiab) OR RSA [tiab] OR Africa, Southern(mh:noexp)OR Southern Africa(tiab))
#1	Search (Multimorbidity OR multi-morbidity OR multimorbidity(tiab) OR "multi morbidities" OR multimorbidity(mh) OR multimorbidit* OR multimorbid OR multimorbidities OR multi-morbidit* OR "multiple morbidities" OR "multiple-morbidit*" OR multidisease* OR multi-disease* OR "multiple disorder" OR "multiple illness")

Foundation to expedite systematic reviews by semiautomating the initial screening of titles and abstracts.⁴² The full-text of potentially relevant articles will be retrieved and independently reviewed by two review authors (RAR and EBT) for eligibility.

Eligible citations will be uploaded into a web-based electronic system, the Burden of Disease Review Manager (BODRevMAN). This system was designed by the Burden of Disease Research Unit of the South African Medical Research Council to facilitate, systemise and manage the process of systematic review, the risk of bias assessment and provide a summary of data extracted.³⁷ BODRevMAN is tailored to the systematic review of observational studies. It facilitates the independent quality assessment and extraction of information from included full-text articles. Any disagreements will be resolved through discussion or another review author (VP-vW or BvW) will add input to enable a consensus. A PRISMA flow diagram will detail the study selection decisions made.

The researchers will not be blinded to the authors, titles and institutions of potentially eligible studies. Where there are multiple studies from the same dataset, the most appropriate data will be included. Where additional information is needed, the authors of the study will be contacted. One reviewer will email the corresponding author and a maximum of two attempts will be made, separated by one week.

Quality assessment

Two reviewers will independently assess study characteristics and the risk of bias of each study. The reviewers will use a modified checklist⁴³ based on the Hoy *et al*⁴⁴ risk of bias tool for population-based prevalence studies and the Newcastle-Ottawa Scale⁴⁵ for assessing the quality of non-randomised studies (online supplemental appendix 2). The tool has been described previously.^{37 46} Results from the two researchers will be compared and differences will be discussed between them. Where consensus is not reached, a third reviewer (VP-vW) will be called on to arbitrate. Studies with a high risk of bias will be excluded and the reasons for their exclusion will be noted.

Data extraction

Two reviewers will independently extract data using BODRevMAN. The data extraction facilitated by BODRevMAN is in accordance with recommendations by Munn *et al*³⁶ for prevalence systematic reviews. The following data will be extracted:

- ▶ Citation details: authors, title, journal and year.
- ▶ Study details: study design, study setting (community or health facility), timeframe for data collection, geographical location and sample size.
- ▶ Case definition: how multimorbidity was defined and how disease conditions were measured.
- ▶ Participant characteristics: age, sex, urban/rural, socioeconomic characteristics.
- ▶ Description of main results: percentage prevalence of multimorbidity (n/N) and 95% CIs. Prevalence of conditions stratified by age and sex. Information on the most common disease clusters in the study sample.

In addition, the aims of the study, the method of data analysis used and any points of difference that may affect the interpretation of findings³⁶ will be noted.

Data synthesis

The results will be presented in accordance with the PRISMA statement. Studies that are deemed to have a moderate or low risk of bias will be included in the analysis. Where appropriate, graphs will be used to display the information from included articles. The quantitative results will be summarised for individual studies and will include point estimates and interval estimates (eg, 95% CIs). The prevalence data will be broken down by age, sex and disease clusters if the information is available. Differences and similarities between studies will be documented. Possible trends will also be noted.

If articles are amenable to meta-analysis, this will be done using Stata V.15 (College Station, Texas). A random effects meta-analysis will be used. Estimates will be pooled to obtain a summary estimate and 95% CI. A χ^2 test will be used to assess statistical heterogeneity and the I^2 statistic will be used to assess the degree of homogeneity.^{47 48} Where there are more than ten studies, publication bias will be assessed with a funnel plot and an egger test.⁴⁹

Where sufficient data exist, subgroup analysis will be conducted based on multimorbidity case definition used, study setting (eg, community or health facility), age groups, sex and time periods. Ideally, multimorbidity prevalence will be estimated by age group and sex.

If it is not possible to do a meta-analysis, the findings from included articles will be presented in summary tables that will include the year of data collection, the study type and setting (community or health facility-based), location of study, the definition of multimorbidity used in each study, the diseases and number of diseases included in the study and how they were ascertained (eg, measured or self-reported).

Patient and public involvement

No patients will be involved directly in this study.

ETHICS AND DISSEMINATION

This systematic review will be the first to review all available studies reporting on the prevalence of multimorbidity in South Africa. This study will provide estimates that will be valuable to health services planning. It will also provide much needed information on multimorbidity on the African continent and in LMICs in general.

The findings from this systematic review will be written up using the PRISMA guidelines. It will be disseminated through publication in a peer-reviewed journal article and/or conference proceedings.

This study is a secondary analysis of published studies. The data from published studies cannot be linked to individuals. This review received ethics approval as part of a larger project by the University of the Western Cape Biomedical Science Research Ethics Committee (BM20/5/8).

Contributors RAR, VP-vW, BvW conceptualised the study. RAR wrote the first draft of the protocol. VP-vW, BvW, EBT provided input for subsequent drafts. All authors gave approval for publication.

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