BMJ Global Health

Multimorbidity in African ancestry populations: a scoping review

Michelle Kamp ,[1,2] Okechinyere Achilonu ,[2] Isaac Kisiangani ,[3] Daniel Maina Nderitu ,[3] Phelelani Thokozani Mpangase ,[2] Girmaw Abebe Tadesse ,[4] Kayode Adetunji,[2] Samuel Iddi ,[3] Skyler Speakman,[4] Scott Hazelhurst ,[2,5] Gershim Asiki ,[3,6] Michèle Ramsay ,[1,2] as members of the MADIVA Research Hub and the DS-I Africa Consortium

To cite: Kamp M, Achilonu O, Kisiangani I, *et al*. Multimorbidity in African ancestry populations: a scoping review. *BMJ Glob Health* 2023;**8**:e013509. doi:10.1136/bmjgh-2023-013509

Handling editor Seye Abimbola

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjgh-2023-013509).

Received 24 July 2023
Accepted 1 November 2023

For numbered affiliations see end of article.

Correspondence to
Professor Michèle Ramsay; Michele.Ramsay@wits.ac.za

ABSTRACT

Objectives Multimorbidity (MM) is a growing concern linked to poor outcomes and higher healthcare costs. While most MM research targets European ancestry populations, the prevalence and patterns in African ancestry groups remain underexplored. This study aimed to identify and summarise the available literature on MM in populations with African ancestry, on the continent, and in the diaspora.

Design A scoping review was conducted in five databases (PubMed, Web of Science, Scopus, Science Direct and JSTOR) in July 2022. Studies were selected based on predefined criteria, with data extraction focusing on methodology and findings. Descriptive statistics summarised the data, and a narrative synthesis highlighted key themes.

Results Of the 232 publications on MM in African-ancestry groups from 2010 to June 2022—113 examined continental African populations, 100 the diaspora and 19 both. Findings revealed diverse MM patterns within and beyond continental Africa. Cardiovascular and metabolic diseases are predominant in both groups (80% continental and 70% diaspora). Infectious diseases featured more in continental studies (58% continental and 16% diaspora). Although many papers did not specifically address these features, as in previous studies, older age, being women and having a lower socioeconomic status were associated with a higher prevalence of MM, with important exceptions. Research gaps identified included limited data on African-ancestry individuals, inadequate representation, under-represented disease groups, non-standardised methodologies, the need for innovative data strategies, and insufficient translational research.

Conclusion The growing global MM prevalence is mirrored in African-ancestry populations. Recognising the unique contexts of African-ancestry populations is essential when addressing the burden of MM. This review emphasises the need for additional research to guide and enhance healthcare approaches for African-ancestry populations, regardless of their geographic location.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Multimorbidity (MM) is a growing global health challenge. While much research focuses on high-income countries and mostly European-ancestry populations, people with African-ancestry are largely under-represented. Even when included, African Americans are often the primary focus and are known to be poorly representative of continental African populations. The definition of MM and study methodologies vary across studies making global comparisons challenging.

WHAT THIS STUDY ADDS

⇒ This study is the first comprehensive literature review on MM in African-ancestry populations. It shows that African-ancestry populations are not homogeneous and treating them as such may lead to erroneous conclusions and inappropriate public health interventions. The analysis of the literature identified crucial differences between MM studies and outcomes when comparing continental and diaspora African-ancestry populations and highlighted the pitfalls of using studies on African American populations as sole representatives for all African-ancestry populations.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ By emphasising the under-representation of studies focused on African and African-ancestry populations, this study encourages more inclusive research. It cautions against over-relying on diaspora African-ancestry populations as proxies for continental African groups and makes a plea for prioritising more nuanced and larger studies from Africa. Furthermore, it underscores significant gaps in MM research and calls on the global scientific and health communities to include more diverse African-ancestry communities from the continent and the diaspora, and to be more context-aware in their methodologies, interpretations and conclusions.

INTRODUCTION

Multimorbidity (MM), the co-occurrence of two or more chronic conditions in an

individual, is a growing global challenge.[1 2] MM is associated with increased premature mortality,[2] lowered quality of life,[3] diminished mental health,[4 5] increased polypharmacy risk[6] and intensified health services utilisation and associated costs, particularly in resource-poor settings.[7]

There are, however, different interpretations of the MM definition and a lack of global consensus. Some use the above-described definition but highlight that there is no index condition or dominant disease in the affected individual.[8 9] This is consistent with the WHO's definition emphasising the chronic and long-term nature of conditions and the absence of hierarchy or clustering of diseases.[10] Comorbidity, on the other hand, refers to additional conditions in patients with a primary condition of interest. The distinction between MM and comorbidity is important but not always clear, despite its critical importance for accurate phenotyping, research analyses and in healthcare settings. Additionally, there is variability in the nature and number of chronic diseases included in MM studies and the measurement methods used to assess MM across studies, as highlighted by a recent Delphi study.[11]

Improved life expectancy resulting from global health efforts has led to a rise in MM due to ageing populations and shifting lifestyle risk factors, including obesity and physical inactivity.[1 12–14] MM encompasses various combinations of chronic conditions, with concordant MM sharing origins and treatment requirements, and discordant MM involving unrelated or differently managed conditions.[15] As reviewed by Roomaney *et al*,[16] in low and middle-income countries (LMICs), MM is further complicated by overlapping infectious disease burdens, poverty-related environmental stressors, limited social infrastructure and under-resourced healthcare settings. It is estimated that at least one-third of adults residing in LMICs have multiple chronic conditions,[17] yet the epidemiology of MM in these regions remains relatively unknown.

Despite the substantial growth in MM studies, most have been conducted in high-income countries or among those of European-ancestry, limiting the generalisability of findings.[16 18] Although studies involving diverse ancestries, particularly European and African American (AA) populations, indicate increased MM risk and adverse health outcomes among individuals of African-ancestry,[19 20] the analyses are primarily focused on AAs and often based on small sample sizes. Moreover, most studies examine single disease outcomes or comorbidities with an index disease, leaving the true burden of MM, its epidemiological characteristics and healthcare strategies in African-ancestry populations largely unknown.[21]

This scoping review is timely as the global health community is advocating for diversity and inclusion in research studies, a viewpoint strongly echoed by researchers, healthcare professionals, policymakers and pharma. It is well recognised that African and African-ancestry populations are under-represented and understudied[19] and this review and critical analysis of the published studies are, therefore, important to raise awareness. When global studies report continent-wide prevalence, the projections for African populations are often based on a few small studies on selected communities. They do not reflect the heterogeneity across Africa and in diaspora populations, providing false impressions that could lead to disastrous public health interventions in communities where the data and findings do not apply.

In addition to the limited representation of diverse populations, MM studies face several methodological challenges, including the lack of international consensus on the definition of MM and the frequent use of non-standardised phenotype and laboratory-based measurement methods. These inconsistencies hinder research, comparative assessments and the translation of findings into guidelines and interventions.[22]

This scoping review seeks to identify, evaluate and summarise existing evidence on MM prevalence, patterns, associated factors, and research gaps specific to African-ancestry populations. It provides insight into similar and divergent trends among continental and diaspora African-ancestry individuals, in order to inform the most appropriate and relevant future research priorities.

The following research questions were addressed to guide the scoping review: (1) How many studies have been done on this topic, and what are the geographical locations of the studied populations? (2) Which definitions of MM and what study designs are commonly used in MM studies that include African-ancestry populations? (3) What are the common MM disease clusters among African-ancestry populations living on the continent and in the diaspora? (4) How does MM prevalence differ across sociodemographic characteristics and are these patterns consistent across continental and diasporic African populations?

METHODS

To assess MM within African-ancestry populations, a scoping review methodology was employed rather than a systematic review or meta-analytic approach as a scoping review is more appropriate when aiming to assess an emerging field of literature and identify research gaps.[23] This review began with the establishment of a research team consisting of members with expertise in epidemiology, demography, clinical medicine, genetics and data science research in Africa. Members were from several African countries (Kenya, Nigeria, South Africa, Ghana and Uganda) and advised on the broad study aim and protocol, including search terms, databases and thematic synthesis. A review protocol for this study is not available.

Search strategy and database search

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews.[24] The initial search was implemented in July 2022 and included a comprehensive literature search by one researcher (MK) in consultation with a librarian and field experts. Five electronic databases (PubMed,

Table 1 Search term strategy

	Search themes	MeSH terms
1	Multimorbidity	'comorbidity' OR 'co-morbidity' OR 'multimorbidity' OR 'multi-morbidity' OR 'multiple chronic conditions' OR 'chronic conditions' OR 'chronic disease'
2	African populations	'Africa' OR 'African' OR 'African population' OR 'African ancestry' OR 'African-ancestry'

Scopus, Science Direct, Web of Science and JSTOR) were searched to identify relevant publications on MM in individuals of African-ancestry. The search strategy incorporated a combination of MeSH (Medical Subject Headings) terms and keywords, including 'multimorbidity', 'comorbidity' and 'African population' and their synonyms. The final search terms are listed in table 1 and detailed in online supplemental materials. Search terms relating to MM were derived from previous systematic reviews, and search themes 1 and 2 were combined using the Boolean operator 'AND'. The search was limited to the title and abstract fields only, as a trial search found searching full text reduced the ability to detect relevant papers. Similarly, for this reason, a list of African countries was not included in the search strategy. Although the search terms were consistent across all databases, the search query was tailored to the specific requirements of each database.

The publication time frame was limited to 1 January 2010–31 June 2022, as research on MM has increased significantly since 2010, with approximately 80% of publications published after this date.[18]

Citation management and study selection

After conducting database searches, the search output citations were downloaded in BibTeX format and uploaded to an electronic screening and data management website, Rayyan.[25] The deduplication function was employed to remove duplicates. For the first level of screening, only the title and abstracts of unique entries were reviewed to avoid wasting resources on articles that did not meet the minimum inclusion criteria. Entries were screened independently and blindly by MK and three other reviewers (IK, DMN and GAT), and studies deemed irrelevant were discarded. A third group (GA and MR) assisted with conflict resolution.

Eligibility criteria

The inclusion criteria were studies reporting epidemiological data on MM or comorbidity in individuals of African-ancestry aged 18 years and above from continental Africa and studies including populations of African-ancestry in other global regions (eg, Caribbean, Europe, North America). Studies written in French were included to mitigate missing data from Francophone Africa.

The definition of MM used in this review was based on the Academy of Medical Sciences definition—the

Table 2 Study inclusion/exclusion criteria for the scoping review

	Inclusion	Exclusion
Methodology	► MM defined as a combination of recognised diseases/conditions (eg, self-report or International Classification of Disease 9th revision (ICD-9) or 10th revision (ICD-10) codes)	► MM defined as a combination of symptoms or pre-disease conditions, not defined as ICD-9 or ICD-10 diseases (eg, predisease, frailty, disability and quality of life) ► Transitions or trajectories within a single disease or from one condition into another (eg, cancer progression)
Study design	► Cross-sectional studies ► Longitudinal quantitative studies, including retrospective and prospective cohort studies ► Qualitative studies	► Systematic reviews ► Meta-analyses ► Case studies ► Expert opinion/committee reports
Population	► Adult humans (18+ years) ► African continent ► African-ancestry diaspora	► Infants, children or adolescents (<18 years) ► Animal research
Publication date	► 01 January 2010–31 June 2022	► Prior to 01 January 2010 ► Post 31 June 2022
Publication type	► Peer-reviewed journal articles ► Clinical trials	► Case reports ► Reviews ► Editorials ► Letters
Language	► English ► French	► Other languages

MM, multimorbidity.

coexistence of two or more chronic conditions, which included conditions in the following categories: physical non-communicable disease (NCD) of long duration, such as cardiovascular disease or cancer, a mental health condition of long duration, such as a mood disorder or dementia, or an infectious disease of long duration, such as HIV or hepatitis.[21] The term 'comorbidity' was included, as it has been used interchangeably with MM in the past, although it is now recognised as a distinct concept.[22] As per the Academy of Medical Sciences definition, acute conditions (<6 months) were not included in our definition. We use the term diaspora to specifically refer to populations of African-ancestry who no longer reside on the African continent, contrasting them to continental African populations residing in Africa. Table 2 provides a detailed summary of our inclusion and exclusion criteria.

Studies were excluded when both initial reviewers indicated that they did not meet the eligibility criteria. When their responses were discordant, a third reviewer assessed the abstract, and in some cases, reviewed the full publication before deciding whether the publication met inclusion criteria.

Data extraction and analyses

All citations deemed relevant after title and abstract screening underwent full-text review. Four reviewers (IK, MK, DMN and GAT) independently assessed the full texts (more than one person evaluated some citations), and study characteristics were captured electronically using a template to extract relevant data (online supplemental table S1). Data on MM definition, the approach to measuring MM, the conditions included, and the characteristics of the population under investigation were extracted. Studies were categorised by geographical location, participant ancestry and study design. The chronic conditions assessed to define MM were collected and organised into categories based on the body system affected.[11] Five reviewers independently extracted data and updated the extraction spreadsheet (OA, IK, MK, DMN and GAT). For the extracted variables (online supplemental table S1), the mean and SD, the absolute number or the percentage were recorded as appropriate.

To effectively analyse and interpret the extensive range of diseases evaluated, a categorisation approach was employed. Diseases were grouped into nine broader clusters (table 3). These clusters were derived using a body system approach with nuances to reflect the major global mortality and morbidity disease burdens over the last decade[26] and through consultation with clinicians.

Data summary and synthesis

The data extraction spreadsheet was imported into Microsoft Excel[27] for validation and coding. The data were then exported into R Statistical Computing Tool (V.4.3)[28] for analysis. Descriptive statistics were calculated

Table 3 Disease clusters and the associated definition and diseases

Cluster	Cluster detail	Example conditions
Cancer	Diseases in which abnormal cells divide uncontrollably and can invade nearby tissues.	Breast, lung, colon, cervical, and prostate cancers, Kaposi Sarcoma, etc.
Cardiovascular	Chronic diseases that affect the heart and blood vessels.	Arrhythmias, atrial fibrillation, cardiomyopathy, coronary artery disease, heart failure, hypertension, peripheral artery disease, stroke, etc.
Infectious	Conditions caused by persistent infections; including bacterial, viral or parasitic infections.	Chronic viral hepatitis (hepatitis D, E and G), hepatitis B, hepatitis C, HIV, human papillomavirus (HPV), long-COVID, tuberculosis, etc.
Metabolic	Chronic diseases that affect the body's metabolic system.	Dyslipidaemia, fatty liver disease, metabolic syndrome, obesity, type 2 diabetes mellitus, etc.
Musculoskeletal	Chronic conditions that affect the bones, joints and muscles.	Chronic back pain, osteoarthritis, osteoporosis, rheumatoid arthritis, back syndrome with radiating pain, back syndrome with non-radiating pain, etc.
Neurological	Conditions that affect the brain and nervous system.	Alzheimer's disease, dementia, epilepsy, multiple sclerosis, Parkinson's disease, autistic spectrum disorder, etc.
Psychiatric	Disorders that affect mood, thinking and behaviour.	Attention deficit hyperactivity disorder (ADHD), bipolar, depression, generalised anxiety disorder (GAD), substance use disorders, post-traumatic stress disorder (PTSD), schizophrenia, etc.
Renal	Chronic diseases that affect the kidneys.	Chronic kidney disease, renal failure, end-stage renal disease, etc.
Respiratory	Chronic diseases that affect the lungs.	Asthma, bronchiectasis, chronic obstructive pulmonary disease (COPD), cystic fibrosis, sleep apnoea, pneumonia, etc.

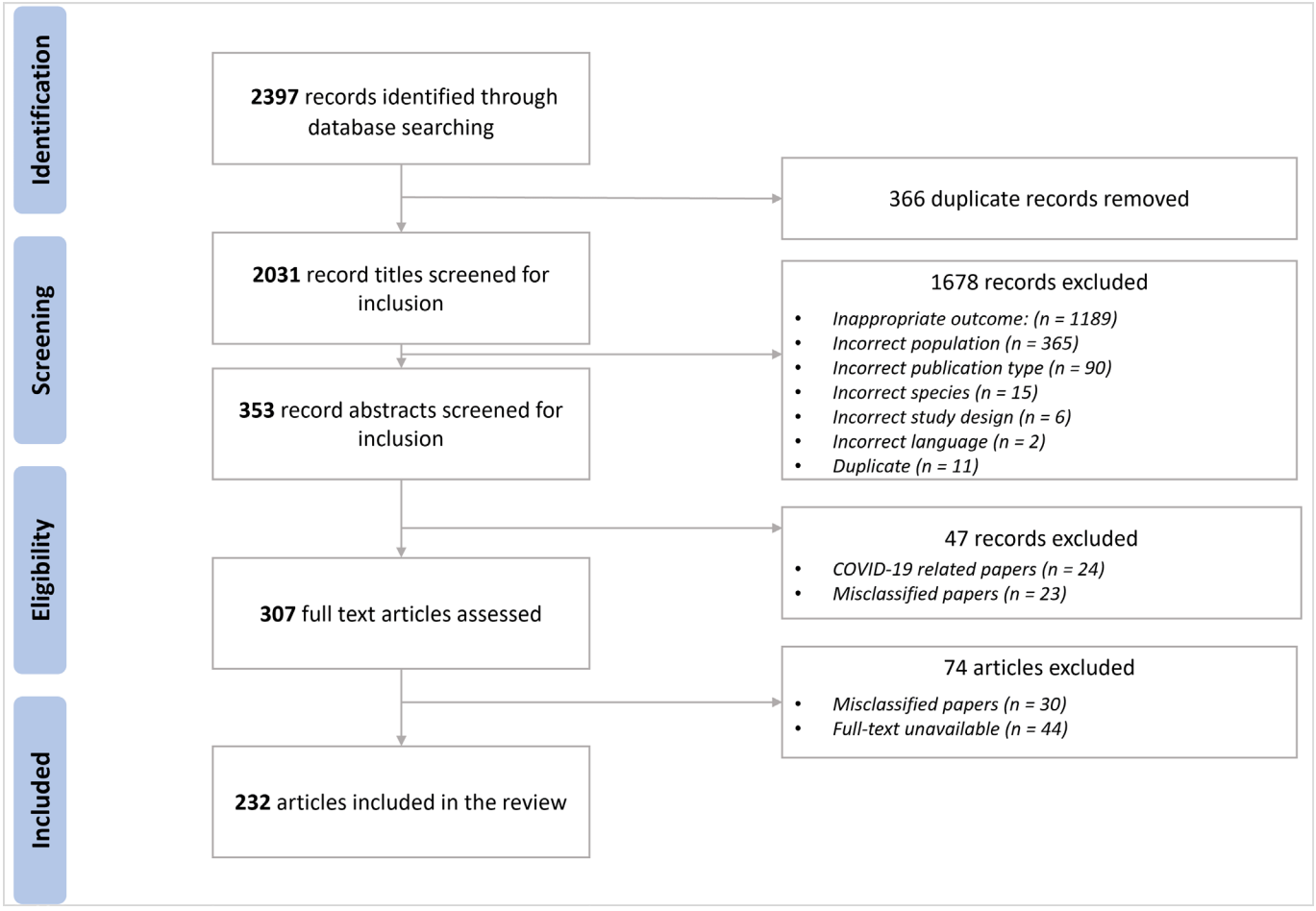

Figure 1 PRISMA-ScR flow diagram of the study selection process. Misclassified papers refer to those that on further analysis did not meet the inclusion criteria, for example, inappropriate outcome (did not meet the criteria for MM), Incorrect publication type (not original research). MM, multimorbidity; PRISMA-ScR, Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews.

to summarise the data, with frequencies and percentages utilised to describe nominal data. An UpSet plot[29] for the two groups of African-ancestry populations was constructed to visualise the disease clusters. A thematic synthesis was used to identify key themes emanating from the included articles.

Patient and public involvement

Patients and the public were not involved in this study. Clinicians known by the authors and working in MM across Africa were invited to comment.

RESULTS

Below we describe the results of our article search, the analyses of the included papers, and the themes identified through content analyses.

Search results

Figure 1 provides an overview of the search results. The initial search yielded 2397 articles, and after removing duplicates (366), 2031 unique records remained. Out of these, 1678 articles were excluded after screening. During the title and abstract screening phase, reviewers had disagreements on the exclusion/inclusion of 15% of the articles, which were resolved through discussion. A total of 353 abstracts were evaluated for eligibility, with 47 articles excluded due to misclassification (n=23) and the exclusion of papers focusing on MM in COVID-19 severity (n=24). 307 full-text articles were assessed, and an additional 74 exclusions were made due to misclassification (n=30) or the full text being unavailable (n=44). The BibTex citation file of analysed articles is available on GitHub (https://github.com/MADIVA-DSI/MM-in-African-ancestry-pops.git).

While multiple criteria led to paper exclusion, only one reason was assigned to each study. The most common exclusion reason was 'inappropriate outcome', indicating the research question did not address MM (as defined by the Academy of Medical Sciences) in African-ancestry populations, the focus of this review. These studies often examined comorbidity or broader chronic disease prevalence, prevention, and treatment strategies.

Study characteristics

The number of publications increased over the past decade from 5 in 2010 to 11 in 2022 (figure 2). While

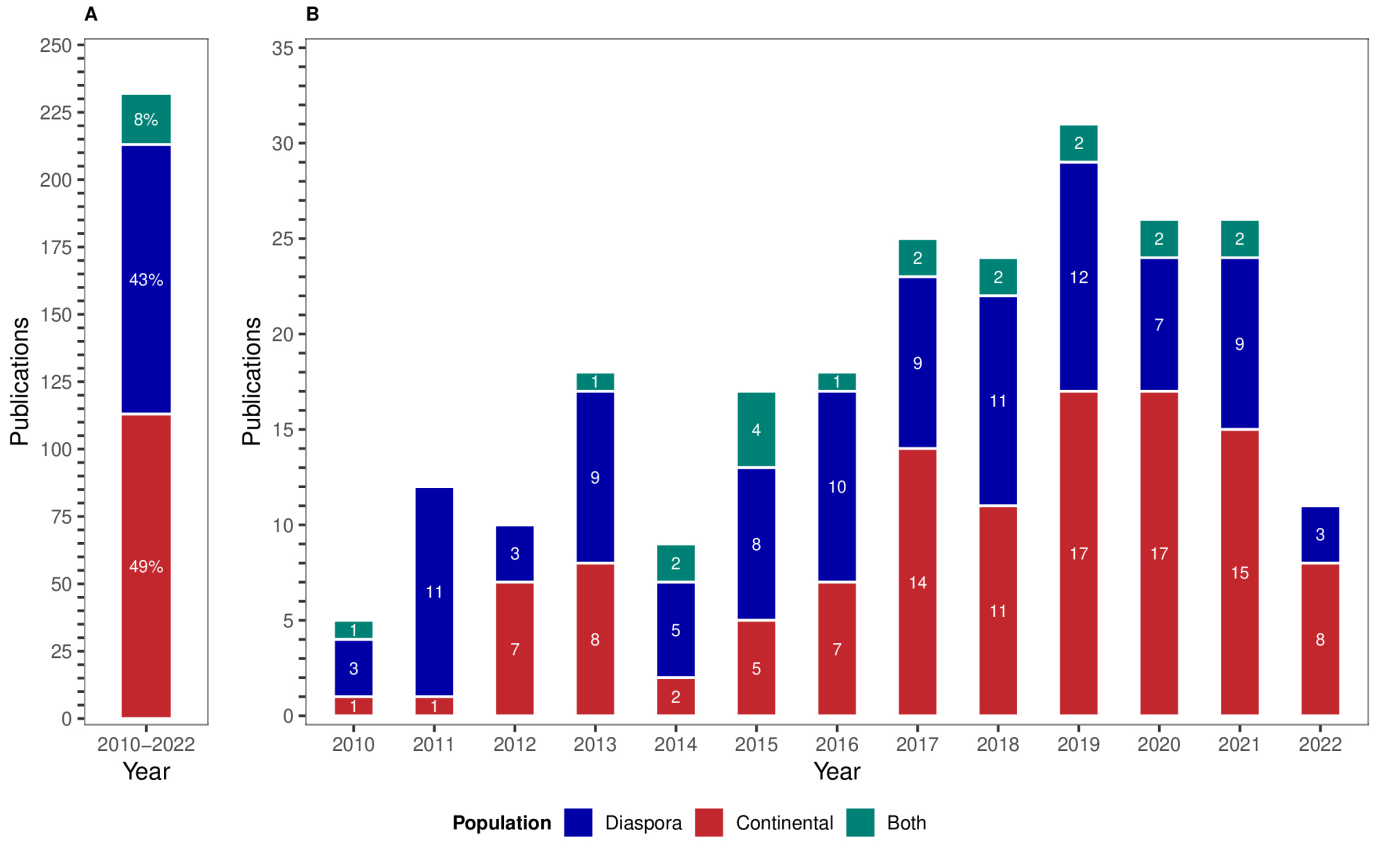

Figure 2 Number of publications by African-ancestry population geographic origin. (A) Proportion of publications by population group over the full assessed timeframe (January 2010–June 2022) (n=232). (B) Proportion of papers by African-ancestry population origin per year.

there was a decline in papers addressing MM in African-ancestry populations from 2020 to 2022, the upward trend persisted when including papers related to MM and COVID-19. During this period, we identified 23 publications associating MM as a risk factor for severe COVID-19 in African populations (2020: 8 studies, 2021: 10 studies, 2022: 5 studies).

Geographical location of African-ancestry populations studied

Figure 2 shows the number of publications per year by African ancestry population, distinguishing between those from the diaspora and the continent. The data show there were slightly more publications among continental populations (49%, n=113) than diaspora (43%, n=100), with 8% conducted in multiple countries involving both populations (n=19).

Figure 3 illustrates the global distribution of studies investigating MM in African-ancestry populations. Figure 3A presents the overall coverage of papers, while figure 3B displays the proportion of papers originating from different regions. Among the 113 papers focused on continental populations, the majority (55%) were conducted in Southern Africa (n=61), followed by East Africa (22%, n=24) and West Africa (15%, n=17). Less than 5% of studies included multiple African regions (n=3).

Diaspora studies were concentrated in North America (95%, n=94), specifically among AA, who were often part of diverse ancestry studies examining the influence of race on MM-related health outcomes. In Europe, diaspora studies typically involved recently migrated individuals (born in Africa or first-generation migrants).

In continental and diaspora groups, epidemiological studies focused on determining disease clusters and prevalence in specific populations. The most common study designs were cross-sectional (67%, n=155) and longitudinal (31%, n=73). Incidence measurement of MM was primarily observed in diaspora studies. Around two-thirds of the studies were conducted in hospital settings, including primary care and clinical settings, while 36% involved the general population. In the diaspora, secondary analysis of large cohorts or databases was prominent (64% of diaspora studies), while continental studies often utilised prospective hospital-based cohorts (32%). Continental studies had smaller sample sizes (median (range)=990 (14 to 417 786)) compared with diaspora studies (median (range)=2022 (20 to 3 739 528)).

Studies examined various risk factors for MM, including sociodemographic variables like age, sex and socioeconomic status (SES). Research conducted in North America was particularly interested in comparing

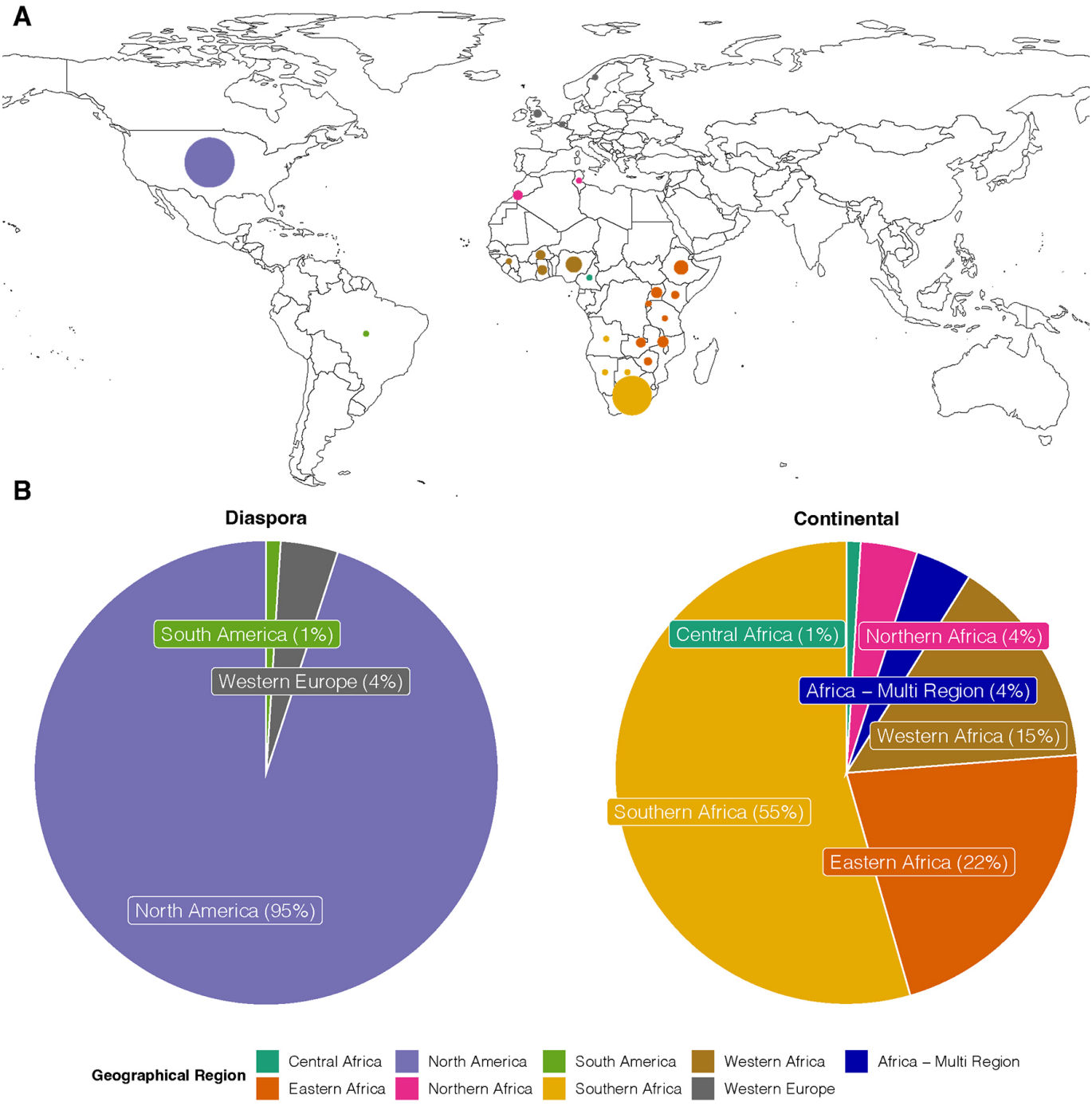

Figure 3 (A) Global location of participants from 213 multimorbidity studies in populations of African-ancestry. Studies including representation from both continental and diaspora populations (n=19) are not shown. (B) Distribution of papers in diaspora (n=100) and continental (n=113) African-ancestry populations by geographical region (n=213). Regional distribution is based on the five regions of Africa described by the United Nations Statistics Division (online supplemental table S2). 'Africa' includes countries from multiple regions.

MM between what they identified as race/ethnic groups. Some studies explored the impact of MM on mortality, morbidity, hospital resource utilisation, polypharmacy, adverse drug reactions and care integration.

Disease and MM ascertainment

We considered a study to have a clear definition of MM when it was stated in the objectives, methodology or discussion of the study. Our literature search found that most studies lacked clear MM definitions and showed considerable variability in disease inclusion. The terms MM and comorbidity were often used interchangeably, particularly in earlier studies.

Studies commonly employed disease counts to identify MM, but diseases included varied widely from 2 to over 200. Many studies used an author-developed disease list or, in some cases, a tool used to determine MM, such as

the Charlson Comorbidity Index.[30 31] These lists were available in 105 continental studies and 93 diaspora studies. In studies employing electronic health records or chart review, patient disease was identified mostly by ICD9 or ICD10 codes, based on clinical diagnosis. In smaller cohort studies, primarily in Africa, disease was determined through self-reporting or proxy variables such as medication use, or when clinical biomarkers were outside normal ranges. Although more cost-effective and feasible in resource-constrained research environments, the latter, particularly self-reporting, can introduce biases like recall errors and misclassification, potentially skewing the accuracy and prevalence of diagnoses.

Figure 4 illustrates the frequency of MM combinations in continental and diaspora studies. The most studied cluster in continental studies was cardiovascular-infectious-metabolic diseases (n=16). In the diaspora, psychiatric conditions (represented by more than one condition but grouped for simplicity) were most frequent (n=11), followed by cardiovascular-metabolic (n=10) and

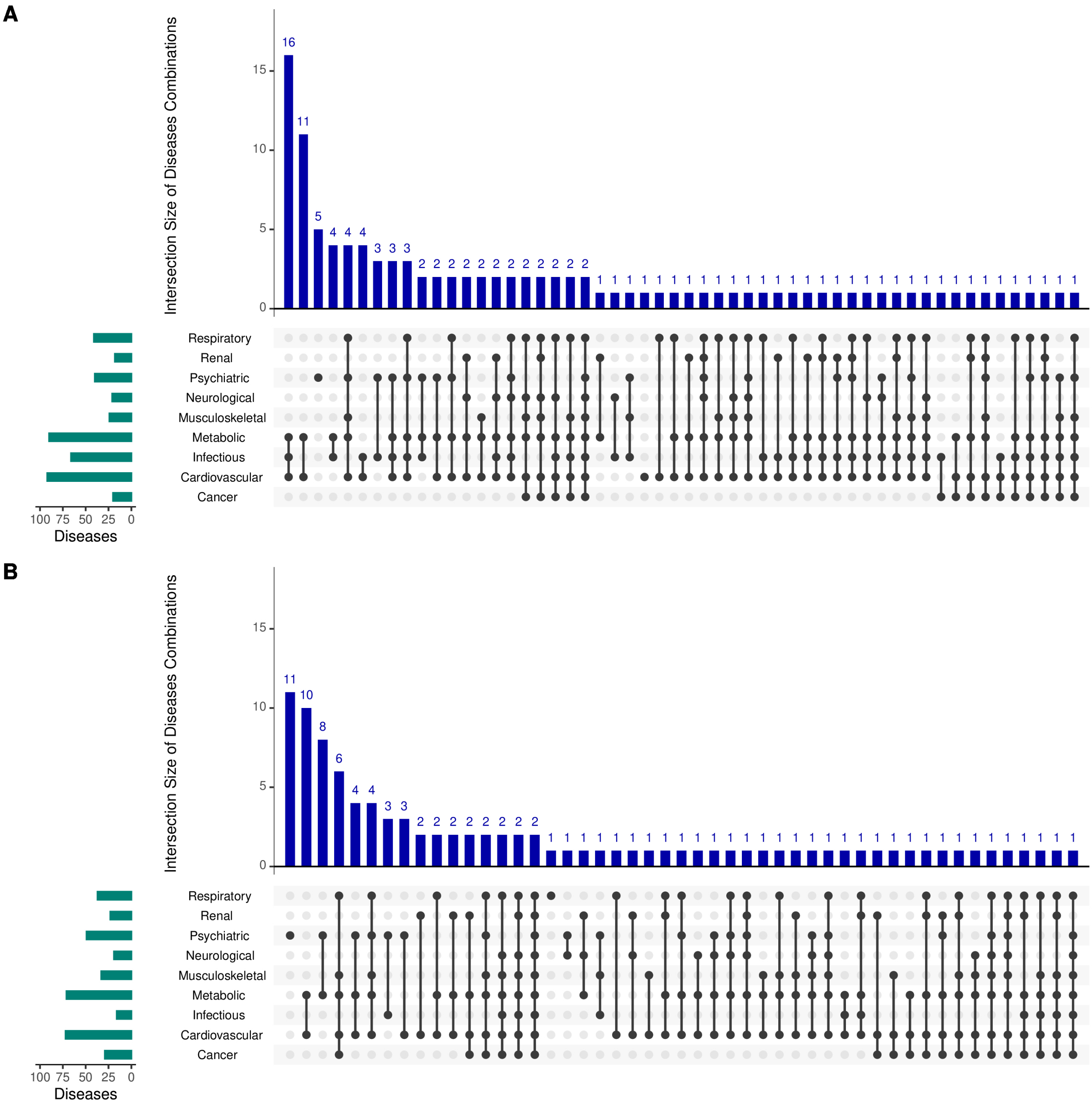

Figure 4 Distribution of disease cluster combinations (cancer, cardiovascular, infectious, metabolic, musculoskeletal, neurological, psychiatric, renal and respiratory) across 213 studies, stratified by (A) continental (113 studies) and (B) diaspora African-ancestry populations (100 studies). upSet plots generated using RStudio.

metabolic-psychiatric (n=8) clusters. Cardiovascular (eg, hypertension) and metabolic diseases (eg, diabetes) were the most widely included in both groups. In continental populations, 80% of studies assessed cardiovascular (n=92) or metabolic (n=90) diseases, while in the diaspora, at least 70% focused on these conditions (cardiovascular (73%, n=72); or metabolic (72%, n=71)) (see figure 4).

In contrast, the diaspora and continental studies differ greatly in their assessment of infectious diseases (predominantly HIV, Tuberculosis (TB) and malaria). Infectious diseases were more prevalent in continental studies (58%) compared with the diaspora (16%), whereas renal diseases, cancer, neurological and musculoskeletal disorders were under-represented in both groups.

Sociodemographic characteristics such as age, sex, household income and SES were examined in relation to MM prevalence and cumulative disease counts in studies involving continental and diaspora populations. Older individuals, particularly those aged 60 years and above, were found to have a higher risk of MM in both continental and diaspora populations. However, among continental populations, MM was also observed in relatively younger adults, approximately 45 years and below.[32–35]

Differences in MM by sex were identified, with women often showing a higher prevalence of MM, particularly in cardiovascular-metabolic clusters.[35–41] Low SES and income were generally associated with MM, but there were some population-specific differences. In the diaspora, lower SES was linked to higher MM prevalence and increased disease count,[42–44] while in continental studies, the impact of SES was variable. Lower SES was associated with higher MM[45–50] ; but differences were observed. For example, studies in South Africa,[51 52] Burkina Faso[41] and Ghana[53] found that higher income was associated with concordant cardiometabolic MM, while lower incomes were associated with infectious disease-related MM.[46 48] In both populations, some studies revealed no effect of SES.[32 54–56] Ancestry effects in diaspora studies varied depending on recent migrations to Europe or AA in North America. In the USA, AA ethnicity consistently posed a risk factor for MM across most MM clusters.[19 57–61] One study assessing MM risk among men in a racially balanced and economically homogenous cohort in the USA found no difference in MM risk between AA and whites when in the same social environment.[62] Conversely, studies on recent migrations indicated lower MM prevalence among African-ancestry migrant populations.[63]

Studies also identified significant geographic variations in MM prevalence and patterns.[40 64] Using a population-based survey in South Africa, Akindele *et al*[40] observed distinct provincial differences, with lower rates of multiple chronic lifestyle diseases among residents of Limpopo, and Wong *et al*[64] demonstrated the intricate geospatial complexities of MM disease clusters within a rural community in Kwa-Zulu Natal.

The impact of behavioural risk factors, such as smoking, alcohol consumption and physical activity, on MM and treatment outcomes was assessed in some studies. When assessed, physical activity was noted as being largely negatively associated with MM, particularly within cardiometabolic MM, due to its impact on cardiometabolic risk factors, such as obesity and waist circumference.[65] Alcohol and substance use were largely controlled for or considered as disorders themselves in most studies and, therefore, their effect on MM was not well described.[32 46] However, assessment of studies examining alcohol use and smoking behaviour showed conflicting effects. For example, smoking and alcohol consumption was positively associated with multimorbid patients suffering from post-traumatic stress disorder in South Africa[66] but negatively associated with multimorbid women newly diagnosed with breast cancer; however, these bivariate associations did not persist in multinomial models.[67]

Thematic analysis

An in-depth review of included papers was used to extract recurring themes from the data. These themes were further reviewed and refined in consultation with the authorship team. While the quality of individual studies was not assessed in this review, caution was exercised in comparing the studies due to their diverse approaches in exploring MM in different settings. The themes below should not be viewed in isolation from one another, as they overlap somewhat and need to be integrated when considering solutions. First, we describe the limitations in terms of non-standardised terminology and data collection, a feature common across many disciplines, but we then highlight the heterogeneity among the combinations of chronic conditions that have been included in MM, but that in both African and diaspora studies the cardiovascular and metabolic clusters are most commonly studied.

Heterogeneity and inconsistency in terminology and methodological approaches

Similar to previous systematic reviews,[16 33 68] our findings highlight substantial heterogeneity in the terminology and methodological approaches used in the identified studies. This variability is not surprising given the relatively recent emergence of MM as a concept in healthcare research and the ongoing debates surrounding its definition and measurement.[11] Most studies used cross-sectional designs to estimate MM prevalence, while fewer employed longitudinal designs, possibly due to convenient and cost-effective participant recruitment. Continental African studies, with smaller sample sizes and reliance on self-reported data, may lead to biased prevalence and outcome estimates.

MM can be measured by counting the number of morbidities or using an MM index that considers both the number and severity of diseases, but the latter may be limited by data requirements.[68] Variability in MM measurement is influenced by national health priorities and data availability. Furthermore, debates around disease clusters and groupings persist, with some advocating conditions

on the same spectrum or targeting the same organ system collectively rather than separately,[69] particularly for well-managed conditions like hypertension.[70]

Dominance of cardiovascular-metabolic disease clusters

Distinct regional variation in disease clusters was observed. Continental populations exhibited a co-occurrence of cardiometabolic clusters and chronic infectious diseases, while the diaspora showed a dominance of psychiatric conditions, often combined with cardiometabolic diseases. This aligns with previous research highlighting depression and cardiometabolic disorders as commonly observed MM clusters.[16 71–73] Nonetheless, it is important to acknowledge that the available data suggest that the prevalence of condition clusters is strongly influenced by the context and population in which the research is conducted. Thus, when electronic health records were available, or when utilising large international cohorts, the number of diseases assessed to determine MM were much greater than smaller hospital or community-based cross-sectional cohorts.

In LMICs, such as those in Africa, chronic infectious illnesses like HIV/AIDS and TB are more prevalent. This is partially attributable to the longer life expectancies made possible by antiretroviral therapy, and the subsequent increase in susceptibility to NCDs at older ages.[21] Additionally, the cardiometabolic-infectious cluster may be exacerbated by the adverse effects of antiretroviral therapies on cardiovascular health.[74–76]

The dominance of specific clusters limits the understanding of the prevalence of concordant and discordant conditions and their associations with other diseases and health outcomes. However, one continental study found similar prevalence rates for concordant and discordant MM (approximately 12% each),[41] suggesting their comparable significance. Another study examining the association between physical MM and depression in six LMICs, including Ghana and South Africa, demonstrated that physical MM significantly increases the odds of depression, with a dose-dependent relationship as the number of diseases increases.[77]

Diverse effects of age, sex and SES across populations

Factors associated with MM risk in African-ancestry populations, such as age, sex, education, SES and comorbidities, were examined. Similar to studies conducted in high-income countries, older age, female sex and lower SES were identified as risk factors for MM. However, nuances were observes, highlighting the importance of context-specific research.

Older age consistently showed a higher prevalence of MM in both populations; however, in continental populations, infectious disease burden contributed to younger adults being diagnosed with MM.[32 35 64] Women of all ages were at increased risk of MM, potentially influenced by biological differences or social factors such as living and working environments, care-seeking behaviour and income inequalities.[21] The relationship between sex and MM varies depending on the specific diseases considered; as suggested in previous research. We noted men to be more at risk when evaluating psychiatric disorders such as substance abuse disorders. Low SES, typically measured by education, income, occupation or a composite of these, was identified as a risk factor for MM, with some disease-group intricacies. Also, SES may influence other factors such as sedentary lifestyles, health awareness and access to healthcare.[48 54] Furthermore, disentangling social context and ethnicity in MM risk among diaspora populations remains challenging.

Diaspora studies often include race as a covariate to compare MM prevalence among different racial groups. However, variations in study methodology and terminology make it challenging to synthesise and interpret interethnic differences in MM risk. It remains unclear whether genuine disparities exist beyond differences in diagnosis or survival rates. USA-based diaspora studies suggested significant differences in MM prevalence and health outcomes across ethnicities, with AAs often having a higher prevalence. For example, Mochari-Greenberger and Mosca,[78] reported higher readmission rates among hypertensive Hispanic and AA patients with comorbid diabetes than Whites. Clements *et al*[79] noted that AA had increased odds of most multiple chronic condition combinations compared with Whites as well as and an increased risk of mortality even when adjusting for disease combinations. However, psychiatric disorders, such as depression and anxiety, were noted as being more prevalent in European-ancestry populations,[19 80] likely due to under-reporting or underdiagnosing, particularly among men who may be more reticent to seek help from mental health services, compared with non-AA. A recent migration study in the Netherlands revealed that ethnic inequalities in MM persisted when adjusting for the lower SES of ethnic minority groups.[81]

Integrating care to address complex health outcomes associated with MM

The literature consistently showed that MM is associated with higher levels of health resource utilisation (eg, medications, primary care, emergency services) and adverse health outcomes (eg, mortality, hospitalisations and reduced quality of life), irrespective of disease clusters. Several studies, including those by Aparasu *et al*,[82] Bhagavathula *et al*[50] and Simakoloyi *et al*,[83] support these findings. Although patients with MM require frequent healthcare access, social determinants such as SES, geographic location and healthcare system factors can hinder access. Perry *et al*[84] described these factors as significant barriers to quality patient-centred care for older multimorbid AA men, despite their higher MM burden.

Multiple studies have highlighted the limitations of traditional healthcare systems that focus on single diseases and have recommended a shift towards an integrated care model (ICM) where practitioners from various specialties collaborate in managing patients with multiple conditions.[64 85–87] Wong *et al*[64] emphasised the

need for integrated management after observing high rates of uncontrolled hypertension (57.5%), diabetes (70.4%) and untreated TB in a rural South African population despite successful HIV management—78% of their cohort had undetectable HIV-1 RNA viral loads. However, implementing ICM poses challenges due to the increased complexity and time required for treating unrelated conditions. Limited evidence exists on the effective management of multiple conditions, particularly in resource-constrained settings like Africa. Nonetheless, Khabala *et al*[87] noted that ICM could improve the flexibility of care delivery and reduce clinician workload among patients with mixed chronic conditions in Kenya, and, in South Africa, ICM reduced HIV stigma in health facilities due to the non-segregation of patients,[88] and with consolidated guidelines, patient education materials and information systems, this could improve treatment and care for MM patients.[89 90] Implementing ICM in South Africa is estimated to have minimal additional costs, approximately USD1.06 (SD:0.33) per patient visit, over the current mean cost of USD4.94 (SD:0.70).[91]

Insufficient data exist to quantify the burden of NCDs in health facilities in sub-Saharan Africa (SSA) and their readiness to manage the growing NCD epidemic. Some studies, mainly in South Africa, have investigated the possibility of expanding HIV clinics to address cardiovascular diseases like hypertension and diabetes.[92] Despite the potential of integrated care to improve patient care and decrease individual and healthcare system costs, a significant gap in clinic and hospital staff training remains a barrier to effective implementation.[93–96]

Challenges in statistical analysis approaches

Studies primarily employed univariate descriptive analysis, while logistic regression was the preferred method for assessing the relationship between MM and exposure variables or MM's impact on an outcome. While simple modelling techniques offer interpretability advantages,[97] there is room for additional analyses through advanced machine learning (ML) and robust computational approaches. These approaches could reduce dependence on hand crafting by domain experts and scalability for the growing size of data and the number of variables.[97 98] Few studies reported model goodness-of-fit assessment or variable selection approaches to refine multivariate models. Using the best subset of variables that contribute to the outcome of interest can lead to more useful and informative models.

Despite the advantages of imputing missing data and available software for implementation, few studies addressed missingness. There was limited assessment of the spatial and temporal distribution of coexisting diseases, which could provide valuable information on MM hotspots and associated factors. Such studies can also offer insights into the future MM population profile and the likely change in MM prevalence.

DISCUSSION

This scoping review identified 232 relevant articles and used thematic analysis to address the aim of the review; to identify, evaluate and summarise the available published evidence on MM in African-ancestry populations and identify research gaps and future recommendations. The themes are often interdependent and should not be viewed in isolation.

Overview of included articles

The review revealed significant heterogeneity in MM terminology, methodology and disease measurement. While cardiovascular-metabolic disease clusters were dominant, regional variations were observed. Risk factors for MM in African-ancestry populations were similar to those found in European populations and high-income countries, including older age, female sex and lower SES,[99 100] with important exceptions. Therefore, the nuanced differences, highlighting the need for context-specific research and the identification of major gaps, need to be considered in the interpretation of MM in these populations.

Research gaps and recommendations for future research

Based on the included literature, we identified six research gaps and below we describe how they could be mitigated. These interconnected areas describe crucial interventions that would advance evidence-based research on MM and thereby potentially enhance patient care and health outcomes.

Paucity of data globally (sample size and complexity of data)

Limited data availability and a lack of large-scale epidemiological studies on MM, particularly in African-ancestry populations, hinder our understanding of MM prevalence and patterns in diverse populations. Future studies should increase sample size and undertake longitudinal population-based studies to better understand MM's longitudinal trajectory. Additionally, including genetic data in these studies can offer valuable insights into MM causation and the interplay between genetic and environmental factors. Gathering comprehensive data will improve our understanding of MM and facilitate more targeted interventions.

Lack of representation (many African countries and ethnic groups have no published data)

African-ancestry populations are under-represented in the MM literature, both within and outside of Africa. Furthermore, other socioeconomic and health factors impact MM prevalence in groups and marginalised communities. More research is needed in African-ancestry individuals in Central and South America as well as recent and growing migrant populations in Europe and elsewhere, who may have unique MM experiences. The Research on Obesity and Diabetes among African Migrants (RODAM) study highlights the influence of migration on MM risk factors in people originating from Ghana and emphasises the importance of understanding

the sociodemographic, cultural, and healthcare contexts of African-ancestry migrants for a comprehensive understanding of MM.[101]

Underrepresented disease areas (health priority mismatch)

On assessing the Global Burden of Disease (GBD) morbidity estimates both globally and within SSA, a mismatch between health priorities and the diseases investigated is evident (GBD morbidity estimates are found in online supplemental figure S1). Cardiometabolic and infectious diseases are the leading disease burdens in SAA,[26] which aligns with the focus of continental studies. This alignment is also true for cardiovascular diseases globally. However, mental health conditions among adults younger than 50 years and cancer among individuals older than 50 also account for a significant health burden in SSA, yet these clusters, particularly cancer, appear to be rarely assessed in continental MM studies. Additionally, as life expectancy rises in Africa, musculoskeletal and neurological diseases associated with the elderly will become more prevalent and should be investigated.

Moreover, there is a paucity of evidence on how clusters of conditions develop and change over time, making it challenging to predict how disease burdens might change within an individual's life, and to identify the best interventions and care approaches. Key factors to consider when assessing long-term health in SSA include not only infectious and NCD but also the combined effects of childhood malnutrition, and high rates of maternal HIV infection.[64]

Lack of standardised study designs and data collection protocols

The absence of standardised definitions and measurements and uncertainties about the applicability and validity of MM assessment tools in African-ancestry populations must be addressed. Moving forward, it is crucial to establish standardised criteria and methods to ensure consistent and accurate identification of MM across populations and regions while recognising the importance of context-specific assessments. This should be applied both to study communities that remain unexplored and to all the different disease clusters.

Need to leverage additional data analysis approaches

In addition to traditional statistical approaches to epidemiological research, recent studies beyond African populations have utilised emerging ML techniques to understand the complex nature of MM.[102 103] These ML techniques can be categorised into pairwise, probabilistic, factorisation and temporal methods.[102] Pairwise methods are relatively simple but limited in capturing complex interactions and multiple co-occurring diseases common in ageing populations. Probabilistic methods, such as Hidden Markov Models, provide an overall view of disease relationships. Factorisation methods, like non-negative matrix factorisation, offer interpretability but may struggle with encoding suppressiveness among diseases. Advanced ML techniques, including deep learning, show promise in unravelling the complexity of MM.[102] These techniques can infer co-occurring diseases, assess data trustworthiness, identify patterns, analyse longitudinal aspects, integrate multiple data sources and provide interpretable insights.[104–106] Future studies should also consider employing ML and prediction modelling approaches, building on successful collaborations between domain experts and ML researchers.

Invest in translational research

To comprehensively understand the interplay between MM, the healthcare system and the cultural/religious context, diverse perspectives must be considered. The gaps described above, therefore, need to be addressed in the specific milieu of the study communities and adapted to suit the context, while striving to generate interoperable data fit for use in comparative studies. Despite it being crucial to explore patients' experiences, caregivers' challenges and clinicians' perspectives regarding MM in African-ancestry populations, there is currently limited research in these domains. Additionally, cultural and religious beliefs will likely influence perceptions and behaviours related to MM. Assessing the financial and social costs of MM is also necessary. This knowledge can inform policy shifts, treatment approaches and clinical guidelines, leading to improved diagnosis, risk prediction, and treatment strategies.

Strengths and limitations of this scoping review

This scoping review is the first to summarise the literature on MM prevalence and patterns in African-ancestry populations worldwide. Dividing studies into continental and diaspora African-ancestry populations revealed important differences. By involving a multidisciplinary team of epidemiologists, demographers, clinicians, geneticists and data scientists, with representation from multiple African countries, we optimised the inclusion of relevant studies and ensured cultural sensitivity during the writing process. However, limitations such as limiting our search strategy to title and abstract only, and assessing open access texts or those available through institutional logins may have resulted in some literature being excluded. The literature did not lend itself to a systematic review or meta-analysis and, therefore, we did not perform quality assessment on the publications using standardised tools. Nevertheless, our results emphasise the necessity for additional research on MM in African-ancestry populations and the development of context-specific guidelines for prevention and management across different geographic locations.

CONCLUSION

In reviewing the literature on MM in populations with African-ancestry, we observed distinct disease clusters and varying effects of social determinants of health on MM. We provide strong evidence that Black Americans (also referred to as AAs), the most widely studied

African-ancestry group, are not a good proxy for all Africans. Furthermore, continental African regions and populations are highly diverse in their health profiles, exposures and behaviours. To address MM effectively in African-ancestry populations, we identified six research gaps: limited data availability, inadequate representation, under-represented disease clusters, absence of standardised study designs and data collection protocols, the need for innovative data analysis approaches and the need for more translational research. Additionally, considering the complexities observed among populations, it is crucial to account for location, resources and environmental context when developing interventions to mitigate the burden of MM, especially in African-ancestry populations.

Author affiliations
[1]Division of Human Genetics, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa
[2]Sydney Brenner Institute for Molecular Bioscience, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa
[3]African Population and Health Research Center (APHRC), APHRC Campus, Nairobi, Kenya
[4]IBM Research Africa, Nairobi, Kenya
[5]School of Electrical and Information Engineering, Faculty of Engineering and the Built Environment, University of the Witwatersrand, Johannesburg, South Africa
[6]Department of Women's and Children's Health, Karolinska Institute, Stockholm, Sweden

Twitter Michelle Kamp @michelleukamp and Girmaw Abebe Tadesse @girmaw_abebe

Acknowledgements We would like to thank the broader MADIVA research hub for their input into study design and interpretation.

Contributors MR, GA, SH and MK conceived the study and participated in the design of the study. MK, OA, IK, DMN, GAT, KA and SI undertook the literature review process. MK, OA and PTM undertook data analysis and visualisation. MK drafted the manuscript with input from OA. MR is acting as guarantor. All authors read and approved the final manuscript.

Funding Research reported in this publication was supported by the Fogarty International Center of the National Institutes of Health under Award Number U54TW012077. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This is a review of already published material; therefore, no ethics approval needed.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available. Data sharing is not applicable as no datasets were generated and/or analysed for this study. The BibTex file containing the articles included in this review is available on GitHub (https://github.com/MADIVA-DSI/MM-in-African-ancestry-pops.git).

ORCID iDs
Michelle Kamp http://orcid.org/0000-0002-4334-6883
Okechinyere Achilonu http://orcid.org/0000-0003-2911-0011
Isaac Kisiangani http://orcid.org/0000-0002-1107-4334
Daniel Maina Nderitu http://orcid.org/0000-0001-9800-2431
Phelelani Thokozani Mpangase http://orcid.org/0000-0001-8280-8940
Girmaw Abebe Tadesse http://orcid.org/0000-0002-2648-9102
Samuel Iddi http://orcid.org/0000-0002-2366-2774
Scott Hazelhurst http://orcid.org/0000-0002-0581-149X
Gershim Asiki http://orcid.org/0000-0002-9966-1153
Michèle Ramsay http://orcid.org/0000-0002-4156-4801

REFERENCES

1 Navickas R, Petric V-K, Feigl AB, *et al*. Multimorbidity: what do we know? What should we do. *J Comorb* 2016;6:4–11.
2 Nunes BP, Flores TR, Mielke GI, *et al*. Multimorbidity and mortality in older adults: a systematic review and meta-analysis. *Arch Gerontol Geriatr* 2016;67:130–8.
3 Fortin M, Lapointe L, Hudon C, *et al*. Multimorbidity and quality of life in primary care: a systematic review. *Health Qual Life Outcomes* 2004;2:51.
4 Cheng GJ, Wagner AL, O'Shea BQ, *et al*. Multimorbidity and mental health trajectories among middle-aged and older U.S. adults during the COVID-19 pandemic: longitudinal findings from the COVID-19 coping study. *Innov Aging* 2022;6:igac047.
5 Fortin M, Bravo G, Hudon C, *et al*. Psychological distress and multimorbidity in primary care. *Ann Fam Med* 2006;4:417–22.
6 Calderón-Larrañaga A, Poblador-Plou B, González-Rubio F, *et al*. Multimorbidity, polypharmacy, referrals, and adverse drug events: are we doing things well. *Br J Gen Pract* 2012;62:e821–6.
7 Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. *Arch Intern Med* 2002;162:2269–76.
8 Salisbury C, Johnson L, Purdy S, *et al*. Epidemiology and impact of multimorbidity in primary care: a retrospective cohort study. *Br J Gen Pract* 2011;61:e12–21.
9 Boyd CM, Fortin M. Future of multimorbidity research: how should understanding of multimorbidity inform health system design *Public Health Rev* 2010;32:451–74.
10 World Health Organization. *Multimorbidity: Technical Series on Safer Primary Care*. Geneva, Switzerland, 2016.
11 Ho ISS, Azcoaga-Lorenzo A, Akbari A, *et al*. Measuring multimorbidity in research: Delphi consensus study. *BMJ Med* 2022;1:e000247.
12 Skou ST, Mair FS, Fortin M, *et al*. Multimorbidity. *Nat Rev Dis Primers* 2022;8:48.
13 Hajat C, Stein E. The global burden of multiple chronic conditions: a narrative review. *Preventive Medicine Reports* 2018;12:284–93.
14 Marengoni A, Angleman S, Melis R, *et al*. Aging with multimorbidity: a systematic review of the literature. *Ageing Res Rev* 2011;10:430–9.
15 Barnett K, Mercer SW, Norbury M, *et al*. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012;380:37–43.
16 Roomaney RA, Wyk BV, Wyk V-V. Decolonising multimorbidity? Research gaps in low and middle-income countries. *Pan Afr Med J* 2022;41:140.
17 Nguyen H, Manolova G, Daskalopoulou C, *et al*. Prevalence of multimorbidity in community settings: a systematic review and meta-analysis of observational studies. *J Comorb* 2019;9:2235042X1987093.

18 Xu X, Mishra GD, Jones M. Mapping the global research landscape and knowledge gaps on multimorbidity: a bibliometric study. *J Glob Health* 2017;7:10414.
19 Alshakhs M, Jackson B, Ikponmwosa D, *et al*. Multimorbidity patterns across race/ethnicity as stratified by age and obesity. *Sci Rep* 2022;12:1–16.
20 Kalgotra P, Sharda R, Croff JM. Examining multimorbidity differences across racial groups: a network analysis of electronic medical records. *Sci Rep* 2020;10:13538.
21 Academy of Medical Sciences. *Multimorbidity: a priority for global health research*. London, UK, 2018.
22 Johnston MC, Crilly M, Black C, *et al*. Defining and measuring multimorbidity: a systematic review of systematic reviews. *Eur J Public Health* 2019;29:182–9.
23 Peters MDJ, Godfrey CM, Khalil H, *et al*. Guidance for conducting systematic scoping reviews. *Int J Evid Based Healthc* 2015;13:141–6.
24 Tricco AC, Lillie E, Zarin W, *et al*. PRISMA extension for scoping reviews (PRISMA-SCR): checklist and explanation. *Ann Intern Med* 2018;169:467–73.
25 Ouzzani M, Hammady H, Fedorowicz Z, *et al*. Rayyan-a web and mobile app for systematic reviews. *Syst Rev* 2016;5:210.
26 Institute for Health Metrics and Evaluation (IHME). GBD compare data visualization. 2020. Available: https://www.healthdata.org/data-visualization/gbd-compare [Accessed 04 May 2023].
27 Microsoft Corporation. *Microsoft Excel*. 2018.
28 R Core Team. R: A language and environment for statistical computing. 2021. Available: https://www.r-project.org/
29 Lex A, Gehlenborg N, Strobelt H, *et al*. Upset: visualization of intersecting SETS. *IEEE Trans Vis Comput Graph* 2014;20:1983–92.
30 Charlson ME, Pompei P, Ales KL, *et al*. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.
31 Sundararajan V, Henderson T, Perry C, *et al*. New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. *J Clin Epidemiol* 2004;57:1288–94.
32 Chang AY, Gómez-Olivé FX, Payne C, *et al*. Chronic multimorbidity among older adults in rural South Africa. *BMJ Glob Health* 2019;4:e001386.
33 Sharman M, Bachmann M. Prevalence and health effects of communicable and non-communicable disease comorbidity in rural Kwazulu-natal, South Africa. *Trop Med Int Health* 2019;24:1198–207.
34 Hopkins KL, Hlongwane KE, Otwombe K, *et al*. The substantial burden of non-communicable diseases and HIV-comorbidity amongst adults: screening results from an integrated HIV testing services clinic for adults in Soweto, South Africa. *EClinicalMedicine* 2021;38:101015.
35 Wade AN, Payne CF, Berkman L, *et al*. Multimorbidity and mortality in an older, rural black South African population cohort with high prevalence of HIV findings from the HAALSI study. *BMJ Open* 2021;11:e047777.
36 Boake M, Mash R. Diabetes in the Western Cape, South Africa: a secondary analysis of the diabetes cascade database 2015 - 2020. *Prim Care Diabetes* 2022;16:555–61.
37 Ntiyani N, Letamo G, Keetile M. Prevalence of and factors associated with hypertension, diabetes, stroke and heart attack multimorbidity in Botswana: evidence from STEPS 2014 survey. *PLoS One* 2022;17:e0265722.
38 Gaziano TA, Pandya A, Steyn K, *et al*. Comparative assessment of absolute cardiovascular disease risk characterization from non-laboratory-based risk assessment in South African populations. *BMC Med* 2013;11.
39 Mohamed SF, Haregu TN, Uthman OA, *et al*. Multimorbidity from chronic conditions among adults in urban slums: the AWI-Gen Nairobi site study findings. *Glob Heart* 2021;16.
40 Akindele MO, Useh U. Multimorbidity of chronic diseases of lifestyle among South African adults. *Pan Afr Med J* 2021;38:332.
41 Odland ML, Payne C, Witham MD, *et al*. Epidemiology of multimorbidity in conditions of extreme poverty: a population-based study of older adults in rural Burkina Faso. *BMJ Glob Health* 2020;5:e002096.
42 Cook JA, Burke-Miller JK, Steigman PJ, *et al*. Prevalence, comorbidity, and correlates of psychiatric and substance use disorders and associations with HIV risk behaviors in a multisite cohort of women living with HIV. *AIDS Behav* 2018;22:3141–54.
43 Vennu V, Abdulrahman TA, Alenazi AM, *et al*. Associations between social determinants and the presence of chronic diseases: data from the osteoarthritis initiative. *BMC Public Health* 2020;20:1323.
44 Diaz E, Poblador-Pou B, Gimeno-Feliu L-A, *et al*. Multimorbidity and its patterns according to immigrant origin. A nationwide register-based study in Norway. *PLoS One* 2015;10:e0145233.
45 Mthoko NFN, Pazvakawambwa L, Leonhardt M, *et al*. Physical comorbidity among patients attending mental health services at Windhoek central hospital, Namibia. *Pan Afr Med J* 2022;41:270.
46 Peltzer K. Tuberculosis non-communicable disease comorbidity and multimorbidity in public primary care patients in South Africa. *Afr J Prim Health Care Fam Med* 2018;10.
47 Weimann A, Dai D, Oni T. A cross-sectional and spatial analysis of the prevalence of multimorbidity and its association with socioeconomic disadvantage in South Africa: a comparison between 2008 and 2012. *Soc Sci Med* 2016;163:144–56.
48 Ataguba JEO. Inequalities in multimorbidity in South Africa. *Int J Equity Health* 2013;12:64.
49 Chikezie UE, Otakpor AN, Kuteyi OB, *et al*. Depression among people living with human immunodeficiency virus infection/acquired immunodeficiency syndrome in Benin city, Nigeria: a comparative study. *Niger J Clin Pract* 2013;16:238–42.
50 Bhagavathula AS, Seid MA, Adane A, *et al*. Prevalence and determinants of multimorbidity, polypharmacy, and potentially inappropriate medication use in the older outpatients: findings from Euroageism H2020 ESR7 project in Ethiopia. *Pharmaceuticals (Basel)* 2021;14:844.
51 Mutyambizi C, Chola L, Groot W, *et al*. The extent and determinants of diabetes and cardiovascular disease comorbidity in South Africa - results from the South African national health and nutrition examination survey (SANHANES-1). *BMC Public Health* 2017;17:745.
52 Alaba O, Chola L. The social determinants of multimorbidity in South Africa. *Int J Equity Health* 2013;12:63.
53 Kunna R, San Sebastian M, Stewart Williams J. Measurement and decomposition of socioeconomic inequality in single and Multimorbidity in older adults in China and Ghana: results from the WHO study on global ageing and adult health (SAGE). *Int J Equity Health* 2017;16:79.
54 Nimako BA, Baiden F, Sackey SO, *et al*. Multimorbidity of chronic diseases among adult patients presenting to an inner-city clinic in Ghana. *Global Health* 2013;9:61.
55 Zelnick LR, Katz R, Young BA, *et al*. Echocardiographic measures and estimated GFR decline among African Americans: the Jackson heart study. *Am J Kidney Dis* 2017;70:199–206.
56 Gabriel A, Zare H, Jones W, *et al*. Evaluating depressive symptoms among low-socioeconomic-status African American women aged 40 to 75 years with uncontrolled hypertension: a secondary analysis of a randomized clinical trial. *JAMA Psychiatry* 2021;78:426–32.
57 Dibato JE, Montvida O, Zaccardi F, *et al*. Association of cardiometabolic multimorbidity and depression with cardiovascular events in early-onset adult type 2 diabetes: a multiethnic study in the U.S. *Diabetes Care* 2021;44:231–9.
58 Erving CL, Frazier C. The association between multiple chronic conditions and depressive symptoms: Intersectional distinctions by race. *J Health Soc Behav* 2021;62:599–617.
59 Roth GA, Abate D, Abate KH, *et al*. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the global burden of disease study 2017. *Lancet* 2018;392:1736–88.
60 Yang J, Ju X, Liu F, *et al*. Prediction for the risk of multiple chronic conditions among working population in the United States with machine learning models. *IEEE Open J Eng Med Biol* 2021;2:291–8.
61 Heckman BD, Merrill JC, Anderson T. Race, psychiatric comorbidity, and headache characteristics in patients in headache subspecialty treatment clinics. *Ethn Health* 2013;18:34–52.
62 Thorpe RJ Jr, Bell CN, Kennedy-Hendricks A, *et al*. Disentangling race and social context in understanding disparities in chronic conditions among men. *J Urban Health* 2015;92:83–92.
63 Marzà-Florensa A, Boateng D, Agyemang C, *et al*. Multimorbidity among migrant and non-migrant Ghanaians: the RODAM study. *Int J Public Health* 2021;66:1604056.
64 Wong EB, Olivier S, Gunda R, *et al*. Convergence of infectious and non-communicable disease epidemics in rural South Africa: a cross-sectional, population-based multimorbidity study. *Lancet Glob Health* 2021;9:e967–76.
65 Romano E, Ma R, Vancampfort D, *et al*. Multimorbidity and obesity in older adults from six Low- and middle-income countries. *Preventive Medicine* 2021;153:106816.
66 Pengpid S, Peltzer K. Mental morbidity and its associations with socio-behavioural factors and chronic conditions in rural

middle- and older-aged adults in South Africa. *J Psychol Afr* 2020;30:257–63.
67 Ayeni OA, Norris SA, Joffe M, *et al*. The multimorbidity profile of South African women newly diagnosed with breast cancer. *Int J Cancer* 2020;147:361–74.
68 Stirland LE, González-Saavedra L, Mullin DS, *et al*. Measuring multimorbidity beyond counting diseases: systematic review of community and population studies and guide to index choice. *BMJ* 2020;368:m160.
69 Fortin M, Stewart M, Poitras M-E, *et al*. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. *Ann Fam Med* 2012;10:142–51.
70 Lee ES, Koh HL, Ho EQ-Y, *et al*. Systematic review on the instruments used for measuring the association of the level of multimorbidity and clinically important outcomes. *BMJ Open* 2021;11:e041219.
71 Sinnige J, Braspenning J, Schellevis F, *et al*. The prevalence of disease clusters in older adults with multiple chronic diseases--a systematic literature review. *PLoS One* 2013;8:e79641.
72 Violan C, Foguet-Boreu Q, Flores-Mateo G, *et al*. Prevalence, determinants and patterns of multimorbidity in primary care: a systematic review of observational studies. *PLoS One* 2014;9:e102149.
73 Prados-Torres A, Calderón-Larrañaga A, Hancco-Saavedra J, *et al*. Multimorbidity patterns: a systematic review. *J Clin Epidemiol* 2014;67:254–66.
74 Gottlieb S. Antiretroviral therapy increases risk of heart attack. *BMJ* 2003;327:1186–0.
75 Jarwani B. Cardiovascular disease and antiretroviral therapy. *J Glob Infect Dis* 2019;11:91–2.
76 Dubé MP, Lipshultz SE, Fichtenbaum CJ, *et al*. Effects of HIV infection and antiretroviral therapy on the heart and vasculature. *Circulation* 2008;118:e36–40.
77 Smith L, Shin JI, Butler L, *et al*. Physical multimorbidity and depression: a mediation analysis of influential factors among 34,129 adults aged ≥50 years from low- and middle-income countries. *Depress Anxiety* 2022;39:376–86.
78 Mochari-Greenberger H, Mosca L. Differential outcomes by race and ethnicity in patients with coronary heart disease: a contemporary review. *Curr Cardiovasc Risk Rep* 2015;9:20.
79 Clements JM, West BT, Yaker Z, *et al*. Disparities in diabetes-related multiple chronic conditions and mortality: the influence of race. *Diabetes Res Clin Pract* 2020;159:107984.
80 Breslau J, Aguilar-Gaxiola S, Kendler KS, *et al*. Specifying race-ethnic differences in risk for psychiatric disorder in a USA national sample. *Psychol Med* 2006;36:57–68.
81 Verest WJGM, Galenkamp H, Spek B, *et al*. Do ethnic inequalities in multimorbidity reflect ethnic differences in socioeconomic status? the HELIUS study. *Eur J Public Health* 2019;29:687–93.
82 Aparasu RR, Mort JR, Brandt H. Polypharmacy trends in office visits by the elderly in the United States, 1990 and 2000. *Res Social Adm Pharm* 2005;1:446–59.
83 Simakoloyi N, Erasmus E, van Hoving DJ. The characteristics of geriatric patients managed within the resuscitation unit of a district-level emergency centre in Cape town. *Afr J Emerg Med* 2022;12:39–43.
84 Perry RG, Mitchell JA, Hawkins J. The role of age and multimorbidity in shaping older African American men's experiences with patient–provider communication. *Geriatrics (Basel)* 2018;3:74.
85 Myers B, Joska JA, Lund C, *et al*. Patient preferences for the integration of mental health counseling and chronic disease care in South Africa. *Patient Prefer Adherence* 2018;12:1797–803.
86 Segafredo G, Kapur A, Robbiati C, *et al*. Integrating TB and non-communicable diseases services: pilot experience of screening for diabetes and hypertension in patients with tuberculosis in Luanda, Angola. *PLoS One* 2019;14:e0218052.
87 Khabala KB, Edwards JK, Baruani B, *et al*. Medication adherence clubs: a potential solution to managing large numbers of stable patients with multiple chronic diseases in informal settlements. *Trop Med Int Health* 2015;20:1265–70.
88 Ameh S, D'Ambruoso L, Gómez-Olivé FX, *et al*. Paradox of HIV stigma in an integrated chronic disease care in rural South Africa: viewpoints of service users and providers. *PLoS One* 2020;15:e0236270.
89 Matima R, Murphy K, Levitt NS, *et al*. A qualitative study on the experiences and perspectives of public sector patients in Cape town in managing the workload of demands of HIV and type 2 diabetes multimorbidity. *PLoS One* 2018;13:e0194191.
90 Godongwana M, De Wet-Billings N, Milovanovic M. The comorbidity of HIV, hypertension and diabetes: a qualitative study exploring the challenges faced by healthcare providers and patients in selected urban and rural health facilities where the ICDM model is implemented in South Africa. *BMC Health Serv Res* 2021;21:647.
91 Lebina L, Kawonga M, Oni T, *et al*. The cost and cost implications of implementing the integrated chronic disease management model in South Africa. *PLoS One* 2020;15:e0235429.
92 Mayosi BM, Lawn JE, van Niekerk A, *et al*. Health in South Africa: changes and challenges since 2009. *The Lancet* 2012;380:2029–43.
93 Adjei KK, Kikuchi K, Owusu-Agyei S, *et al*. Women's overall satisfaction with health facility delivery services in Ghana: a mixed-methods study. *Trop Med Health* 2019;47:41.
94 Lebina L, Oni T, Alaba OA, *et al*. A mixed methods approach to exploring the moderating factors of implementation fidelity of the integrated chronic disease management model in South Africa. *BMC Health Serv Res* 2020;20:617.
95 Peck CC, Goulet J-P, Lobbezoo F, *et al*. Expanding the taxonomy of the diagnostic criteria for temporomandibular disorders. *J Oral Rehabil* 2014;41:2–23.
96 Peck R, Mghamba J, Vanobberghen F, *et al*. Preparedness of Tanzanian health facilities for outpatient primary care of hypertension and diabetes: a cross-sectional survey. *Lancet Global Health* 2014;2:e285–92.
97 Ley C, Martin RK, Pareek A, *et al*. Machine learning and conventional statistics: making sense of the differences. *Knee Surg Sports Traumatol Arthrosc* 2022;30:753–7.
98 Cruz JA, Wishart DS. Applications of machine learning in cancer prediction and prognosis. *Cancer Inform* 2006;2:117693510600200.
99 Bezerra de Souza DL, Oliveras-Fabregas A, Espelt A, *et al*. Multimorbidity and its associated factors among adults aged 50 and over: a cross-sectional study in 17 European countries. *PLoS One* 2021;16:e0246623.
100 Ofori-Asenso R, Chin KL, Curtis AJ, *et al*. Recent patterns of multimorbidity among older adults in high-income countries. *Popul Health Manag* 2019;22:127–37.
101 Asogwa OA, Boateng D, Marzà-Florensa A, *et al*. Multimorbidity of non-communicable diseases in low-income and middle-income countries: a systematic review and meta-analysis. *BMJ Open* 2022;12:e049133.
102 Hassaine A, Salimi-Khorshidi G, Canoy D, *et al*. Untangling the complexity of multimorbidity with machine learning. *Mech Ageing Dev* 2020;190:111325.
103 Uddin S, Wang S, Lu H, *et al*. Comorbidity and multimorbidity prediction of major chronic diseases using machine learning and network analytics. *Expert Systems with Applications* 2022;205:117761.
104 Koedel U, Schuetze C, Fischer P, *et al*. Challenges in the evaluation of observational data trustworthiness from a data producers viewpoint (FAIR+). *Front Environ Sci* 2022;9:737.
105 Wang H, Tang J, Wu M, *et al*. Application of machine learning missing data imputation techniques in clinical decision making: taking the discharge assessment of patients with spontaneous supratentorial intracerebral hemorrhage as an example. *BMC Med Inform Decis Mak* 2022;22:1–14.
106 Polessa Paula D, Barbosa Aguiar O, Pruner Marques L, *et al*. Comparing machine learning algorithms for multimorbidity prediction: an example from the Elsa-Brasil study. *PLoS One* 2022;17:e0275619.