Multimorbidity of cardiometabolic diseases and effectiveness of integrated healthcare system response in sub-Saharan Africa

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COLOFON

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Multimorbidity of Cardiometabolic Diseases and Effectiveness of Integrated Healthcare System Response in sub-Saharan Africa

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ABBREVIATIONS

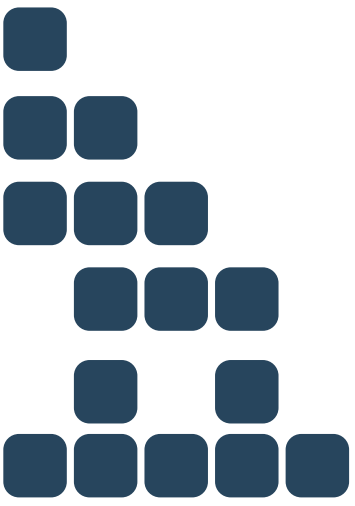
aBIC	Adjusted Bayesian Information Criterion
ADL	Activities of daily living
DBP	Diastolic blood pressure
ACGCMS	Adjusted Clinical Groups Case-Mix System
aOR	Adjusted odds ratio
APHRC	African Population and Health Research Center
aPR	Adjusted prevalence ratio
BMI	Body mass index
BP	Blood Pressure
CAIC	Akaike information criterion
CCI	Charlson Comorbidity Index
CHVs	Community health volunteers
CI	Confidence interval
CINAHL	Nursing and Allied Health Literature
CIRS	Cumulative Illness Rating Scale
CMEs	Continuous medical education
CVDs	Cardiovascular diseases
DiD	Difference-in-difference
EA	Enumeration areas
ECG	Electrocardiogram
EPOC	Effective Practice and Organization of Care
FBS	Fasting blood sugar
FGD	Focus group discussions
GBDS	Burden of Disease Study
GRADE	Grading of Recommendation, Assessment, Development, and Evaluation
HbA1c	Glycated haemoglobin
HCA	Hierarchical cluster analysis
HIC	High-income countries
HMIS	Health Management Information System
HRQoL	Health-related quality of life
ICT	Information, communication and technology
IPTW	Inverse Probability of Treatment Weighting using Propensity Scores
KIIs	Key informant interviews
LCA	Latent class analysis
LFK	Luis Furuya Kanamori
LMIC	Low- and middle-income countries

MD	Mean difference
MPA	Moderate-to-vigorous physical activity
NCDs	Non-communicable diseases
NGOs	Non-governmental organisations
NHIF	National Health Insurance Fund
PRISMA	Preferred Reporting Items for Systematic Reviews
PROSPERO	Prospective Register for Systematic Reviews
PS	Propensity Score
QoL	Quality of life
RBS	Random Blood Sugar
RCTs	Randomised controlled trials
RMIC	Rainbow Model of Integrated Care
SAGE	Survey of ageing and adult health
SARAM	Service Availability and Readiness Assessment Mapping
SBP	Systolic blood pressure
SES	Socio-economic status
SSA	sub-Saharan Africa
STEPS	STEPwise approach to non-communicable disease risk factor surveillance
UHC	Universal health coverage
VPA	Vigorous physical activity
WHO	World Health Organization
WHO-PEN	World Health Organization Package of Essential Non-communicable Diseases
WHOQOL	World Health Organization Quality of Life

This thesis is dedicated to my late dad
MAURICE OTIENO JASUNGA, who incidentally inspired me to study multimorbidity.
Your experiences in navigating the healthcare system remind me to never give up.
My heart remains dedicated to this cause in honor of you and your fighting spirit!

“The sum of our conditions is not a burden but a reflection of our capacity for resilience”

Anonymous



1

General introduction

Cardiometabolic multimorbidity

Cardiometabolic diseases are a group of preventable chronic conditions that include type 2 diabetes, dyslipidemia, hypertension and cardiovascular diseases (CVDs) (1). These conditions share four main lifestyle risk factors: physical inactivity, harmful alcohol use, unhealthy diet, and tobacco use (2). People with cardiometabolic diseases often suffer multiple conditions concurrently (3). This phenomenon referred to as *cardiometabolic multimorbidity* (4). Multimorbidity is a distinct concept from comorbidity. The former refers to the coexistence of a chronic illness in the context of an index disease (5). Cardiometabolic multimorbidity can be either concordant (similar) or discordant (dissimilar) with respect to pathophysiology, or disease management, and can either support or compete with the care for cardiometabolic diseases (6). Examples of coexisting chronic conditions with similar pathology, commonly known as concordant multimorbidity include hypertension, type 2 diabetes and CVDs (6). Common examples of discordant cardiometabolic multimorbidities include the coexistence of cardiometabolic diseases and conditions such as depression, chronic lung diseases, and musculoskeletal disorders (7-9).

Cardiometabolic multimorbidity is a major global public health challenge (10-12). Three in every five deaths occurring globally are due to cardiometabolic diseases (13). Three-quarters of cardiometabolic disease-related mortalities in the world occur in low and middle-income countries (LMICs) (14-16). Cardiometabolic multimorbidity significantly contributes to higher excess mortality in LMICs than expected from each cardiometabolic disease separately (14-16). The care pathways for patients with multimorbidity are complex and demanding for the healthcare system in sub-Saharan Africa (SSA) due to in part the co-existing burden of infectious diseases (17). People living with multimorbidities require a holistic continuum of care to attain optimal health outcomes (18). However, the existing care pathways in SSA have routinely focused on a single disease approach, leading to inadequate care (19). Furthermore, the management of multimorbidity is complex due to polypharmacy and high treatment burden (20). Despite these challenges, evidence of the burden and health system response to cardiometabolic multimorbidity in SSA is still scarce.

While previous studies identify multimorbidity as a major public health problem (14-16), a huge body of evidence is limited to non-specific forms of multimorbidities, with little emphasis on specific chronic diseases that tend to cluster together (21). Without strong empirical evidence on the burden and health system response to chronic diseases that cluster together such as cardiometabolic diseases, health service providers, and policy-makers will have limited guidance on preventive and therapeutic interventions. Evidence of the burden of cardiometabolic multimorbidity is crucial for supporting the development of robust user-centred chronic care models that are responsive to the healthcare needs of people living with cardiometabolic multimorbidity in SSA.

Patterns and clusters of cardiometabolic multimorbidity in sub-Saharan Africa

Although there is a growing recognition of the rising burden of multimorbidity in SSA, most studies have focused on single diseases (5). The majority of studies on multimorbidity are from HIC (22). Studies conducted in the United States, Germany, the United Kingdom, and Spain, for instance, show that the prevalence of cardiometabolic multimorbidity ranges from 34% to 82% (23-26). One study conducted in South Africa found that three-quarters of persons aged 15 years and above with type 2 diabetes also suffered from CVDs (27). Another study evaluating cardiometabolic multimorbidity among adults aged 18 years and above in Nigeria, Ghana, and Kenya found that 71% of the patients with type 2 diabetes also suffered from hypertension (28). The competing public health priorities and limited resources point to the need for evidence on the patterns and clusters of cardiometabolic multimorbidity in SSA to inform the design of targeted interventions.

The vast majority of studies on the burden of cardiometabolic multimorbidity globally are not only limited by the complexities in the conceptualization and operationalization of multimorbidity including the absolute number of disease combinations but also the geographical scope**.** Two main types of measurements of the burden of multimorbidity have been previously used in literature: simple count of chronic diseases, and indices estimated from the weights of multimorbidities (29). Although simple counts remain the most commonly used method to assess the burden of multimorbidity, other methods that include the Charlson Comorbidity Index (CCI) (30), the Cumulative Illness Rating Scale (CIRS) (31), and the Johns Hopkins University Adjusted Clinical Groups Case-Mix System (ACGCMS) (32) exist. The CCI, CIRS, and ACGCMS have been previously used in studies examining the burden of multimorbidity, however, they are more complex than simple disease count methods since they were originally developed to estimate mortality risks and healthcare costs rather than the prevalence of multimorbidity (33). Despite its simplicity and ease of use, the simple disease count method provides inadequate information on the most common clusters of chronic diseases (17). Identification of the clusters of chronic diseases is a pragmatic approach that recognizes the epidemiological peculiarities of multimorbidities and fosters a greater understanding of the burden of the most common disease combinations.

Risk factors for cardiometabolic multimorbidity in sub-Saharan Africa

As postulated by the theories of population growth, the previous century was characterized by rapid global epidemiological and demographic transitions (34, 35). This implies an unprecedented increase in life expectancy and prolonged exposure to “lifestyle risks” for cardiometabolic multimorbidities (36-38). Although epidemiological and demographic transitions remain a global health problem, the patterns, determinants,

and rapidity vary significantly across SSA countries (39). According to the 2019 Global Burden of Disease Study (GBDS), the variability in the demographic and epidemiologic transitions is attributable to four main risk factors: unhealthy diets, harmful alcohol consumption, tobacco use, and physical inactivity (40). However, the findings from the 2019 GBDS suggest inter-country disparities in the changes in behavioural risk factors for cardiometabolic multimorbidity in SSA (40).

Compared to HICs, SSA is the world's fastest-urbanizing region (41). In 2018, a total of 472 million people lived in urban areas in SSA (42). The rapid urbanization in SSA and globalization have led to dietary transitions and increased exposure to unhealthy lifestyles including unhealthy diets, harmful alcohol consumption, tobacco use, and physical inactivity (43-45). Additionally, socioeconomic disparities in the behavioural risk factors for cardiometabolic multimorbidity are common phenomena at both national and sub-national levels. Studies from HICs show that people with low socio-economic status (SES) when compared to the non-poor are more likely than those with high SES to report all the behavioural risk factors for cardiometabolic multimorbidity (22, 46, 47). Similarly, evidence from SSA shows that behavioural risk factors such as smoking, harmful alcohol use, and inadequate consumption of fruits and vegetables are more likely to be reported by people with low SES while overweight and obesity are prevalent among people with both low and high SES (48-51). There is a huge variation in the distribution of behavioural risk profiles across the socio-economic strata within and between countries in SSA (40). The onset of cardiometabolic multimorbidities can be prevented by reducing exposure to lifestyle risk factors (52, 53). To do this, evidence on the most common combinations of lifestyle risk factors for cardiometabolic multimorbidity is needed to prioritize targeted interventions (54).

Association of cardiometabolic multimorbidity clusters with healthcare utilization, functional disability and quality of life

Planning health system capacity and response to multimorbidity requires rigorous knowledge of the frequency of healthcare utilization for different disease clusters. With the global increase in the proportion of older persons and the increasing prevalence of cardiometabolic multimorbidity, there have been fears regarding the likelihood of reversing the gains made on healthy life expectancy (55). Functional disability is an umbrella term for bodily function problems including persistent limitation in daily life activities and disengagement from real-life situations (56). Estimation of the burden of multimorbidity on functional disability is crucial in providing evidence for improving quality of life and long-term care (57).

A study conducted in Sweden found that adults aged 78 years and above with cardiometabolic multimorbidity spent more than three-quarters of their remaining years with disability (58). A different study reported severe functional disability being

significantly higher in South Africa and Ghana than in China and Mexico (59). The decline in quality of life among people living with cardiometabolic multimorbidity may be exacerbated by the high treatment burden and fragmented care in addition to polypharmacy and psychosocial factors such as poverty and weak social networks (60). Previous studies in LMICs show a positive linear association between multimorbidity and frequency of outpatient visits, hospitalization and quality of life (61-65). However, the chronic disease counts used to measure multimorbidity in these studies lack adequate information on the specific disease clusters to guide the health system response (33, 66). Understanding the burden of specific multimorbidity clusters on healthcare utilization and quality of life is important for optimising resources to accommodate the unique needs of people living with cardiometabolic multimorbidity.

Effectiveness of integrated care for cardiometabolic multimorbidity in sub-Saharan Africa

Integrated chronic disease management refers to *"a set of patient-centred and multidisciplinary care activities coordinated by two or more collaborating service providers within or across the healthcare sector including community and social environments"* (67). Many of the current integrated chronic care models have adopted Wagner's chronic care model (68). The Wagner's chronic care model outlines important elements required for effective chronic disease management including patient self-management support, community resources, clinical information systems, delivery system redesign, decision support, and community resources (68). Patient self-management support and community resources aim to make chronic care more patient-centred by enabling patients to control their own health and improve their access to health care; while the other elements are focused on restructuring health care delivery to better meet patients' needs during chronic disease management (69). Most of Wagner's chronic care models have been tested in HICs (70, 71). Thus, the operational descriptions of well-functioning chronic care models in resource-constrained settings that are appropriate for SSA countries are currently unavailable (72).

A systematic review conducted a decade after the introduction of Wagner's chronic care model concept revealed that its implementation improved health outcomes (73). However, evidence supporting chronic care models has been largely inferred from studies focusing on single chronic diseases. Furthermore, most of these studies have been conducted in HICs (74-76). Consequently, there is an enduring knowledge gap on what a functioning health system entails for the management of cardiometabolic multimorbidity in the context of SSA. Due to the variations in the health system's structures and socio-economic development across countries, there is never a "one size fits all" solution to strengthening the capacity of primary health care to manage cardiometabolic multimorbidity (77-79). It is therefore critical to evaluate the

applicability of Wagner's chronic care model in SSA and unearth the components that are suitable for integrated management of cardiometabolic multimorbidity in SSA.

Readiness to provide integrated management of cardiometabolic multimorbidity in sub-Saharan Africa

The management of multimorbidity is complex and demanding for both patients and the healthcare system in SSA (80). The Rainbow model of integrated care framework for monitoring and evaluation of the health system performance highlights the domains that are intrinsic to the integrated management of multimorbidity (81). These include systems integration, professional integration and clinical integration (81). However, the extent to which countries in SSA apply the elements of care integration remains unknown. Health systems in most SSA countries have been designed to manage infectious diseases rather than non-communicable diseases (NCDs). Thus, primary care for chronic diseases may not be sufficiently equipped to handle the rising burden of multimorbidity (82).

The development of sustainable care models for cardiometabolic multimorbidity requires an understanding of the care integration capacity of the health system. A scoping review of the care integration capacity of 47 African countries revealed that none of the countries were ready to provide integrated care in primary care settings (83). In addition, less than a third of the countries had national guidelines for management of NCDs and only 10% (less than 5 countries) reported the availability of all the essential drugs for chronic diseases in primary care facilities (83). Thus, narrowing the gap between the unmet needs for integrated management of chronic diseases and unresponsive healthcare systems in SSA is imperative. Understanding the gaps in the provision of integrated care in the SSA context may inform the design of care models that are contextually appropriate.

Effect of multimorbidity on self-management and patient-led peer support group interventions for cardiometabolic diseases in sub-Saharan Africa

People with multimorbidity perform complex self-care activities (84-86). Home-based self-management is a form of care in which patients monitor their conditions at home (87-90). This includes home-based measurements of blood pressure and fasting blood sugar (91). The blood pressure or sugar measurements can be recorded by the patient and shown to the health professional during a regular visit (92). Alternatively, the recordings can be directly transmitted electronically to the clinic using mobile applications (93). Patient support groups thus provide an environment that would encourage better self-management and have been shown in HIC to improve the management of some chronic diseases (94).

Self-management support and peer support groups not only provide a foundation for navigating self-care activities but also improves patient autonomy (84). Indeed self-management support may reduce hospital admissions, healthcare costs and mortality (55, 95, 96). Previous studies have shown that home-based self-measurement of blood pressure increased patients' awareness (97), decreased therapeutic inertia, and eventually reduced BP (92). Despite these promising approaches, most self-management and patient support group interventions have not led to a radical improvement in existing care for cardiometabolic diseases and most have only been tested as add-ons to usual clinic-based care, thereby increasing the bureaucratic burden on healthcare providers and patients.

Conceptual framework

This thesis adopts and extends the WHO's theoretical framework on the social determinants of multimorbidity (98), as shown in Figure 1. The framework recognizes the complex pathways through which macro, meso, and micro-level factors contribute to the burden of multimorbidity. This framework has also been used in previous studies investigating the risk factors for multimorbidity in LMICs (99-101). The primary outcome was modified to include clustering of obesity, hypocholesteremia, hypertension, type 2 diabetes, heart attack, angina, stroke (concordant multimorbidity) and unrelated conditions such as arthritis, asthma, chronic lung disease, cataracts, and depression (discordant multimorbidity). The secondary outcomes included functional disability, quality of life and healthcare utilization patterns such as frequency of outpatient visits and hospitalization.

The conceptual framework depicts three key categories of determinants of cardiometabolic multimorbidity: distal, intermediate, and proximal. The distal determinants are expressed through the macro-level factors including urbanization, and legislative and policy environment such as governance and financial structures. The intermediate determinants comprise the meso and micro-level factors. The meso-level factors consist of chronic care models such as healthcare organization, delivery system design, decision support systems, clinical information systems, self-management support, and community resources. The micro-level factors comprise socioeconomic characteristics such as education, employment, income and wealth.

The proximal determinants of cardiometabolic multimorbidity comprise the micro-level factors including behaviours such as unhealthy diet, physical inactivity, harmful alcohol use, and smoking, and biological risks such as age and sex. The framework shows a bidirectional association of cardiometabolic multimorbidity with functional disability and quality of life. Indeed previous studies have shown that on the one hand, multimorbidity may impair the instrumental activities of daily living and quality of life (102, 103). On the other hand, functional impairment and poor quality of life may impact

the severity and burden of multimorbidity, leading to a vicious circle (104). However, the circle may be modified by the patient's characteristics such as socioeconomic status, lifestyle risks and other underlying factors such as the policy environment and the organization of healthcare services (60). Thus, the effects of macro, meso, and micro-level factors emerge as central to assessing the determinants and the burden of cardiometabolic multimorbidity in SSA.

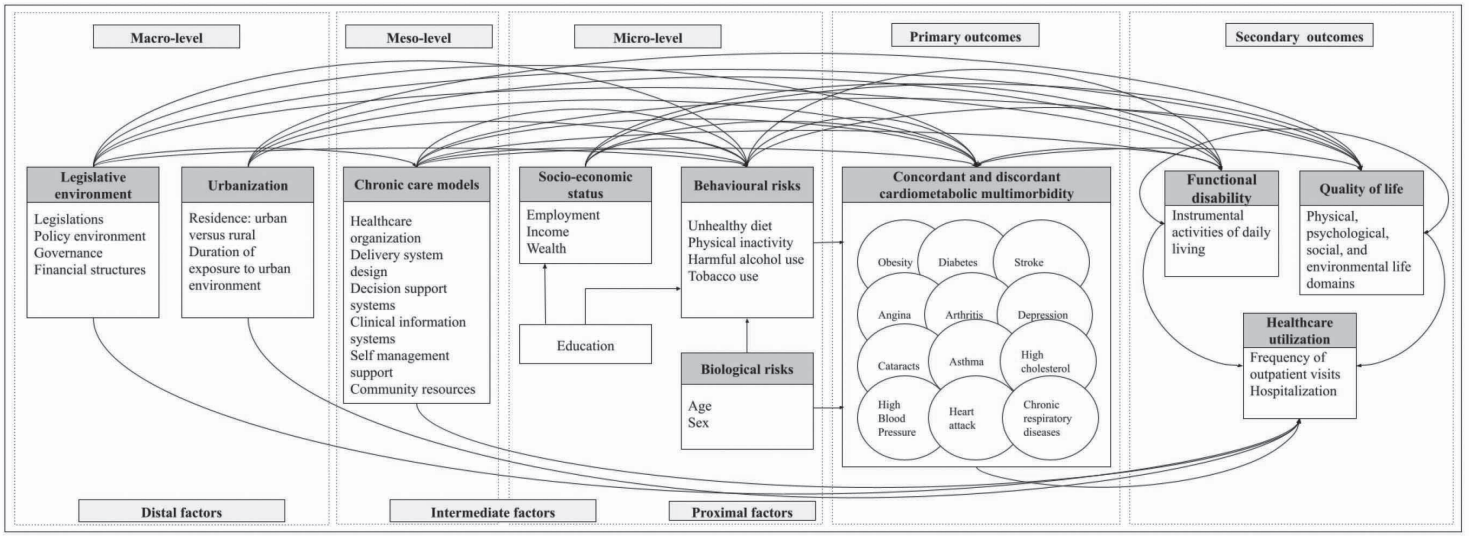
Aims and Objectives

The overarching aim of this thesis is to strengthen the responsiveness of healthcare systems to the management of cardiometabolic multimorbidity in SSA. More specifically, this thesis investigated four main issues on cardiometabolic multimorbidity in SSA: 1) the burden of cardiometabolic multimorbidity; 2) chronic care models; 3) the readiness of healthcare facilities to provide integrated chronic disease management; and 4) the effect of multimorbidity on self-care interventions.

The thesis has seven key objectives:

1. To determine the patterns of cardiometabolic multimorbidity and associated risk factors in SSA.
2. To identify the clusters of cardiometabolic multimorbidity associated with moderate and severe disabilities in Ghana and South Africa.
3. To determine the association of different cardiometabolic multimorbidity combinations with healthcare utilization and quality of life in Ghana.
4. To evaluate the effectiveness of integrated chronic care models for cardiometabolic multimorbidity in SSA.
5. To assess the readiness of healthcare facilities to provide integrated management of CVDs and type 2 diabetes in Kenya.
6. To determine the perceived health system facilitators and barriers to the integrated management of hypertension and type 2 diabetes in Kenya.
7. To examine whether multimorbidity moderates the effects of a patient support group intervention on blood pressure management among low and middle-income patients with hypertension in Kenya.

Figure 1: *Conceptual Framework for the social determinants of cardiometabolic multimorbidity*



Source: WHO 2005; the framework was modified to include macro, meso, and micro-level determinants multimorbidity.

Outline of thesis

This thesis is presented in four parts to address the seven key objectives. Part one (chapters 2, 3 and 4) describes the patterns and risk factors for common clusters of cardiometabolic multimorbidity in SSA and the association of different cardiometabolic multimorbidity combinations with functional disability, healthcare utilization and quality of life in Ghana and South Africa. Part two (Chapter 5) presents a systematic review and meta-analysis of the effectiveness of integrated chronic care models for cardiometabolic multimorbidity in SSA. Part three (chapters 6 and 7) presents a readiness assessment of healthcare facilities' capacity to provide integrated management of CVDs and type 2 diabetes in Kenya and a qualitative study of the health system facilitators and barriers to integrated care in Kenya. The effect of patient peer support groups for hypertension on blood pressure among patients with and without multimorbidity in Kenya is presented in part four (Chapter 8). Table 1 summarises the studies presented in this thesis.

Table 1: Overview of studies presented in this thesis

Objective	Chapter	Study design	Data source
PART 1: The burden of cardiometabolic multimorbidity in SSA			
1. Patterns of cardiometabolic multimorbidity and associated risk factors in SSA	2	Cross-sectional	WHO STEPS surveys (2014-2017)
2. Clusters of cardiometabolic multimorbidity associated with moderate and severe disabilities in Ghana and South Africa	3	Cross-sectional	WHO SAGE surveys (Ghana & South Africa) Wave 2 (2015)
3. Association of different cardiometabolic multimorbidity combinations with healthcare utilization and quality of life in Ghana	4	Cross-sectional	WHO SAGE survey (Ghana) Wave 2 (2015)
PART 2: Chronic care models for cardiometabolic multimorbidity in SSA			
4. Effectiveness of integrated chronic care models for cardiometabolic multimorbidity in SSA.	5	Systematic review and meta-analysis	Systematic review
PART 3: Health system capacity to manage cardiometabolic multimorbidity in Kenya			
5. Readiness of healthcare facilities to provide integrated management of CVDs and type 2 diabetes in Kenya	6	Cross-sectional	National facility assessment survey in Kenya (2019-2020)

Table 1: Continued

Objective	Chapter	Study design	Data source
6. Health system facilitators and barriers to the integrated management of hypertension and type 2 diabetes in Kenya.	7	Qualitative study	In-depth interviews and focus group discussions with patients and key-informant interviews with health stakeholders in Kenya (2019-2020)
PART 4: Effect of multimorbidity on self-care interventions for cardiometabolic diseases in Kenya			
7. Effect of patient peer support groups for hypertension on blood pressure among patients with and without multimorbidity in Kenya	8	Longitudinal cohort	*Ngao ya Afya* study in Kenya (2019-2020)

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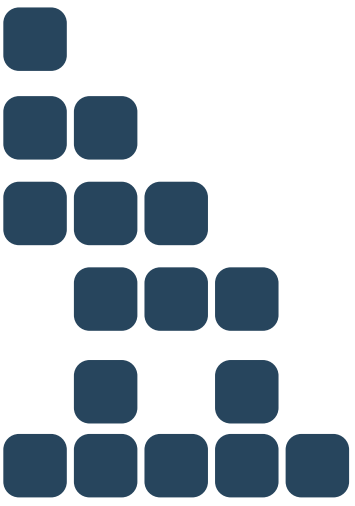
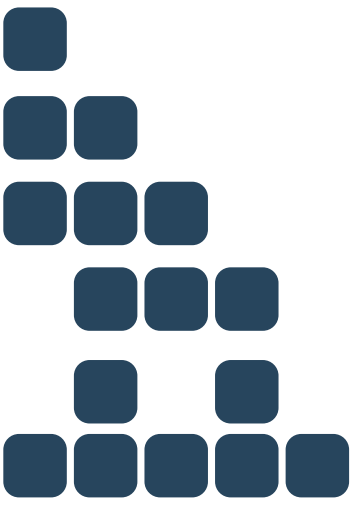


PART 1

The burden of Cardiometabolic Multimorbidity in sub-Saharan Africa



2

Multimorbidity of cardiometabolic diseases: a cross-sectional study of patterns, clusters and associated risk factors in sub-Saharan Africa

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Abstract

Objective: To determine the patterns of cardiometabolic multimorbidity and associated risk factors in sub-Saharan Africa (SSA).

Design: We used data from the World Health Organization STEPwise approach to non-communicable disease risk factor surveillance (STEPS) crossectional surveys conducted between 2014 and 2017.

Participants: The participants comprised 39, 658 respondents aged 15-69 years randomly selected from nine SSA countries using a multistage stratified sampling design.

Primary outcome measure: Using latent class analysis and agglomerative hierarchical clustering algorithms, we analysed the clustering of cardiometabolic diseases including high blood sugar, hypercholesterolemia, hypertension, and cardiovascular diseases (CVDs) such as heart attack, angina, and stroke. Clusters of lifestyle risk factors: harmful salt intake, physical inactivity, obesity, tobacco, and alcohol use were also computed. Prevalence ratios (PR) from modified Poisson regression were used to assess the association of cardiometabolic multimorbidity with sociodemographic and lifestyle risk factors.

Results: Two distinct classes of cardiometabolic diseases were identified: a relatively healthy group with minimal cardiometabolic diseases (95.2%) and a cardiometabolic multimorbidity class comprising participants with high blood sugar, hypercholesterolemia, hypertension, and CVDs (4.8%). The clusters of lifestyle risk factors included alcohol, tobacco, and harmful salt consumption (27.0%), and physical inactivity and obesity (5.8%). The cardiometabolic multimorbidity cluster exhibited unique sociodemographic and lifestyle risk profiles. Being female (PR=1.7, 95% CI (1.5-2.0), middle-aged (35-54 years) (3.9 (3.2-4.8)), compared to age 15-34 years, employed (1.2 (1.1-1.4)), having tertiary education (2.5 (2.0-3.3)), versus no formal education and clustering of physical inactivity and obesity (2.4 (2.0-2.8)) were associated with a higher likelihood of cardiometabolic multimorbidity.

Conclusion: Our findings show that cardiometabolic multimorbidity and lifestyle risk factors cluster in distinct patterns with a disproportionate burden among women, middle-aged, persons in high socioeconomic positions, and those with sedentary lifestyles and obesity. These results provide insights for health systems response in SSA to focus on these clusters as potential targets for integrated care.

Keywords: multimorbidity, cardiometabolic diseases, clustering, latent class analysis, hierarchical clustering, sub-Saharan Africa

Article Summary

Strengths and limitations of this study

- Data used in this analysis are from nationally representative population-based surveys conducted in nine countries in SSA using a standardised WHO-STEPS protocol. Hence, the findings are generalizable to the populations of these countries.
- The screening for cardiometabolic diseases is based on direct measures of blood pressure, anthropometry, key biomarkers, and self-reports thereby allowing for an objective assessment of multimorbidity.
- This study provides crucial evidence on population-based cardiometabolic multimorbidity patterns among broader age ranges comprising young, middle-aged older persons.
- Data used in the analysis are from cross-sectional studies thus it is not possible to draw causal inferences for cardiometabolic multimorbidity and temporal associations with socio-demographic and lifestyle risk factors. However, the findings provide useful insights for policymakers and health service providers to prioritize risk-centered approaches for prevention, early detection and treatment of cardiometabolic multimorbidity.

Introduction

Cardiometabolic diseases are the leading cause of global mortality and disability (1). Over half of the global burden of non-communicable diseases (NCDs) is attributable to cardiometabolic diseases that share four major risk factors: harmful alcohol use, unhealthy diet, tobacco use, and physical inactivity (2, 3). Three-quarters of the global cardiometabolic disease-related mortality occurs in low and middle-income countries with 30% classified as premature deaths (4). People living with cardiometabolic diseases often present with multiple conditions including diabetes mellitus, hypercholesterolemia, hypertension, and stroke (5-7). Hence the concept of cardiometabolic multimorbidity.

Although cardiometabolic diseases are estimated to take away up to 12 years in life expectancy (8, 9), their onset can be prevented or postponed by the elimination of lifestyle risk factors (10, 11). Most studies have consistently identified cardiometabolic multimorbidity as a common cluster (12-15). However, there are still several knowledge gaps on the multimorbidity spectrum in SSA. First, literature is scarce on clustering cardiometabolic diseases and behavioural risk factors because extant evidence has not applied statistical methods to separate the random and non-random co-occurrence (16-19). Moreover, most studies have mainly focused on analysing the most prevalent combinations of cardiometabolic diseases (16-20). The prevalence of different disease combinations is significantly associated with the prevalence of the individual comorbid diseases in question. Hence, a high prevalence of a particular multimorbidity combination does not provide sufficient evidence to support a non-random co-occurrence (21). Accounting for the random co-existence of multimorbidity requires rigorous assessment of multimorbidity clusters and lifestyle risk factors (22).

Evidence of clustering of cardiometabolic diseases and lifestyle risk factors is needed to prioritize healthcare services for the most frequently co-occurring combinations (23). However, the methodological differences in the conceptualization of multimorbidity in previous studies have hindered the comparison of findings (13, 24). Furthermore, most studies have been conducted among older age groups in primary care settings where multimorbidity are more likely to occur (13, 24). To date, little research in SSA has investigated multimorbidity patterns among broader age ranges from the general population.

This study, therefore, sought to investigate patterns and clusters of cardiometabolic multimorbidity and associated factors among persons aged 15 to 69 years using nationally representative World Health Organization (WHO) STEPwise surveys from nine countries in SSA.

Methods

Study design

We used data from the WHO STEPwise approach to NCD risk factor surveillance (STEPS) surveys in SSA. Details of the data collection methods have been published elsewhere (25). Briefly, STEPS surveys are nationally representative population-based cross-sectional surveys of risk factors for NCDs in participants aged 15 to 69 years. The WHO STEPS surveys aims to provide baseline national estimates for NCD indicators to inform health policies in the study countries (26).

A standard sampling protocol for the WHO STEPS survey was used in all the study countries (27). The participants were selected using a multistage stratified sampling design. First, sampling clusters or enumeration areas (EAs) were selected using probability proportional to the size of the number of households in the cluster. Second, samples of households were randomly drawn from a household listing in the cluster. Eligible participants comprised all listed household members aged 18 to 69 years residing in the sampled households for at least six months preceding the survey. In some countries, the minimum age was 15 years (28-30). Finally, the Kish sampling grid was used to randomly select one study participant from a list of all eligible household members (25).

Data abstraction

Data used in the current study were collected using interviewer-administered structured questionnaires modified from the WHO STEPS tool (25). The data were from self-reports and direct measurements of anthropometry and key biomarkers. The variables were measured using the WHO criteria (27). Self-reported information comprised sociodemographic characteristics such as age, sex, education, and employment; behavioural risk factors such as physical inactivity, tobacco and alcohol use, harmful salt consumption; and clinical histories of high blood sugar, hypercholesterolemia, hypertension and cardiovascular diseases (heart attack, angina, and stroke). The physical measurements comprised screening for blood pressure and anthropometrics such as weight (kg) and height (m). The biochemical measurements comprised fasting blood samples for cholesterol and blood sugar measurements in mmol/L or mg/dL. Random blood glucose (RBS) was collected for 117/39,658 participants who failed to fast as instructed. The measurements of the variables used in this study are shown in Table 1.

Table 1: measurements of study of the variables

Variable	Measurement
Sociodemographic factors	
Age	Young age (15-34 years), Middle-age (35-54years), Older age (55-69 years)
Sex	Male, Female
Education	No formal education, Primary, Secondary, or Tertiary
Employment	Unemployed, Employed
Self-reported lifestyle risk factors	
Physical activity	≥150mins/week of MPA* or ≥75mins/week of VPA† or ≥150mins/week of MVPA‡
Harmful salt intake	Always or often adding salt to cooked food
Alcohol use	Current alcohol use
Current tobacco use	Current smoking and/or tobacco use
Body Mass Index	
Obesity	BMI ≥ 30kg/m^2 for adult participants (18+ years) or BMI-for-age-sex ≥95th percentile in participants aged<18 years
Cardiometabolic diseases	
High blood sugar	FBS concentration of ≥ 7 mmol/L (126 mg/dL) or RBS concentration of ≥ 11.1 mmol/L (200 mg/dL) and/or a previous diagnosis of diabetes mellitus by a professional health care provider and/or being on treatment for diabetes.
Cardiovascular Disease	Having a previous diagnosis of heart attack or angina or a stroke
Hypertension	SBP ≥140 or DBP ≥90 mm Hg and/or a previous diagnosis of hypertension by a professional health care provider and/or being on antihypertensive therapy.
Hypercholesterolemia	Total cholesterol levels ≥5.2 mmol/l (202.8 mg/dL) or having a previous diagnosis of high cholesterol by a professional health care provider and/or being on treatment for elevated cholesterol

*MPA; moderate-to-vigorous physical activity, † VPA; vigorous physical activity, ‡MVPA; moderate-to-vigorous physical activity, FBS: Fasting blood sugar, RBS; Random blood sugar. SBP; systolic blood pressure; DBP, diastolic blood pressure, BMI: Body Mass Index.

Data inclusion and exclusion criteria

We used a two-stage inclusion criteria for the present study (See supplementary file 1). The first step involved the selection of eligible study countries while in the second step, eligible participants were selected from the latest round of the STEPS survey in each of the study countries (See supplementary file 2). In the first step, a country was eligible for inclusion in the analysis if it met the following criteria: (1) Had data collected between 2000 to 2020; (2) The survey was nationally representative; and (3) Had data on key variables comprising blood sugar, cholesterol, body mass index, blood pressure, and

CVD status. Others comprised age, sex, education, employment, alcohol consumption, smoking, diet, and physical activity. In the second step, eligible participants were included in the analysis if they were not pregnant. In the end, data from nine countries with 39, 658 participants were included in the analysis (See supplementary file 3).

Definition of variables

The outcome variable for the present analysis was defined as the clustering of cardiometabolic diseases comprising high blood sugar, hypercholesterolemia, hypertension, and CVDs (heart attack, angina, and stroke). The explanatory variables included sociodemographic characteristics: age, sex, education level, and employment status. Other covariates comprised clusters of multiple lifestyle risk factors including harmful salt intake, physical inactivity, obesity, tobacco use, and alcohol consumption. Clusters were named based on their unique dominant cardiometabolic diseases and risk profiles.

Data analysis

Applying sample weights

We accounted for the complex survey design using the *svyset* command in Stata, by defining clusters and sampling weights. The original country-level datasets were weighted using the probability of selection at each stage of sampling. Thus, the participants' weight was equal to the inverse of the product of the probability of the selection of the enumeration area or sampling cluster, the probability of household selection, the probability of selection within the household, and the age-sex distribution of the study country.

Characteristics of participants were summarised using frequencies and percentages. Given the exclusion of participants with missing data on the key variables, we compared the characteristics of the participants with complete data and those with incomplete data and found no differences between the two groups based on age, sex, and employment status. (See supplementary file 4).

Latent class analysis

We used latent class analysis (LCA) to identify distinct groups of cardiometabolic multimorbidity and lifestyle risk factors. The LCA is a structural equation modelling-based approach used to identify groups of participants with homogenous response patterns to a set of observed variables (31). We determined the optimal number of latent classes using the adjusted Bayesian Information Criterion (BIC). The BIC has been previously used as a robust indicator for determining the optimal number of classes for latent variables (32, 33). First, the BIC was used to compare several plausible models. The model with the lowest values of BIC was finally selected as the best-fitting model (34, 35). The posterior probabilities were used to determine the likelihood of class membership. Finally, the participants were grouped into the classes with the highest-class probability.

Hierarchical cluster analysis

We conducted a supplementary analysis of the cardiometabolic multimorbidity patterns and clustering of lifestyle risk factors using the agglomerative hierarchical cluster analysis (36). First, the proximity index grouped individual cardiometabolic diseases and lifestyle risk factors into a single cluster. Second, the individual clusters were gradually merged with the most closely related clusters until a single cluster with all the elements was obtained. We used the average linkage method to accommodate the spread of the clusters (36). The number of clusters was assessed using a dendrogram and Jaccard similarity coefficient. In summary, the Jaccard coefficient is a measure of similarity between two sets or clusters expressed as a percentage. The higher the percentage, the more similar the two clusters are (37).

Modified Poison Regression

We used modified Poisson regression to assess the sociodemographic variables and clusters of lifestyle risk factors associated with cardiometabolic multimorbidity. The sociodemographic variables comprising age, sex, education level, employment status and clusters of lifestyle risk factors were regressed against a dummy outcome variable indicating whether the participant was in class 1 (healthy class with minimal cardiometabolic diseases) or class 2 (cardiometabolic multimorbidity). The selection of the sociodemographic and lifestyle risk factors for the multivariable model was based on the variables conceptualized from the WHO's theoretical framework on the social determinants of non-communicable diseases (38) as more traditional level p values such as 0.05 used to select variables can fail in identifying variables known to be important (39). We adjusted for country of residence by including the country dummy variable in the models, as in previous publications from WHO surveys (40-42). We found no multicollinearity among the independent variables based on the assessment of variance inflation factors (43). The adjusted prevalence ratios (PR) and 95% CI from modified Poisson regression were used to determine the sociodemographic and lifestyle risk factors associated with cardiometabolic multimorbidity. All statistical analyses were carried out in Stata version 15 (StataCorp, College Station, TX, USA).

Patient and public involvement

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

Results

Characteristics of participants

In total, 39,658 participants were included in the analysis. Table 2 shows the characteristics of the study participants. In general, most of the participants were women, belonged to the youngest age group (15-34 years), had a primary level of education, and were unemployed.

Harmful salt intake (37.5%) and alcohol use (27.9%) were the most prevalent lifestyle risk factors. The most prevalent cardiometabolic disease was hypertension (24.9%). Varying patterns in the distribution of cardiometabolic diseases and lifestyle risk factors were observed among the study countries. Tobacco use (20.7%), harmful salt intake (98.6%), physical inactivity (25.6%) and hypertension (36.2%) were highest in Botswana. Ethiopia had the highest prevalence of alcohol use (43.3%). Obesity and hypercholesterolemia were highest in Swaziland (19.5%) and Benin (13.9%). Sudan and Zambia had the highest prevalence of high blood sugar (7.4%) while CVD prevalence was highest in Uganda (9.2%).

Table 2: Sociodemographic and health characteristics of the study participants

	Benin n=4,645	Botswana n=3,302	Ethiopia n=8,184	Kenya n=3,986	Malawi n=3,640	Sudan n=6,559	Swaziland n=2,461	Uganda n=3,413	Zambia n=3,468	Pooled data n= 39,658
Age										
15-34	56.5	62.3	64.5	57.6	54.3	55.9	64.7	56.3	59.2	59.2
35-54	33.9	28.0	27.3	32.3	35.0	33.7	24.9	32.6	32.2	31.2
55-69	9.6	9.7	8.2	10.1	10.6	10.3	10.4	11.1	8.6	9.6
Sex										
Male	52.1	51.4	56.0	50.5	48.9	55.9	48.2	49.6	50.8	53.1
Female	47.9	48.6	44.0	49.5	51.1	44.1	51.8	50.4	49.2	46.9
Education										
No formal education	46.7	7.0	41.3	11.7	10.6	40.1	5.9	15.1	7.1	27.6
Primary	30.9	20.9	47.2	45.9	66.7	27.9	46.6	42.1	44.6	43.3
Secondary	15.9	53.4	7.1	31.5	20.1	21.0	38.6	34.4	40.4	21.5
Tertiary	6.5	18.7	4.4	10.9	2.6	11.1	9.0	8.5	7.9	7.6
Employment										
Unemployed	26.6	72.5	92.6	40.0	61.6	51.3	63.9	37.0	49.3	61.0
Employed	73.4	27.5	7.4	60.0	38.4	48.7	36.1	63.0	50.7	39.0
Lifestyle risk factors										
Tobacco use	9.9	20.7	4.9	13.2	12.4	15.8	8.3	11.7	15.8	11.0
Alcohol use	37.2	34.0	43.3	24.6	21.6	2.5	18.1	36.1	27.3	27.9
Harmful salt intake	11.4	98.6	60.2	23.2	17.6	32.1	17.9	21.6	38.7	37.5
Physical inactivity	17.7	25.6	7.1	7.9	4.3	17.5	17.5	5.6	14.5	9.8

Table 2: Continued

	Benin n=4,645	Botswana n=3,302	Ethiopia n=8,184	Kenya n=3,986	Malawi n=3,640	Sudan n=6,559	Swaziland n=2,461	Uganda n=3,413	Zambia n=3,468	Pooled data n= 39,658
Obesity	8.6	11.7	1.1	9.1	5.1	10.1	19.5	4.6	7.2	5.8
Cardiometabolic diseases										
Hypercholesterolemia	13.9	8.8	3.3	6.5	5.6	11.1	8.5	4.8	4.7	6.2
High blood sugar	6.5	3.9	2.2	2.5	1.8	7.4	5.5	1.8	7.4	3.7
Hypertension	31.0	36.2	18.1	27.2	20.3	33.0	30.9	27.4	24.5	24.9
CVD	4.8	7.3	3.4	5.7	7.8	3.4	4.7	9.2	3.6	4.9

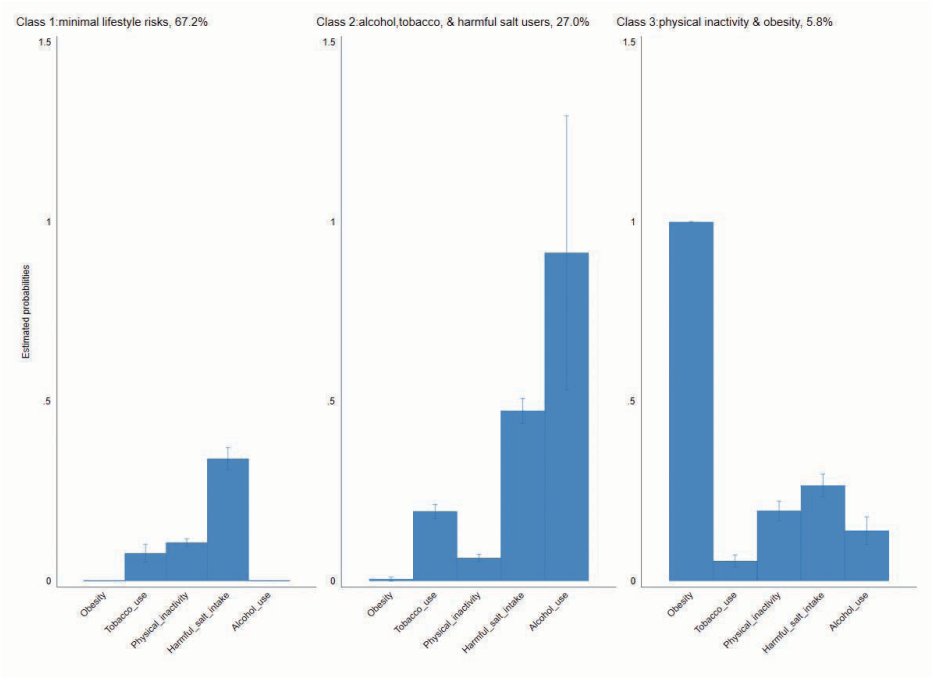
Notes: Data presented as weighted row %, unless otherwise specified, CVD; cardiovascular diseases: heart attack, angina, and stroke

Findings of Latent Class Analysis

Clustering of lifestyle risk factors

The classes of lifestyle risk factors are shown in Figure 1. We compared LCA models with 1 to 4 classes (See supplementary file 5). The three-class model had the lowest BIC and thus was selected as the best-fit model. Class one comprised participants with minimal lifestyle risks (67.2%). Class two included participants with high probabilities of alcohol use, smoking and harmful salt consumption (27.0%). Class three comprised participants with the highest probability of physical inactivity and obesity (5.8%).

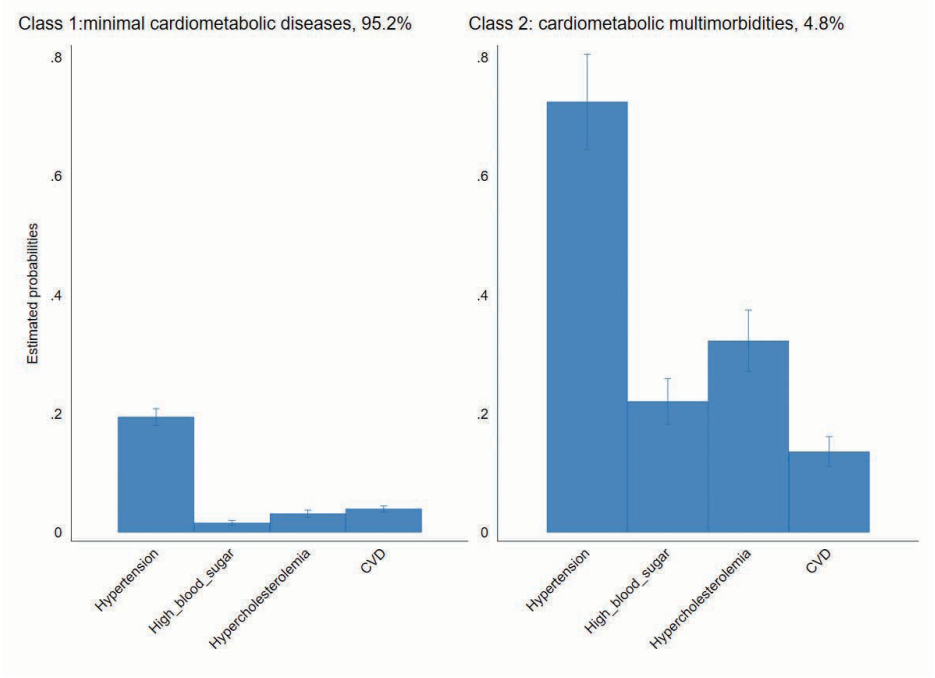
Figure 1: Latent classes of lifestyle risk factors



Cardiometabolic multimorbidity classes

The classes of cardiometabolic diseases are shown in figure 2. We ran LCA models from 1 to 4 classes selecting the two-class model based on indices of fit (See supplementary file 5). The two-class model had the lowest BIC and thus was selected as the best-fit model. Class one (interpreted as the "relatively healthy group") comprised participants with minimal multimorbidity (95.2%). Class two (cardiometabolic multimorbidity) included participants with the highest probability of high blood sugar, hypercholesterolemia, hypertension, and CVDs (4.8%).

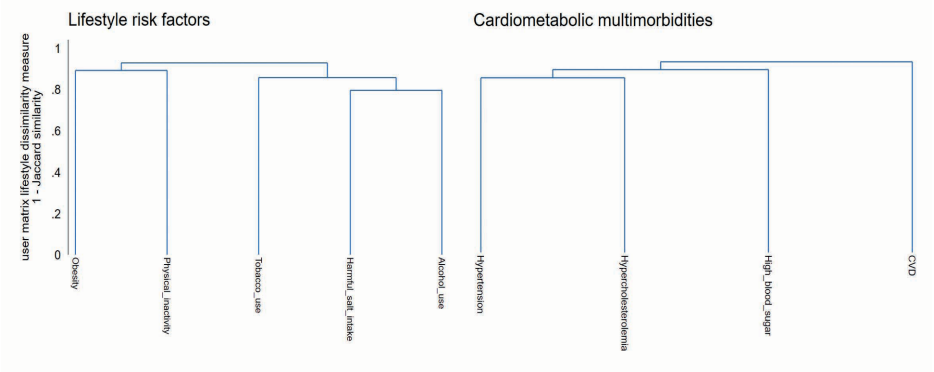
Figure 2: Latent classes of cardiometabolic diseases



Hierarchical cluster analysis findings

As a supplementary analysis, we also calculated cardiometabolic multimorbidity patterns and clustering of lifestyle risk factors using the agglomerative hierarchical cluster analysis. Figure 3 shows the hierarchical tree plot (dendrogram). The dendrogram displays the agglomeration schedules at which cardiometabolic diseases and lifestyle risk factors are combined. In general, the findings were similar to those obtained using LCA. The hierarchical clustering algorithms revealed two distinct groupings of lifestyle risk factors. Based on the proximity coefficients, physical inactivity and obesity formed the first cluster. Alcohol use, harmful salt intake and tobacco use combined to form the second cluster. The proximity coefficients from the hierarchical cluster analysis revealed clustering of hypertension, hypercholesterolemia, high blood sugar, and CVDs.

Figure 3: Dendrogram of lifestyle risk factors and cardiometabolic diseases



Distribution of cardiometabolic multimorbidity by sociodemographic and lifestyle risk factors

The distribution of cardiometabolic multimorbidity by sociodemographic and lifestyle risk factors is presented in table 3. The clustering of cardiometabolic multimorbidity (hypertension, high blood sugar, hypercholesterolemia and CVD) was highest in middle-aged and older participants, females, employed, and those with tertiary education. Varying patterns in the distribution of cardiometabolic comorbidities were observed among the study countries. The prevalence of cardiometabolic multimorbidity was highest in Sudan and Botswana (9.9% and 9.3%) and lowest in Ethiopia (2.0%).

Table 3: Distribution of cardiometabolic multimorbidity by sociodemographic and lifestyle risk factors

Weighted row%	Latent classes Class1: relatively healthy	Class 2: cardiometabolic multimorbidity
	Minimal cardiometabolic diseases	Hypertension, high blood sugar, hypercholesterolemia & CVD
N	36,618	3,040
**Age		
18-34	98.3	1.7
35-54	92.3	7.7
55-69	85.9	14.1
**Sex		
Male	96.3	3.7
Female	93.9	6.1

Table 3: Continued

Weighted row%	Latent classes Class1: relatively healthy	Class 2: cardiometabolic multimorbidity
**Employment		
Unemployed	96.2	3.8
Employed	93.7	6.3
**Education		
No schooling	95.0	5.0
Primary	96.6	3.4
Secondary	94.4	5.6
Tertiary	90.4	9.6
**Country		
Benin	90.7	9.3
Botswana	92.8	7.2
Ethiopia	98.0	2.0
Kenya	95.3	4.7
Malawi	96.7	3.3
Sudan	90.2	9.9
Swaziland	92.4	7.7
Uganda	96.5	3.5
Zambia	94.5	5.5
**Latent classes of lifestyle risk factors		
Class 1:minimal lifestyle risks	95.8	4.2
Class 2:alcohol,tobacco, & harmful salt users	97.0	3.0
Class 3:physical inactivity & obesity	79.9	20.1
Total	95.2	4.8

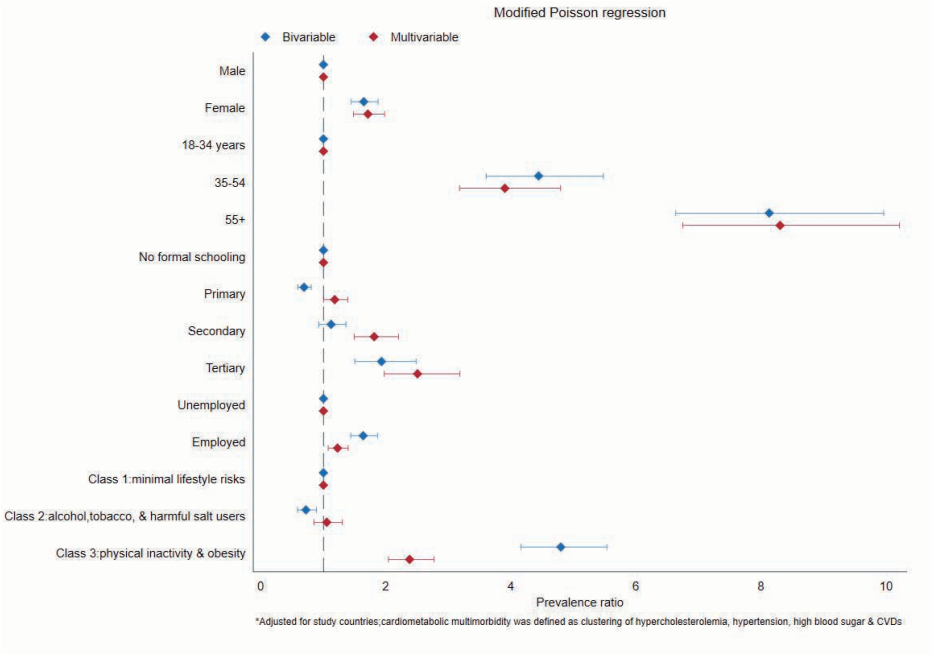
Notes: Data presented as weighted row %, unless otherwise specified, ** p<0.001

Sociodemographic and lifestyle risk factors associated with cardiometabolic multimorbidity

Figure 4 shows the sociodemographic and lifestyle risk factors associated with cardiometabolic multimorbidity. Being female (PR=1.7, 95% CI (1.5-2.0), middle-aged (35-54 years) (3.9 (3.2-4.8)) and older age (55-69 years) (3.9 (3.2-4.8)), compared to age 15-34 years were associated with a higher likelihood of cardiometabolic multimorbidity. Participants in the highest socioeconomic position such as tertiary education (2.5

(2.0-3.3)) versus no formal schooling and those employed (1.2 (1.1-1.4)) versus unemployed were more likely to have cardiometabolic multimorbidity. The likelihood of cardiometabolic multimorbidity was higher among participants with co-occurring physical inactivity and obesity (2.4 (2.0-2.8)) compared to those with minimal lifestyle risk factors.

Figure 4: Sociodemographic and lifestyle risk factors associated and cardiometabolic multimorbidity



Discussion

In this study, we examined the patterns of cardiometabolic multimorbidity and associated risk factors in persons aged 15 years and older in SSA. Two distinct classes of cardiometabolic diseases were identified: a relatively healthy group with minimal cardiometabolic diseases and a cardiometabolic multimorbidity class comprising participants with high blood sugar, hypercholesterolemia, hypertension, and CVDs. Three clusters of lifestyle risk factors were yielded. Class one comprised participants with minimal lifestyle risks. Class two included alcohol users, smokers and harmful salt consumers. Class three comprised clustering of physical inactivity and obesity. Our findings show that cardiometabolic multimorbidity cluster in distinct patterns with a disproportionate burden among women, middle-aged, persons in the highest socioeconomic positions, and those with sedentary lifestyles and obesity.

The clusters of cardiometabolic multimorbidity identified in our study have similarities with findings from other studies in SSA (44, 45). Several underlying pathophysiological mechanisms could explain the clustering of high blood sugar, hypercholesterolemia, hypertension, and CVDs. Insulin resistance is known as a possible mechanism explaining the clustering of cardiometabolic diseases (46-48). The abnormalities in the metabolism process could be due to in part insulin resistance which may also lead to defects in vascular reactivity (49). The clustering of lifestyle risk factors such as smoking, alcohol use and harmful salt consumption in our study could be due to the interplay among various socio-behavioural factors that affect smoking, drinking behaviour and diet (50). This was consistent with findings from other studies in different parts of the world (50-52). Given that cardiometabolic diseases share common lifestyle risk factors (2, 3), our results provide crucial insights into the need to scale up population-level primary and secondary prevention programs. Primary prevention should target co-occurring lifestyle risk factors. Previous studies have shown that healthy lifestyles in early life often persist into adulthood and old age, preventing or delaying cardiometabolic diseases (53). Secondary prevention should target persons living with cardiometabolic diseases, such as regular screening for multimorbidity, self-monitoring, and adopting healthy lifestyles to prevent or delay the onset of multimorbidity.

The gender disparity in the distribution of cardiometabolic multimorbidity observed in our study may be partly attributed to the inequalities in occupational and domestic activities and the gender differences in risk factors for CVDs such as lifestyle and diet (54, 55). Our results suggest that cardiometabolic multimorbidity is not limited to older persons but is a common phenomenon among middle-aged persons in the study countries. These results mirror those of several multimorbidity studies in support of the emerging evidence on the high burden of multimorbidity in middle-aged persons (53, 56-58). Studies conducted in Brazil, Guatemala, India, the Philippines, and South Africa have also shown that people living in LMICs tend to experience cardiometabolic

diseases much earlier in life than their counterparts living in HIC due to socioeconomic hardships and poor access to healthcare services (59-61).

Similar to previous studies (62-64), our results show that increasing levels of educational achievements and being employed were associated with a greater likelihood of cardiometabolic multimorbidity. This may be due to the fact that with higher education and employment also comes affluence (62-64), and greater access to alcohol, tobacco and unhealthy diets (65). However, other studies have also shown that higher education achievement was also associated with a low likelihood of clustering of multiple behavioural risk factors for CVDs, possibly because a higher level of education may also increase both awareness of, and capacity for lifestyle modification (50, 66). Further studies on the socioeconomic determinants of cardiometabolic multimorbidity are needed to elucidate these results.

The likelihood of cardiometabolic multimorbidity was higher among participants with co-occurring physical inactivity and obesity compared to those with minimal lifestyle risk factors. This finding is in line with previous studies that pointed in the same direction (67-69). The mechanisms through which physical activity increases the risk of cardiometabolic multimorbidity are known. Previous physical activity intervention studies have demonstrated consistent improvements in various CVD risk factors such as hypertension (70), high-density lipoprotein cholesterol (71), C-reactive protein, and other inflammatory markers (72, 73). Consequently, further longitudinal studies are needed to elucidate the most critical sociodemographic factors attributable to the clustering of physical inactivity and obesity and its long-term effects on cardiometabolic multimorbidity in SSA.

Overall, our findings have two main implications. First, there is a need for further policy discourse on the integrated management of cardiometabolic diseases in primary care settings in SSA. The clustering of cardiometabolic diseases and lifestyle risk factors in the population is important for clinicians, policymakers, and researchers in prioritizing the needs and care processes for patients living with or at risk of multimorbidity. A paradigm shift towards comprehensive care may enable patients presenting with cardiometabolic diseases at primary care to be regularly screened for other chronic conditions. A shift away from fragmented care may also improve access to quality healthcare services, especially in SSA where persons living with cardiometabolic diseases remain undiagnosed for several years and the majority of those on treatment often remain uncontrolled (74). Secondly, our study provides baseline estimates for future researchers to design longitudinal studies on the burden and aetiology of the most common clusters of cardiometabolic diseases in SSA.

Strengths and limitations

Data used in this analysis are from nationally representative population-based surveys conducted in nine countries in SSA using a standardised WHO-STEPS protocol. Hence, the findings are generalizable to the populations of these countries. Secondly, most previous studies were conducted among older age groups in primary care settings where comorbidities are more likely to occur (13, 24). Our study bridges this gap by providing crucial evidence on population-based multimorbidity patterns among broader age ranges comprising young, middle-aged, and older persons. Third, data used are based on direct measures of blood pressure, anthropometry, key biomarkers, and self-reports allowing for a more objective screening for cardiometabolic diseases than self-reporting used in over three-quarters of previous studies (75).

Limitations stem from the fact that data used in the analysis are from cross-sectional studies thus it is not possible to draw causal inferences for cardiometabolic multimorbidity and temporal associations with socio-demographic and multiple lifestyle risks. Moreover, our study does not give an idea of the index disease in the multimorbidity clusters identified. Second, the screening for CVDs such as heart attack, angina, and stroke was based on self-reported history of clinical diagnosis, which may have led to information bias, possibly underestimating the prevalence of CVDs. Lastly, The current study is based on pooled data sets from several countries; hence, the findings may be limited by the variations in the sociocultural and economic contexts within the study countries.

Conclusions

Our findings show that cardiometabolic multimorbidity and lifestyle risk factors cluster in distinct patterns with a disproportionate burden among persons in the highest socioeconomic positions, women, the middle-aged, and those with sedentary lifestyles and obesity. These results provide useful insights for health systems response in SSA to focus on these clusters as potential targets in the development and segmentation of integrated care for cardiometabolic multimorbidity. We draw attention to the need for healthcare systems in SSA to prioritize risk-centred management of cardiometabolic diseases by incorporating aggressive approaches for prevention, early detection, treatment, and promotion of healthy lifestyles to avert the occurrence of multimorbidity.

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Competing interests: None declared.

Data sharing statement: Data are available in a public, open-access repository. No additional data are available.

Ethics approval: Data used in this study are publicly available on the NCD microdata repository of the WHO (https://extranet.who.int/ncdsmicrodata/index.php/catalog/STEPS) (76). We obtained formal written permission from the WHO for the surveys included. Since we used publicly available data, no additional approval was required from an institutional ethics review board.

Patient consent for publication: Not required.

Author contributions: PO conceptualized the study, reviewed literature, and analysed the data. GA, FW, CW, RS, WW, and CA made substantive contributions to the conceptualization of the study, and data analysis and reviewed the manuscript. All authors read and approved the final manuscript

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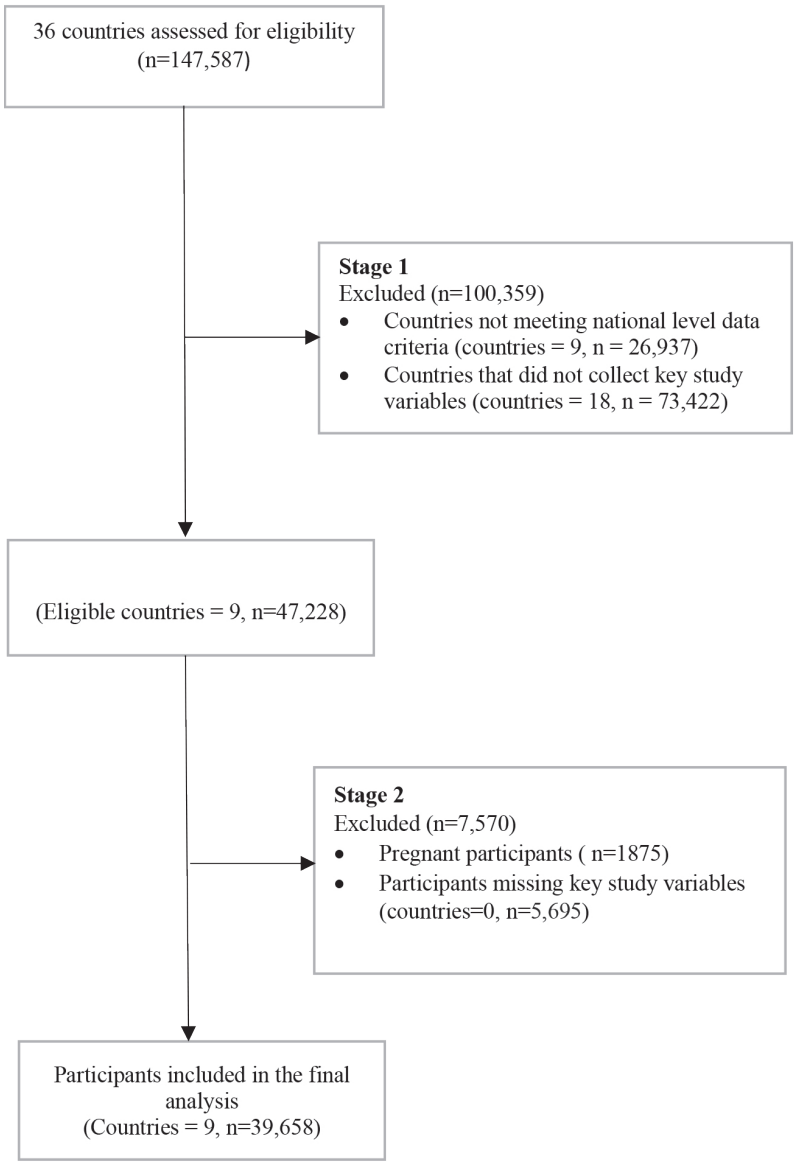
Supplementary files

Supplementary file 1: flow chart.



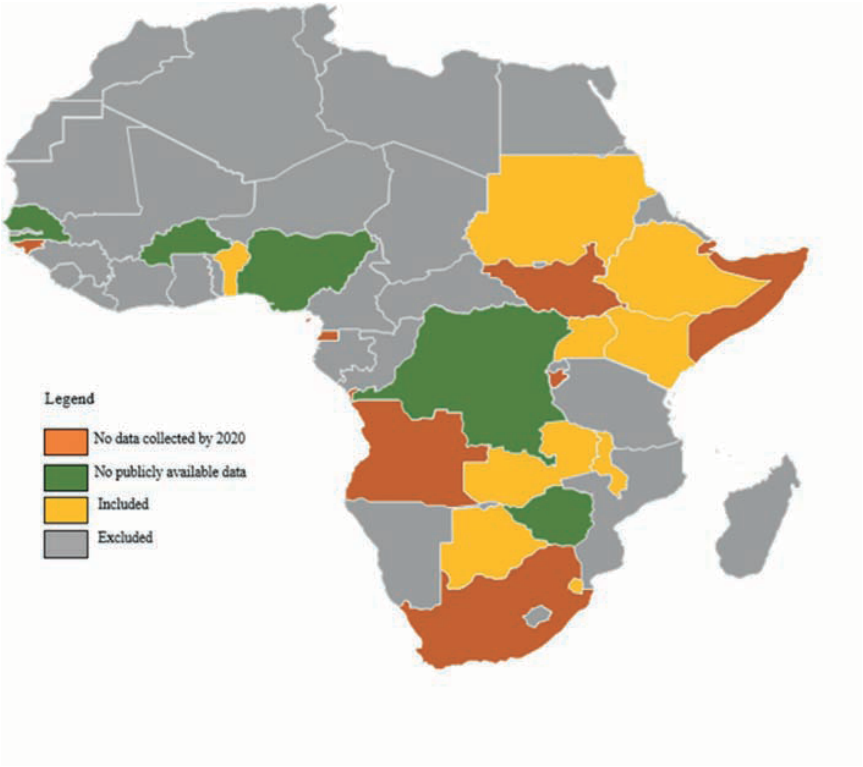
Supplementary file 2: WHO STEPS surveys in Sub-Saharan Africa

#	Countries	Collected WHO STEPS data	Year	National Level data	Publicly accessible
1	Angola	No	-	-	-
2	Benin	Yes	2015	Yes	Yes
3	Botswana	Yes	2014	Yes	Yes
4	Burkina Faso	Yes	2013	Yes	No
5	Burundi	Yes	-	-	-
6	Cape Verde	Yes	2007	Yes	Yes
7	Cameroon	Yes	2003	Yes	Yes
8	Central Africa Republic	Yes	2017	Yes	Yes
9	Chad	Yes	2008	No	Yes
10	Comoros	Yes	2011	Yes	Yes
11	Congo (Brazzaville)	Yes	2004	No	Yes
12	Congo (Democratic Republic)	Yes	2005	No	No
13	Cote d'Ivoire	Yes	2005	No	Yes
14	Djibouti	No	-	-	-
15	Equatorial Guinea	No	-	-	-
16	Eritrea	Yes	2010	Yes	Yes
17	Swaziland	Yes	2014	Yes	Yes
18	Ethiopia	Yes	2015	Yes	Yes
19	Gabon	Yes	2009	No	Yes
20	The Gambia	Yes	2010	Yes	Yes
21	Ghana	Yes	2006	No	Yes
22	Guinea	Yes	2009	No	Yes
23	Guinea-Bissau	No	-	-	-
24	Kenya	Yes	2015	Yes	Yes
25	Lesotho	Yes	2012	Yes	Yes
26	Liberia	Yes	2011	Yes	Yes
27	Madagascar	Yes	2005	No	Yes
28	Malawi	Yes	2017	Yes	Yes
29	Mali	Yes	2013	No	Yes
30	Mauritania	Yes	2006	No	Yes
31	Mauritius	Yes	2004	Yes	No
32	Mozambique	Yes	2005	Yes	Yes
33	Namibia	Yes	2005	Yes	Yes
34	Niger	Yes	2007	Yes	Yes

Supplementary file 2 Continued

#	Countries	Collected WHO STEPS data	Year	National Level data	Publicly accessible
35	Nigeria	Yes	2003	No	No
36	Rwanda	Yes	-	-	-
37	Sao Tome and Principe	Yes	2009	Yes	Yes
38	Senegal	Yes	2015	Yes	No
39	Seychelles	Yes	2004	Yes	Yes
40	Sierra Leone	Yes	2009	Yes	Yes
41	Somalia	No	-	-	-
42	South Africa	No	-	-	-
43	South Sudan	No	-	-	-
44	Sudan	Yes	2016	Yes	Yes
45 (a)	Tanzania	Yes	2012	Yes	Yes
45 (b)	Zanzibar	Yes	2011	Yes	Yes
46	Togo	Yes	2011	Yes	Yes
47	Uganda	Yes	2014	Yes	Yes
48	Zambia	Yes	2017	Yes	Yes
49	Zimbabwe	Yes	2005	No	No

Supplementary file 3: geographical distribution of study countries.



Supplementary file 4: comparison of the characteristics of complete cases and incomplete cases

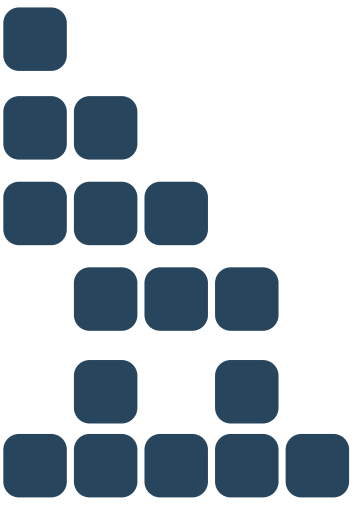
Background Characteristics	Complete cases	Incomplete cases	Std. Diff
Number of study participants	39,658	5,695	
Proportion (%)	87.40%	12.60%	
Mean age: All participants (SD)	37.1 (13.7)	35.7 (13.8)	0.1
Males (SD)	37.4 (14.8)	35.9 (14.0)	0.1
Females (SD)	36.9 (13.6)	35.6 (13.7)	0.1
Employment %	89.0	87.2	0.1

SD: standard deviation, Std Diff: standard difference. Std Diff= Difference in means divided by standard error; imbalance defined as an absolute value greater than 0.2

Supplementary file 5: comparison between latent class models

Number of latent classes	BIC	CAIC
Clustering of lifestyle risk factors		
1	183698.7	183741.7
2	181584.2	181678.7
3	**181386.8**	**181240.8**
4	181408.4	181228.0
Cardiometabolic mulitimorbidity classes		
1	107458.3	107424.0
2	**105290.8**	**105213.5**
3	105310.4	105198.2
4	105335.1	105197.7

Note: Boldface type indicates the selected model. BIC adjusted Bayesian Information Criterion, CAIC consistent Akaike Information Criterion



3

Cardiometabolic Multimorbidity Associated with Moderate and Severe Disabilities: Results from the Study on Global AGEing and Adult Health (SAGE) Wave 2 in Ghana and South Africa

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Abstract

Background: Integrated management of cardiometabolic diseases is crucial for improving the quality of life of older persons. The objective of the study was to identify clusters of cardiometabolic multimorbidity associated with moderate and severe disabilities in Ghana and South Africa.

Methods: Data were from the World Health Organization (WHO) study on global AGEing and adult health (SAGE) Wave-2 (2015) conducted in Ghana and South Africa. We analysed the clustering of cardiometabolic diseases including angina, stroke, diabetes, obesity, and hypertension with unrelated conditions such as asthma, chronic lung disease, arthritis, cataract and depression. The WHO Disability Assessment Instrument version 2.0 was used to assess functional disability. We used latent class analysis to calculate the multimorbidity classes and disability severity levels. Ordinal logistic regression was used to identify the clusters of multimorbidity associated with moderate and severe disabilities.

Results: Data from 4,190 adults aged over 50 years were analysed. The prevalence of moderate and severe disabilities was 27.0% and 8.9%, respectively. Four latent classes of multimorbidity were identified. These included a relatively healthy group with minimal cardiometabolic multimorbidity (63.5%), general and abdominal obesity (20.5%), hypertension, abdominal obesity, diabetes, cataract and arthritis (10.0%), and angina, chronic lung disease, asthma and depression (6.0%). Compared to the participants with minimal cardiometabolic multimorbidity, the odds of moderate and severe disabilities were higher among participants with multimorbidity comprising hypertension, abdominal obesity, diabetes, cataract and arthritis [aOR=3.0; 95% CI 1.6 to 5.6] and those with angina, chronic lung disease, asthma and depression [aOR=2.7; 95% CI 1.6 to 4.5].

Conclusions: Cardiometabolic diseases among older persons in Ghana and South Africa cluster in distinct multimorbidity patterns that are significant predictors of functional disabilities. This evidence may be useful for defining disability prevention strategies and long-term care for older persons living with or at risk of cardiometabolic multimorbidity in Sub-Saharan Africa.

Keywords: Cardiometabolic diseases, multimorbidity, disability, latent class analysis.

Background

Cardiometabolic multimorbidity, defined as having two or more coexisting cardiometabolic diseases, is a major global health challenge to healthcare systems (1, 2). The findings of the 1990-2019 global burden of diseases show that people are living longer, but with more chronic diseases and disabilities (3). The number of people living with cardiometabolic diseases such as coronary artery disease, stroke, hypertension and diabetes has been rising globally (4, 5). Importantly, cardiometabolic diseases often coexist with obesity and insulin resistance (6). Characterizing these disease states reveals that discordant multimorbidity, the simultaneous occurrence of other diseases with unrelated pathophysiology or pharmacological treatments such as chronic lung diseases, and musculoskeletal disorders are common among people with cardiometabolic diseases (7-9).

The population of older persons in sub-Saharan Africa (SSA) is projected to triple to 235.1 million in 2050 from 74.4 million in 2020 (10). Ghana and South Africa are at different stages of epidemiologic and demographic transitions but are experiencing a rapid increase in the proportion of older persons (11). Recent studies show a rising prevalence of cardiometabolic multimorbidity in Ghana and South Africa (12-15). With this rapid demographic transition, active ageing has become a priority for long-term healthcare policies in SSA (16, 17). The main goal of active ageing is to maintain the capacity to perform the activities of daily living (ADL) across the life course (18). Thus, measuring disability severity levels is crucial in understanding the consequences of ageing and planning long-term care programs. Disability is a complex process that transcends physical limitations (19). The International Classification of Functioning Disability and Health defines disability as a decline in three levels of functioning: bodily, person, and societal (20). Hence, disability comprises impairment in bodily functions, limitations in ADLs and restrictions in societal participation (18).

Although recent studies have attributed the functional decline to the presence of multimorbidity, several research gaps still exist (1, 21-25). First, the majority of the existing literature is based on disease counts or indices with inadequate information on specific concordant or discordant multimorbidity clusters to guide clinical or social interventions (26, 27). Second, a lack of homogeneity in the conceptualization of multimorbidity has hindered the comparison of findings (28). Third, a majority of studies have estimated the prevalence of disability using a binary classification approach (29-32). Such an approach may overlook the heterogeneity of the disability severity levels frequently observed among the older population.

Most literature on multimorbidity is available in high-income (HIC) where disease burdens and healthcare systems differ from those in SSA (33). Thus, the need for similar research in SSA. Consequently, the WHO Study on global AGEing and adult health (SAGE)

project was designed to address the emerging evidence gaps on ageing and well-being in LMICs (19). In 2020, one analysis from the SAGE Wave 1 study revealed that the prevalence of severe disability was three to five times higher in South Africa and Ghana than in China and Mexico (34). Whilst the findings of the SAGE study show high levels of severe disability among older adults in Ghana and South Africa, a more comprehensive unpacking of specific multimorbidity clusters may provide opportunities for integrated management of disease combinations with adverse impacts on functional health. Using the 2015 WHO SAGE Wave 2 survey in Ghana and South Africa, the objective of the current study was to determine the concordant and discordant cardiometabolic multimorbidity combinations and explore the associations with levels of disability (i.e., no disability, moderate and severe).

Methods

Study design

Data were from the WHO SAGE Wave 2 survey conducted in Ghana and South Africa in 2015 (35). The study design has been previously published (19). The SAGE survey is an ongoing population-based longitudinal study that aims to provide reliable evidence on ageing and well-being from nationally representative samples of persons aged 50 years and older (11). The primary sampling units were stratified across urban and rural areas in each country to capture socioeconomic differences and lifestyle behaviours. A standard protocol for the WHO SAGE survey was used in all the study countries (19). Briefly, the study participants were selected using a two-stage stratified sampling design. Stage 1 comprised of selection of clusters based on probability proportional to the number of households in the cluster. Households in each cluster were listed in stage two and a simple random sample was drawn from the listing frame. Eligible participants comprised all listed household members aged 50 years and older residing in the sampled households.

Data sources

Data used in the current study were collected using interviewer-administered structured questionnaires modified from the World Health Survey tool (35). Detailed information on the study tools and data collection procedures is provided elsewhere (19). The current analysis focused on the screening outcomes for chronic conditions and functional disability. The chronic conditions comprised cardiometabolic diseases such as angina pectoris, stroke, diabetes, hypertension, obesity and conditions such as arthritis, asthma, chronic lung disease, depression, and cataracts. Other variables included socio-demographic information such as age, sex, place of residence (rural and urban), and employment.

Measurement of variables

The screening for chronic diseases was based on self-reported history of clinical diagnosis, algorithms for symptomatology, physical measurements, and anthropometrics. We extracted the self-reported history of clinical diagnosis of angina pectoris, stroke, diabetes mellitus, hypertension, arthritis, asthma, chronic lung disease, depression, and cataracts. The diagnosis was ascertained using the screening question: "Has a healthcare professional ever told you that you have (disease name)?" In addition, based on the information available, WHO recommended symptomatology algorithms were used to screen for angina pectoris, arthritis, asthma, chronic lung disease, and depression (36-38). Details of the symptomatology algorithms are shown in the supplementary file 1.

The physical measurements comprised screening for systolic blood pressure (SBP), diastolic blood pressure (DBP) and anthropometrics including waist circumference (cm), weight (kg) and height (m). Screening blood pressure was recorded as the average of the last two BP readings. Hypertension was defined as SBP ≥ 140mmHg and/or DBP ≥ 90 mmHg and/or the previous diagnosis of hypertension by a professional health care provider and being on hypertensive therapy (39). Abdominal obesity was defined using WHO guidelines as waist circumference ≥ 94 cm for men or ≥ 80 cm for women (40). General obesity was defined as body mass index ≥30.0 kg/m^2 (41). Participants with a history of clinical diagnosis or treatment for any of the chronic conditions but screened negative based on the symptomatology algorithms or physical measurements were considered to have the condition.

Inclusion and exclusion criteria

The original sample of participants aged 50 years and older surveyed in the two study countries was 5,757 (Ghana: n=3,575 and South Africa: n=2,182). Participants were included in the current analysis if they had valid data on the key variables: disability status, chronic diseases such as angina pectoris, stroke, diabetes mellitus, hypertension, obesity, arthritis, asthma, chronic lung disease, depression, and cataracts and sociodemographic characteristics comprising sex, age and employment. Participants (n=1, 529) for which data on key variables were not captured or judged invalid were excluded. Since the causes of missing information was not ascertained, we did not apply missing data technique to avoid further uncertainty in the imputation models. Thus, the final analysis included 4,190 participants.

Given the exclusion of participants with missing data on the key study variables, the characteristics of the study participants with complete data were compared to those with incomplete data and no differences were found based on age and sex (See supplementary file 2).

Definition of variables

Outcome variable

Disability status was the main outcome variable. The WHO Disability Assessment Instrument version 2.0 (WHODAS 2.0) was used to screen for disability. The WHODAS 2.0 is a cross-culturally validated disability assessment tool comprising six domains assessed using a 12-item scale with two items per domain) (42). The domains comprise self-care, cognition and communication, mobility, life activities, interpersonal relations and participation. The global score is the sum of the 12 items from the six domains expressed on a continuous scale ranging from 0 (no disability) to 100 (full disability) (42).

Explanatory variables

The main explanatory variable was cardiometabolic multimorbidity defined as having two or more concordant or discordant cardiometabolic multimorbidity. Concordant cardiometabolic multimorbidity was defined as the simultaneous presence of two or more cardiometabolic diseases including angina pectoris, stroke, diabetes, hypertension, and obesity (43). Discordant cardiometabolic multimorbidity was defined as the simultaneous presence of at least one cardiometabolic diseases and one or more chronic diseases with unrelated pathophysiology or pharmacological treatment plans such as chronic lung disease, arthritis, cataract and depression (44). We computed clusters of concordant cardiometabolic multimorbidity comprising angina pectoris, stroke, diabetes, hypertension, obesity and discordant multimorbidity including chronic lung diseases, arthritis, cataract and depression. Other explanatory variables comprised sociodemographic factors such as age, sex, marital status, education level, employment status, and place of residence (urban or rural).

Data analysis

We used descriptive statistics comprising frequencies, means and standard deviations to summarize the characteristics of the study participants and disability patterns in a pooled dataset of the study countries while adjusting for survey weights.

Latent class analysis

We used latent class analysis (LCA) to identify distinct groups of multimorbidity classes and disability levels. The LCA is a methodological approach used to identify groups of participants with homogenous response patterns to a set of observed variables (45). We determined the optimal number of latent classes using the adjusted Bayesian Information Criterion (aBIC) and the consistent Akaike Information Criterion (CAIC). The BIC and CAIC have been previously used as robust indicators for determining the optimal number of classes for latent variables (46, 47). First, the aBIC and CAIC were used to compare several plausible models. The models with the lowest values of aBIC and CAIC were finally selected as the best fitting models. (48, 49). The posterior probabilities were used to determine the likelihood of multimorbidity class membership

and levels of disability. Finally, the participants were grouped into the cardiometabolic multimorbidity classes and disability levels with the highest-class probability.

Hierarchical cluster analysis

We conducted a supplementary analysis of the multimorbidity patterns using the agglomerative hierarchical cluster analysis with the average linkage method (HCA) (50). First, a proximity index was used to group the individual chronic diseases into a single cluster. Next, the chronic disease clusters were gradually merged with the most closely related clusters until a single cluster with all the elements was obtained. We used a dendrogram plot and Jaccard similarity coefficient to assess the cardiometabolic multimorbidity patterns (51).

Ordinal regression

Given the ordinal nature of the disability severity levels (i.e., no disability, moderate and severe) identified from the LCA, weighted ordinal regression was used to model the association of cardiometabolic multimorbidity classes with disability levels on pooled dataset from the two study countries. Because of the clustered design of the sample, robust variance estimates (Huber-White sandwich estimator) were used for the correction of standard errors to adjust for the correlation among responses within the same household (52).

Bivariable ordered logistic regression analysis with levels of disability as the outcome variable was first fitted for each of the multimorbidity classes followed by a multivariable model adjusting for socio-demographic characteristics namely age, sex, education, employment status, and place of residence. There was no evidence of violation of the assumption of parallel slopes using the command "*brant*" in Stata 17.0 (StataCorp LP, Texas, USA). The likelihood ratio test was used to compare the goodness of fit of the models. We used the adjusted odds ratio (aOR) and 95% Confident Interval (CI) to interpret the strength and direction of associations.

All statistical analyses were carried out using Stata 17.0 (StataCorp LP, Texas, USA) and accounted for the complex sampling design used in the SAGE survey.

Results

Characteristics of participants

The sociodemographic and health characteristics of the study participants are presented in Table 1. A total of 4,190 participants were included in the analysis. The mean age was 61.6 years. In general, most of the participants were women (54%), had a primary (35.7%) or secondary level of education (32.2%), were self-employed (33.3%) and lived in urban areas (70.9%). The most prevalent cardiometabolic diseases were abdominal obesity (56.4%) and hypertension (48.8%). Concordant and discordant cardiometabolic

multimorbidity were observed in 45.9% and 33.8% of the participants respectively. Varying patterns in the distribution of multimorbidity were observed between the two study countries. The highest prevalence of concordant and discordant cardiometabolic multimorbidity was observed in South Africa (56.3% and 38.4%) respectively.

Table 1: Sociodemographic and health characteristics of the study participants

	Country		Pooled data
Characteristics (%)	**Ghana, n=3,128**	**South Africa, n=1,062**	**Both countries,n=4,190**
Age, (mean) SD	61.9 (9.7)	61.4 (8.4)	61.6 (8.9)
Sex			
Male	47.7	44.9	46.0
Female	52.3	55.1	54.0
Education			
No formal education	41.5	17.0	26.7
Primary	28.3	40.5	35.7
Secondary	26.5	35.8	32.2
Tertiary	3.7	6.6	5.5
Employment			
Public	7.8	9.8	9.0
Private	4.4	43.5	28.0
Self-employed	69.7	9.6	33.3
Informal employment	16.2	29.0	24.0
Unemployed	1.9	8.2	5.7
Place of residence			
Urban	47.9	85.8	70.9
Rural	52.1	14.2	29.1
Chronic diseases			
Abdominal obesity	47.0	62.5	56.4
Hypertension	37.1	56.4	48.8
General obesity	13.4	39.0	28.9
Arthritis	20.4	21.4	21.0
Asthma	8.3	16.3	13.2
Cataract	7.2	9.5	8.6
Diabetes	2.6	12.0	8.3
Angina	8.4	6.0	6.9
Chronic lung disease	4.5	7.4	6.2
Depression	4.5	6.4	5.6

Table 1: Continued

Characteristics (%)	Country		Pooled data
	Ghana, n=3,128	South Africa, n=1,062	Both countries,n=4,190
Stroke	1.2	2.4	1.9
†Concordant cardiometabolic multimorbidity	29.9	56.3	45.9
‡Discordant cardiometabolic multimorbidity	26.6	38.4	33.8

Cells are weighted row percentages unless otherwise specified

† *Concordant cardiometabolic multimorbidity is defined as the simultaneous presence of two or more cardiometabolic diseases including angina pectoris, stroke, diabetes, hypertension, and obesity*

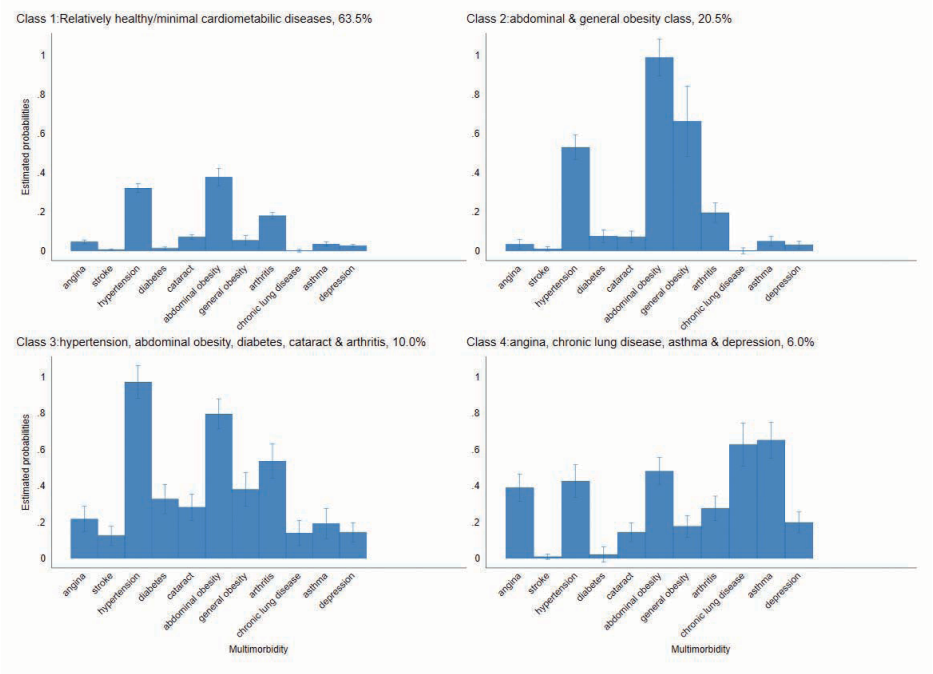
‡ *Discordant cardiometabolic multimorbidity is defined as the simultaneous presence of at least one cardiometabolic disease and one or more chronic diseases with unrelated pathophysiology or pharmacological treatment plans such as chronic lung disease, asthma, arthritis, cataract and depression*

Findings of Latent Class Analysis

Cardiometabolic multimorbidity classes

The multimorbidity classes are shown in figure 1. We compared LCA models with 2 to 5 classes (See supplementary file 3). Although the five-class model had a slightly lower AIC than the four-class (AIC_{5class} = 31748.2 vs. AIC_{4class} = 31791.5), further inspection showed that the four-class model exhibited clearer separation between latent classes and had the lowest aBIC. Thus the four-class model was finally selected. A four-class model exhibited a much clearer separation between latent classes thus this model was finally selected for interpretation of the multimorbidity classes. Class one (interpreted as the "relatively healthy group") comprised participants with minimal cardiometabolic multimorbidity (63.5%). Class two comprised participants with high probabilities of general and abdominal obesity (20.5%). Class three comprised participants with high probabilities of multimorbidity of hypertension, abdominal obesity, diabetes, cataract and arthritis (10.0%). Class four comprised participants with high probabilities of multimorbidity of angina, chronic lung disease, asthma and depression (6.0%).

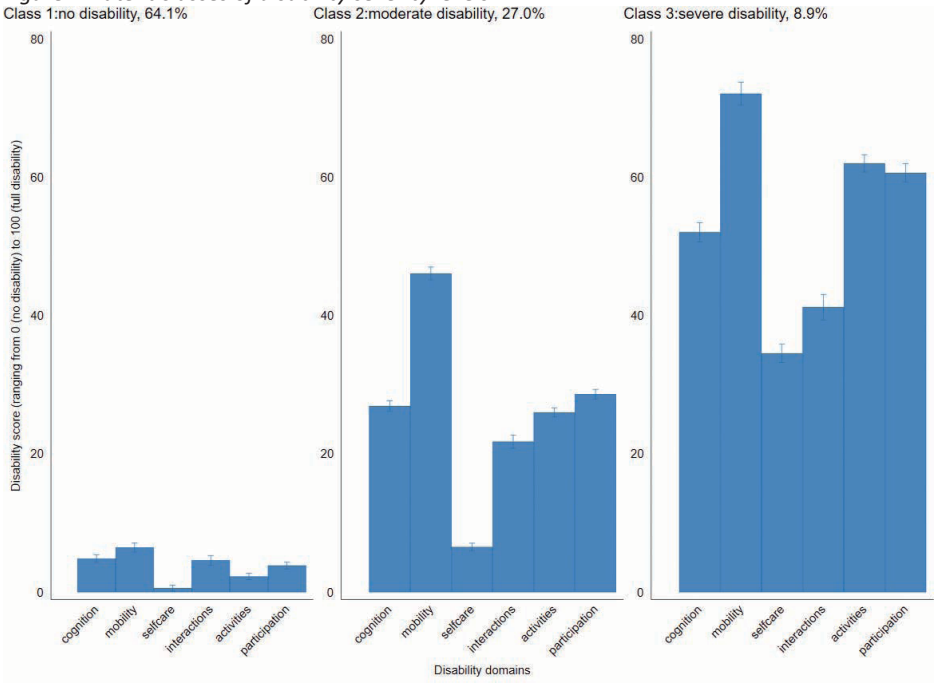
Figure 1: Latent classes of concordant and discordant cardiometabolic multimorbidity.



Disability levels

We ran LCA models from two to four classes selecting the three-class model based on indices of fit. The online supplementary file 3 shows the results of the fit indices. The three-class model had the lowest AIC and aBIC and thus was selected as the best-fit model. Figure 2 shows the disability levels. Class one comprised participants with extremely low WHODAS scores (64.1%) thus labelled “no disability”. Participants with moderate WHODAS scores (27.0%) characterized class two and thus labelled “moderate disability” while those with high WHODAS scores (8.9%) characterized class three and thus labelled “severe disability”.

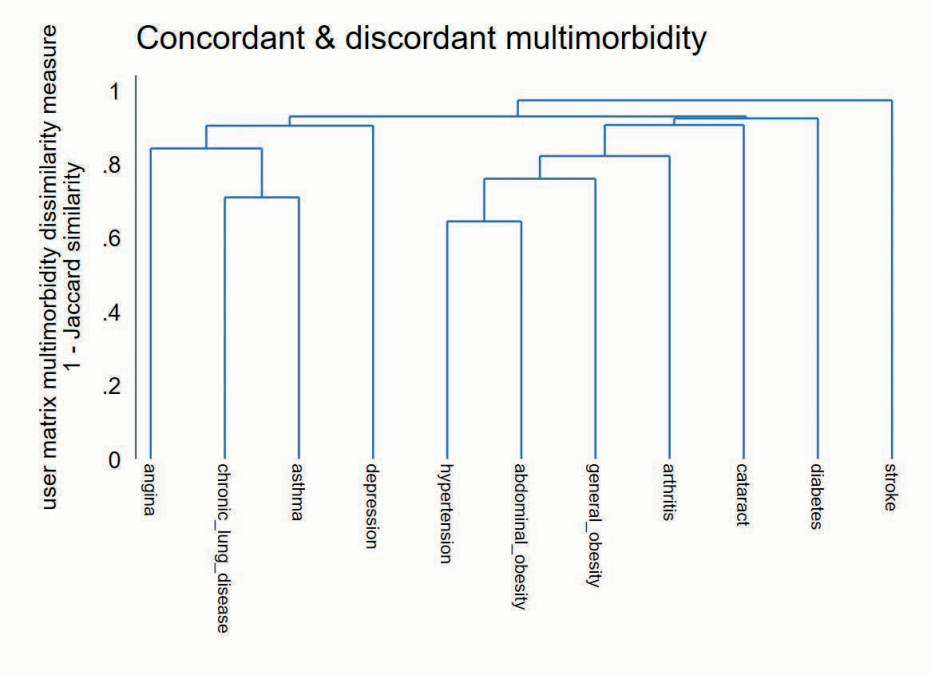
Figure 2: Latent classes of disability severity levels.



Hierarchical cluster analysis findings

As a supplementary analysis, we also calculated multimorbidity patterns using the agglomerative hierarchical cluster analysis. Figure 3 shows the hierarchical tree plot of the multimorbidity clusters (dendrogram). The dendrogram shows a graphical representation of the agglomeration schedules at which multimorbidity clusters are combined. In general, the findings were similar to those obtained using LCA. The hierarchical clustering algorithms revealed distinct groupings of concordant and discordant cardiometabolic multimorbidity in the study sample. Based on the proximity coefficients, the first cluster comprised angina, chronic lung disease, asthma and depression multimorbidity. The second cluster comprised hypertension, abdominal obesity, general obesity arthritis, cataract and diabetes multimorbidity.

Figure 3: Dendrogram of concordant and discordant cardiometabolic multimorbidity clusters.



Distribution of disability severity levels

The distribution of disability severity levels is presented in table 2. Severe disability was highest among older participants, females, unemployed, those with no formal education and participants from South Africa. We found no difference in severity levels of disability between rural and urban residents. Meanwhile, the prevalence of severe disability was highest among participants with discordant cardiometabolic multimorbidity comprising hypertension, abdominal obesity, diabetes, cataract and arthritis (23.5%) and those with angina, chronic lung disease, asthma and depression multimorbidity (20.7).

Table 2: Distribution of disability severity levels

Characteristics	Disability levels		
	No disability	Moderate	Severe
	n=2,387	n=1,425	n= 378
Age, (mean) SD	59.6 (7.6)	63.9 (9.3)	68.4 (11.2)
** Sex			
Male	72.0	22.2	5.8
Female	57.6	30.9	11.5

Table 2: Continued

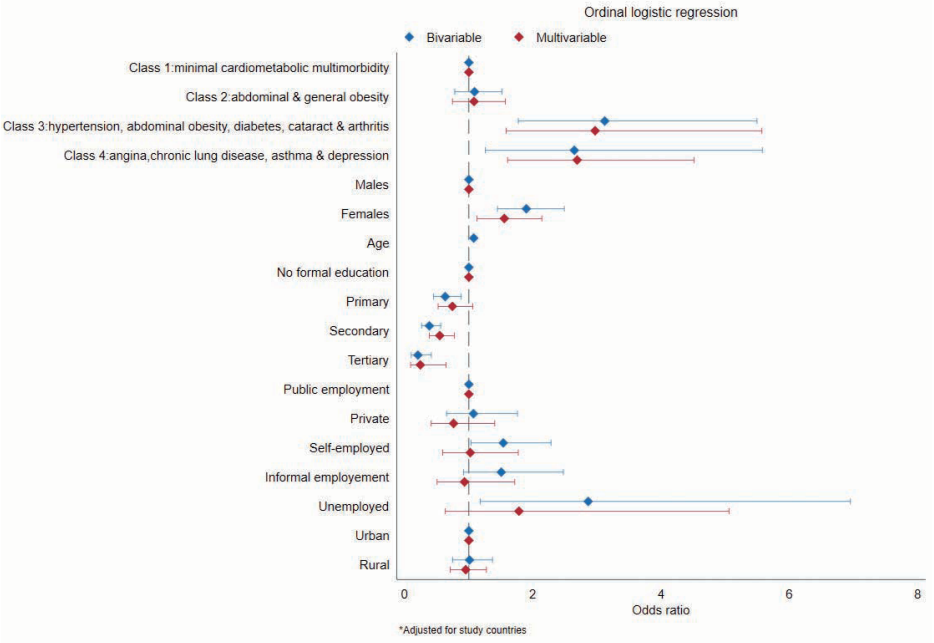
Characteristics	Disability levels		
	No disability n=2,387	Moderate n=1,425	Severe n= 378
**Education			
No formal education	51.0	36.0	13.0
Primary	62.6	27.8	9.5
Secondary	73.7	20.3	6.0
Tertiary	83.3	15.1	1.6
** Employment			
Public	70.3	26.1	3.5
Private	70.4	20.6	9.0
Self-employed	60.4	32.9	6.7
Informal employment	62.3	27.7	9.9
Informal	62.2	27.8	10.0
Unemployed	52.2	22.1	25.7
Residence			
Urban	64.5	26.0	9.5
Rural	63.7	29.1	7.3
*Study country			
Ghana	61.0	31.9	7.1
SA	66.3	23.7	10.0
**Concordant & discordant cardiometabolic multimorbidity classes			
Class 1:minimal cardiometabolic multimorbidity	68.0	26.2	5.9
Class 2:general and abdominal obesity class	66.6	25.5	7.9
Class 3:hypertension, abdominal obesity, diabetes, cataract and arthritis	44.0	32.5	23.5
Class 4:angina, chronic lung disease, asthma & depression	47.5	31.8	20.7
Total	64.1	27.0	8.9

*Cells are weighted row percentages, *p<0.05, ** p<0.001*
Class 1 comprised participants with minimal cardiometabolic multimorbidity. Class 2 comprised participants with high probabilities of general and abdominal obesity. Class 3 comprised participants with high probabilities of hypertension, diabetes, cataract and arthritis. Class 4 comprised participants with high probabilities of angina, chronic lung disease, asthma and depression

Cardiometabolic multimorbidity classes associated with moderate and severe disabilities

Figure 4 shows the results of ordinal logistic regression model. Compared to the participants with minimal cardiometabolic multimorbidity, the odds of moderate and severe disabilities were higher among participants with discordant cardiometabolic multimorbidity comprising hypertension, abdominal obesity, diabetes, cataract and arthritis [aOR=3.0; 95% CI 1.6 to 5.6] and those with angina, chronic lung disease, asthma and depression [aOR=2.7; 95% CI 1.6 to 4.5]. Being older was associated with higher odds of moderate and severe disabilities (aOR=1.1; 95% CI 1.1 to 1.1). The odds of moderate and severe disabilities were lower among those with secondary education (aOR=0.5; 95% CI 0.4 to 0.8) and tertiary education (aOR=0.2; 95% CI 0.1 to 0.6) compared to no formal education.

Figure 4: Ordinal regression of cardiometabolic multimorbidity classes associated with disability.



Discussion

In this study, we examined the latent classes of cardiometabolic multimorbidity associated with moderate and severe disability in Ghana and South Africa. We identified four distinct classes of cardiometabolic multimorbidity including a relatively healthy group with minimal cardiometabolic multimorbidity; general and abdominal obesity; hypertension, abdominal obesity, diabetes, cataract and arthritis; and angina, chronic lung disease, asthma and depression.

The cardiometabolic multimorbidity clusters identified in our study have similarities with findings from a systematic review of multimorbidity patterns in 14 studies drawn from across the world (53). The review identified three broad patterns of multimorbidity comprising cardiometabolic, musculoskeletal and mental health (53). In our study, 10.0% of the participants were classified under hypertension, abdominal obesity, diabetes, cataract and arthritis class, and 6.0% under angina, chronic lung disease, asthma and depression class.

Several underlying biological mechanisms could explain the clustering of concordant and discordant cardiometabolic multimorbidity identified in our study. Insulin resistance is well established in the literature as a possible pathophysiological mechanism explaining the clustering of cardiometabolic diseases (54-56). Insulin resistance may affect the metabolism process and lead to abnormalities of vascular reactivity (6). Modification of lifestyles to reduce metabolic syndrome and therapeutic intervention targeting insulin resistance may reduce the risk of cardiovascular diseases (57). The clustering of angina, chronic lung disease and asthma could be partly explained by inflammation, hypoxia, stress processes and environmental risk factors such as smoking or air pollution (53, 58).

Our results showed that 27.0% and 8.9% of the participants had moderate and severe disabilities with significant sociodemographic differences. Consistent with previous studies, being older, female, and having a low educational level were significantly associated with moderate and severe disabilities (59, 60). Although several previous studies have investigated the prevalence of disability among older adults, the heterogeneity in the definition of disability has hindered the comparison of findings. However, we selected three studies that are important for triangulation. The prevalence of ADL disability ranged from 1.6% to 16.6% in a study conducted in 2012 in South Africa and Ghana (61). Another study evaluating the burden of disability using the SAGE Wave 1 survey found that 38.6% and 44% of older adults in South Africa and Ghana had disabilities (62). Mitra et al. (2017) (32) also estimated the global prevalence of disability to be 14% from a sample of 54 countries. It is important to note that the disability severity levels were not investigated in the aforementioned studies. Moreover, only the physical components of disability were studied while in the current study, we incorporated the diverse dimensions of disability comprising bodily level, person level and societal level (20).

Relative to no disability, moderate and severe disabilities among older persons in Ghana and South Africa were significantly associated with two distinct discordant cardiometabolic multimorbidity classes comprising multimorbidity of hypertension, abdominal obesity, diabetes, cataract and arthritis and multimorbidity of angina, chronic lung disease, asthma and depression. Although previous studies have also attributed disability to the presence of multimorbidity, (1, 21-25), the vast majority of literature is based on disease counts or indices with inadequate information on specific

multimorbidity combinations (26, 27). Our findings add evidence to the discordant cardiometabolic multimorbidity combinations associated with moderate and severe disabilities to guide clinical and social interventions. However, there is still a lack of consensus on the pathway from the accumulation of chronic disease to disability (63). One possible explanation is the fact that multimorbidity may lead to anatomical and structural impairments, which results in functional limitations and finally moderate and severe disabilities (64). Further longitudinal studies are needed to determine the disability causal pathways and chronic disease aggregation.

Strengths and limitations

This study has several strengths. First, data are from nationally representative population-based surveys of chronic conditions using a standardised WHO-SAGE protocol. Hence, the results are generalizable to the populations of the study countries. Second, the data used are based on direct measures of BP, anthropometry, symptomatology algorithms, and self-reports allowing for a more objective screening for chronic diseases than self-reporting used in over three-quarters of previous studies (26). Third, the use of LCA in estimating the disability prevalence takes into consideration the heterogeneity of the disability severity levels frequently observed among the older population. Finally, the replication of the LCA results using the hierarchal cluster analysis of multimorbidity patterns strengthened the internal validity and robustness of the findings.

Our findings should be viewed considering some limitations. First, the screening questions for disability and chronic diseases were partially based on self-report. This may have resulted in the underestimation or overestimation of the true prevalence of disability severity levels and chronic diseases. However, previous studies in Ghana and South Africa have also reported consistent and similar prevalence rates (34, 61, 62). Moreover, several other studies have shown reasonable validity and reliability between self-reported diagnoses and physician-diagnosed conditions (65, 66).

Second, the number of cardiometabolic diseases and discordant chronic multimorbidity in the LCA was limited to those included in the SAGE survey. This may have left out other common chronic conditions among older persons, such as dementia and cancers, resulting in an underestimation of the multimorbidity prevalence. However, the observed prevalence of cardiometabolic multimorbidity in the current study is consistent with the findings of previous studies in Ghana and South Africa (67, 68). Future studies need to include more chronic diseases to increase the external validity. Finally, the cross-sectional design of the data used in the current analysis implies that we cannot make conclusions regarding the temporality or causation between the multimorbidity classes and disability. Future studies should use longitudinal analysis to estimate the incidence of transitions between latent classes and their impact on the disability.

Conclusions

Our results provide insight into the concordant and discordant cardiometabolic multimorbidity clusters associated with disability severity among older adults, using a case example of Ghana and South Africa. Moderate and severe disabilities relative to no disability were associated with two distinct multimorbidity clusters comprising multimorbidity of hypertension, abdominal obesity, diabetes, cataract and arthritis and multimorbidity of angina, chronic lung disease, asthma and depression. This evidence may be useful for defining disability prevention strategies and long-term care for older persons. Primary, secondary and tertiary prevention of functional disability at the population and individual level should target older persons with or at risk of concordant and discordant cardiometabolic multimorbidity comprising hypertension, abdominal obesity, diabetes, cataract and arthritis and multimorbidity of angina, chronic lung disease, asthma and depression.

Ethics approval and consent to participate

This study was approved by the World Health Organization's Ethical Review Board (reference number RPC149). The respondents went through an informed consent process and their participation was voluntary and anonymous. Written consent was provided before participation.

Availability of data and materials

Data used in the current study are publicly available on the microdata repository of the WHO (https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog).

Competing interest

The authors declare that they have no competing interest

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Authors' contributions

PO conceptualized the study, reviewed literature, and analysed the data. GA, CW, RS, WW, DM and CA made substantive contributions to the conceptualization of the study, and data analysis and reviewed the manuscript. All authors read and approved the final manuscript.

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Supplementary files

Supplementary file 1: Symptomatology algorithms

Arthritis	
Q1	During the last 12 months, have you experienced, pain, aching, stiffness, or swelling in or around the joints (like arms, hands, legs, or feet)which was not related to an injury and lasted for more than a month?
Q2	During the last 12 months, have you experienced stiffness in the joint in the morning after getting up from bed, or after a long rest of the joint without movement?
Q3	How long did this stiffness last?—1) less than 30 minutes; 2) more than 30 minutes `
Q4	Did this stiffness go away after exercise or movement in the joint?—1) yes; 2) no
Algorithm If the response to Q1 and 2 was "yes" and the response to questions 3 and 4 was the first option, the respondent was said to have arthritis	
Angina	
Q1	During the last 12 months, have you experienced any pain or discomfort in your chest when you walk uphill or hurry?
Q2	During the last 12 months, have you experienced any pain or discomfort in your chest when you walk at an ordinary pace on level ground?
Q3	What do you do if you get the pain or discomfort when you are walking?—1) stop or slow down; 2) carry on after taking a pain-relieving medicine that dissolves in your mouth; 3) carry on walking
Q4	If you stand still, what happens to the pain or discomfort?—1) relieved; 2) not relieved
Q5	Apart from these questions, respondents were asked to identify the points of pain in the upper part of the body (excluding the head) with the help of a picture depicting the upper parts of the body.
Algorithm If the response to Q1 and Q2 was "yes" and the response to Q3 and 4 was the first option, and in Q5 the respondent indicated that the pain was in the upper left part of the body, the person was said to have angina.	
Chronic Lung Disease	
Q1	During the last 12 months, have you experienced any shortness of breath at rest (while awake)?
Q2	During the last 12 months, have you experienced any coughing or wheezing for 10 minutes or more at a time?
Q3	During the last 12 months, have you experienced any coughing up of sputum or phlegm on most days of the month for at least 3 months?
Algorithm A respondent was ascertained to have chronic lung disease if his/her response was "yes" to Q1 or "yes" to both Q2 and Q3.	

Asthma

Q1 During the last 12 months, have you experienced attacks of wheezing or whistling breathing?

Q2 During the last 12 months, have you experienced an attack of wheezing that came on after you stopped exercising or some other physical activity?

Q3 During the last 12 months, have you had a feeling of tightness in your chest?

Q4 During the last 12 months, have you woken up with a feeling of tightness in your chest in the morning or any other time?

Q5 During the last 12 months, have you had an attack of shortness of breath that came on without an obvious cause when you were not exercising or doing some physical activity?

Algorithm
A respondent was said to suffer from asthma if s/he responded "yes" to Q1 and "yes" to any of the subsequent Q2–Q5.

Depression

Q1 During the last 12 months, have you had a period lasting several days when you felt sad, empty, or depressed?

Q2 During the last 12 months, have you had a period lasting several days when you lost interest in most things you usually enjoy, such as personal relationships, work, or hobbies/recreation?

Q3 During the last 12 months, have you had a period lasting several days when you have been feeling your energy decreased or that you are tired all the time?

If the response to any of the above 3 questions was "yes," then the following set of questions was asked:

Q4 Did this period (of sadness/loss of interest/low energy) last for more than 2 weeks?

Q5 Was this period (of sadness/loss of interest/low energy) most of the day, nearly every day?

Q6 During this period, did you lose your appetite?

Q7 Did you notice any slowing down in your thinking?

Q8 Did you notice any problems falling asleep?

Q9 Did you notice any problems waking up too early?

Q10 During this period, did you have any difficulties concentrating—for example, listening to others, working, watching television, listening to the radio?

Q11 Did you notice any slowing down in your moving around?

Q12 During this period, did you feel anxious and worried most days?

Q13 During this period, were you so restless or jittery nearly every day that you paced up and down and could not sit still?

Q14 During this period, did you feel negative about yourself or like you had lost confidence?

Q15 Did you frequently feel hopeless—that there was no way to improve things?

Q16 During this period, did your interest in sex decrease?

Q17 Did you think of death, or wish you were dead?

Q18 During this period, did you ever try to end your life?

Algorithm

To ascertain depression from this set of questions, 2 sets of variables were computed. The first set of variables was based on Q1–Q5 and Q16. From this set, 3 variables were computed taking the values 0 and 1, as follows:

1. The first variable takes the value 1 if the response to any of Q1, Q4, and Q5 is "yes."
2. The second variable takes the value 1 if the response to Q2 or Q16 is "yes."
3. The third variable takes the value 1 if the response to Q3 is "yes."

The second set of variables was based on Q6–Q15, Q17, and Q18. From these questions, 7 variables were computed.

1. The first variable takes the value 1 if the response to Q14 or Q15 is "yes."
2. The second variable takes the value 1 if the response to Q12 or Q13 is "yes."
3. The third variable takes the value 1 if the response to Q17 or Q18 is "yes."
4. The fourth variable takes the value 1 if the response to Q7 or Q10 is "yes."
5. The fifth variable takes the value 1 if the response to Q11 is "yes."
6. The sixth variable takes the value 1 if the response to Q8 or Q9 is "yes."
7. The seventh variable takes the value 1 if the response to Q6 is "yes."

These newly created variables from the respective sets were added to obtain 2 new variables, the first consisting of the sum of the first set of variables (maximum value 3) and the second consisting of the sum of the second set of variables (maximum value 7). Based on these 2 variables, a respondent was said to suffer from depression if s/he had a value for the first variable of 2 or more and a value for the second variable of 4 or more

Supplementary file 2: Comparison of the characteristics of complete cases and incomplete cases

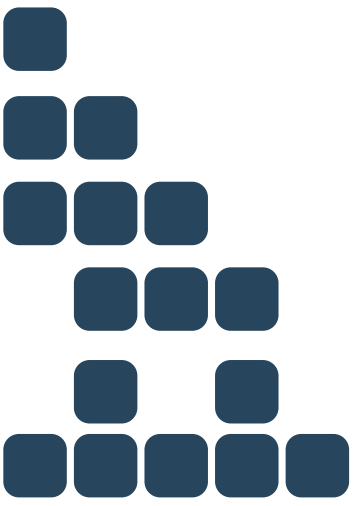
Background Characteristics	Complete cases	Incomplete cases	Std. Diff
Number of study participants	4,190	1,567	
Proportion (%)	72.8%	27.2%	
Mean age: All participants (SD)	64.1 (10.0)	65.8 (11.0)	0.16
Males (SD)	64.9 (10.1)	66.9 (10.9)	0.19
Females (SD)	63.5 (9.9)	65.3 (11.0)	0.17

SD: standard deviation, Std Diff: standard difference. Std Diff= Difference in means divided by standard error; imbalance defined as an absolute value greater than 0.2

Supplementary file 3: Comparison between latent class models

Number of latent classes	CAIC	aBIC
Concordant & discordant cardiometabolic comorbidities		
2	32427.4	32566.9
3	31934.4	32156.3
4	**31791.5**	**32089.5**
5	31748.2	32103.3
Disability (WHODAS scores)		
2	212065.2	212185.6
3	**206668.7**	**206833.5**
4	206682.7	206891.9

Note: Boldface type indicates the selected model. aBIC adjusted Bayesian Information Criterion, CAIC consistent Akaike Information Criterion, WHODAS, World Health Organization Disability Assessment



4

Cardiometabolic multimorbidity and associated patterns of healthcare utilization and quality of life: results from the Study on Global AGEing and Adult Health (SAGE) Wave 2 in Ghana

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Abstract

Understanding the patterns of multimorbidity, defined as the co-occurrence of more than one chronic condition, is important for planning health system capacity and response. This study assessed the association of different cardiometabolic multimorbidity combinations with healthcare utilization and quality of life (QoL). Data were from the World Health Organization (WHO) study on global AGEing and adult health Wave 2 (2015) conducted in Ghana. We analysed the clustering of cardiometabolic diseases including angina, stroke, diabetes, and hypertension with unrelated conditions such as asthma, chronic lung disease, arthritis, cataract and depression. The clusters of adults with cardiometabolic multimorbidity were identified using latent class analysis and agglomerative hierarchical clustering algorithms. We used negative binomial regression to determine the association of multimorbidity combinations with outpatient visits. The association of multimorbidity clusters with hospitalization and QoL were assessed using multivariable logistic and linear regressions. Data from 3,128 adults aged over 50 years were analysed. We identified four distinct classes of multimorbidity: relatively "healthy class" with no multimorbidity (47.9%): abdominal obesity only (40.7%): cardiometabolic and arthritis class comprising participants with hypertension, type 2 diabetes, stroke, abdominal and general obesity, arthritis and cataract (5.7%); and cardiopulmonary and depression class including participants with angina, chronic lung disease, asthma, and depression (5.7%). Relative to the class with no multimorbidity, the cardiopulmonary and depression class was associated with a higher frequency of outpatient visits [β=0.3; 95% CI 0.1 to 0.6] and higher odds of hospitalization [aOR=1.9; 95% CI 1.0 to 3.7]. However, cardiometabolic and arthritis class was associated with a higher frequency of outpatient visits [β=0.8; 95% CI 0.3 to 1.2] and not hospitalization [aOR=1.1; 95% CI 0.5 to 2.9]. The mean QoL scores was lowest among participants in the cardiopulmonary and depression class [β=-4.8; 95% CI -7.3 to -2.3] followed by the cardiometabolic and arthritis class [β=-3.9; 95% CI -6.4 to -1.4]. Our findings show that cardiometabolic multimorbidity among older persons in Ghana cluster together in distinct patterns that differ in healthcare utilization. This evidence may be used in healthcare planning to optimize treatment and care.

Keywords: Cardiometabolic diseases, multimorbidity, healthcare utilization, hospitalization, quality of life, latent class analysis, agglomerative hierarchical cluster analysis.

Background

Sub-Saharan Africa is undergoing more rapid ageing than high-income countries (HIC) (1). This poses potential critical challenges for older persons, central among them is the burden of chronic diseases (2). People living with chronic conditions often have multiple rather than a single condition, commonly referred to as multimorbidity (3). In Ghana, three in every five older persons aged above 50 years live with multimorbidity (4). Cardiometabolic diseases such as hypertension and diabetes account for the highest burden of multimorbidity in Ghana (5). Importantly, cardiometabolic diseases often coexist with other chronic diseases with unrelated pathophysiology such as mental illnesses, chronic lung diseases and musculoskeletal disorders (6-8). This phenomenon is referred to as discordant multimorbidity (9).

The management of multimorbidity is complex and demanding for healthcare systems in Ghana (10, 11). This is because the current chronic disease management guidelines were developed when having a single chronic disease was common and focused on a single disease (12, 13). The recent World Health Organization (WHO) guidelines on multimorbidity question this single-disease management approach and highlight the need for accounting for all multimorbidities when informing the patient about available treatment options (14). However, studies conducted in Ghana show that people living with multimorbidity face several challenges such as fragmented appointments, difficulties with access to information, and a lack of coherence or coordination of care (15, 16). Furthermore, therapeutic interventions for multimorbidity are a major challenge due to polypharmacy and poor medication adherence (17). Integrated management of multimorbidity and a shift of the treatment goals towards medical care that is less disruptive may partly lower the treatment burden (18).

Previous studies show a positive association between the number of co-existing chronic conditions and frequency of outpatient visits, longer hospital stays, and poor health-related quality of life (4, 19-22). However, the multimorbidity counts or indices used in the vast majority of existing studies do not provide adequate information on specific disease clusters to guide integrated care interventions (23, 24). Although the use of disease count is important in establishing the prevalence of multimorbidity, clusters of conditions that tend to co-occur non-randomly is more useful for clinical practice and health policy. Thus, a deeper insight into the multimorbidity burden on healthcare utilization that goes beyond counting the number of coexisting chronic conditions is needed (25). Understanding multimorbidity clusters and healthcare utilization patterns is important for planning health system capacity and response to optimise healthcare resources and accommodate patient needs.

The aim of this study was to identify classes of adults with cardiometabolic multimorbidity and determine the association of different multimorbidity combinations with healthcare utilization and quality of life (QoL).

Methods

Study design

The data for this study are from the WHO Study on Global AGEing and Adult Health (SAGE) Wave 2 survey conducted in Ghana in 2015 (26). The WHO SAGE aims to provide reliable evidence on the health and well-being of older persons aged over 50 years in low and middle-income countries (27). The study design is provided elsewhere (28). In brief, a stratified multistage cluster sampling method was used to collect data from a nationally representative sample of adults aged 50 years and older. Detailed descriptions of sampling methods and data collection procedures have been previously published (28-30).

The original study sample comprised 3,575 older persons aged over 50 years. Participants were included in the current analysis if they had valid data on the key variables: chronic diseases such as angina pectoris, stroke, diabetes mellitus, hypertension, obesity, arthritis, asthma, chronic lung disease, depression, and cataracts and sociodemographic characteristics comprising sex, age, and employment. Participants (n=447) for which data on key variables were not captured or judged as invalid were excluded. Since the causes of missing information were not ascertained, we did not apply missing data techniques to avoid further uncertainty in the imputation models. Thus, the final analysis included 3,128 participants.

Data collection

Data used in the current study were collected using interviewer-administered structured questionnaires (31). Detailed information on the study tools has been published (32). Data were collected on socio-demographic characteristics, chronic conditions, healthcare utilization and QoL. The chronic conditions comprised cardiometabolic diseases such as angina pectoris, stroke, diabetes, obesity and hypertension, and unrelated conditions such as arthritis, asthma, chronic lung disease, depression, and cataracts.

Measurement and definition of variables

Outcome variable.

The outcome variables were frequency of outpatient visits, hospitalization and QoL. The frequency of outpatient visits was measured as the number of times a participant had an outpatient visit in the preceding 12 months. Hospitalization was measured as any overnight stays in the hospital that lasted for at least one night in the past 12 months. An 8-item World Health Organization Quality of Life (WHOQOL) instrument was used to assess the QoL score (33). The WHOQOL comprises two questions across

each of the four main life domains: physical, psychological, social, and environmental (33). Using a five-point Likert scale, ranging from very satisfied to very dissatisfied, the respondents rated their satisfaction with life domains such as health, ability to perform daily activities and meet basic needs, relationships, and environment. The composite score of QoL is the sum of the 8 items from the four domains expressed as a percentage.

Explanatory variables

The main explanatory variable was cardiometabolic multimorbidity defined as the coexistence of at least two cardiometabolic diseases including obesity, angina, stroke, diabetes, hypertension or a discordant multimorbidity comprising at least one cardiometabolic disease and an unrelated chronic disease such as asthma, chronic lung disease, arthritis, cataract and depression. The multimorbidity clusters were named based on their unique dominant chronic diseases.

Self-reported history of diagnosis by a healthcare professional was extracted for cardiometabolic diseases comprising angina, stroke, type 2 diabetes, hypertension and other conditions such as arthritis, asthma, chronic lung disease, depression, and cataract. The WHO symptomatology algorithms (34-36) were used to screen for angina pectoris, arthritis, asthma, chronic lung disease, and depression. Supplementary file 1 shows the details of the symptomatology algorithms. Physical measurements comprised screening for BP and anthropometrics. Hypertension was defined as systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg or previous diagnosis of hypertension by a professional health care provider and/or being on hypertensive therapy (37). Abdominal obesity was defined using WHO guidelines as waist circumference ≥ 94 cm for men or ≥ 80 cm for women (38). General obesity was defined as body mass index ≥30.0 kg/m^2 (39).

Other explanatory variables comprised sociodemographic and health characteristics such as sex, age, education, employment, health insurance coverage, primary source of care (private, public, faith-based/charity hospital) and place of residence (urban or rural).

Data analysis

Descriptive statistics comprising frequencies, means, medians, standard deviations, interquartile range, and Pearson's chi-squared tests were used to summarize the characteristics of the study participants while accounting for sampling weights.

Latent class analysis

Latent Class Analysis (LCA) was used to place participants in a number (K) of clinically meaningful classes of cardiometabolic multimorbidity. The number of multimorbidity classes was defined a priori using the adjusted Bayesian information criterion (BIC), a model selection method that balances fit with parsimony (40). Five plausible LCA models were delineated, characterized by increasing numbers of chronic disease classes from one to five (Supplementary file 2). The model with the lowest value of the BIC index was

selected as the best-fitting model considering interpretability and clinical judgment (40, 41). Posterior probabilities were used to determine the likelihood of class membership. Finally, the participants were grouped into the multimorbidity classes with the highest-class probability (42).

Hierarchical cluster analysis

We identified clinically meaningful clusters of multimorbidity using agglomerative hierarchical clustering algorithms (43). Data used in our analysis are a collection of binary objects arranged in an n×p matrix. The rows represent the (n=3, 128) study participants and the columns represent the (p=11) chronic diseases including abdominal obesity, hypertension, general obesity, arthritis, asthma, cataract, diabetes, angina, chronic lung disease, depression and stroke. The classical approach to the analysis of multimorbidity clusters comprises the grouping of "n" study participants into a set of clusters using the proximity index among the study respondents. This yields an "n×n" proximity matrix that reflects the degree of closeness among the study participants and describes the patterns of disease clusters. However, in the current study, we analysed the multimorbidity patterns by clustering the outcome variables i.e. multimorbidity rather than the observations. This approach is more robust than the former since it reduces the transposed "p×n" data matrix to a much smaller "p×p" proximity matrix among the chronic disease outcomes compared to a potentially large "n×n" proximity matrix (44). First, individual chronic diseases were grouped in a single cluster. Second, the individual disease clusters were gradually merged with the most closely related clusters until a single cluster with all the elements was obtained. To accommodate the spread of the cluster, we used the average linkage method (45). Finally, we assessed the number of clusters using a dendrogram and Jaccard similarity coefficient (43).

Regression analysis

We used negative binomial regression to determine the association of multimorbidity combinations with outpatient visits. Negative binomial regression has inbuilt parameters that account for the overdispersion problem of modelling healthcare utilization frequency (46). The association of multimorbidity combinations with hospitalization and QoL were assessed using multivariable logistic and linear regressions. Bivariable negative binomial regression, logistic and linear regression with the frequency of outpatient visits, hospitalization, and QoL as the outcome variables, were first fitted for each of the multimorbidity classes followed by a multivariable model adjusting for socio-demographic characteristics namely age, sex, education, employment status, health insurance coverage, and place of residence. Because of the clustered design of the sample, robust variance estimates (Huber-White sandwich estimator) were used for the correction of standard errors to adjust for the correlation among responses within the same household (47). The strength of association was interpreted using the adjusted odds ratios (aOR) and 95% confidence intervals (CI) from logistics regression

and beta (β) coefficients from negative binomial and linear regressions (48, 49). P values of <0.05 were considered statistically significant

We assessed the goodness of fit of the bivariate and multivariable models using the likelihood ratio test (50).

All statistical analyses were carried out using Stata 17.0 (StataCorp LP, Texas, USA) and accounted for the complex sampling design used in the WHO SAGE survey.

Ethics approval and consent to participate

All methods were carried out in accordance with the relevant guidelines and regulations. This study was approved by the World Health Organization's Ethical Review Board (reference number RPC149) and the Ethical and Protocol Review Committee, College of Health Sciences, University of Ghana, Accra, Ghana. The respondents went through an informed consent process and their participation was voluntary and anonymous. Written consent was provided before participation.

Results

Characteristics of participants

The sociodemographic and health characteristics of the study participants are presented in Table 1. In total, 3,128 participants were included in the analysis. In general, most of the participants were women, aged between 50-59 years (51.2%), had no formal education (41.5%), self-employed (69.7%), lived in rural areas (52.1%), and sought care from public facilities (41.4%). Only a quarter of the participants had health insurance coverage. The most prevalent chronic diseases were abdominal obesity (47.0%) and hypertension (37.1%). The prevalence of abdominal and general obesity, arthritis angina and depression were significantly higher in females than males.

Table 1: Sociodemographic and health characteristics of the study participants

Characteristics (%)	Both sexes	Males	Females	P value
N	3,128	1,306	1,822	
Age (Years)				0.063
50-59	51.2	52.5	50.0	
60-69	27.5	28.3	26.7	
70+	21.3	19.2	23.3	
Education				<0.001
No formal education	41.5	29.8	52.2	
Primary	28.3	28.7	27.8	
Secondary	26.5	35.9	17.9	
Tertiary	3.7	5.6	2.1	

Table 1: Continued

Characteristics (%)	Both sexes	Males	Females	P value
N	3,128	1,306	1,822	
Employment				<0.001
Public	7.8	11.7	4.3	
Private	4.4	6.7	2.2	
Self-employed	69.7	64.8	74.2	
Informal employment	16.2	15.2	17.2	
Unemployed	1.9	1.7	2.0	
Place of residence				0.785
Urban	47.9	47.5	48.2	
Rural	52.1	52.5	51.8	
Primary source of care				0.013
Private facility	9.3	8.8	9.6	
Public facility	41.4	37.4	45	
Faith-based/charity hospital	4.0	4.3	3.7	
[†] Others	3.6	3.6	3.6	
Never sought care	41.8	45.9	38.1	
Health insurance coverage				
Yes	25.4	21.6	28.9	<0.001
Chronic diseases				
Abdominal obesity	47.0	16.5	74.8	<0.001
Hypertension	37.1	36.7	37.4	0.761
General obesity	13.4	5.9	20.2	<0.001
Arthritis	20.4	17.3	23.2	0.005
Asthma	8.3	8.0	8.6	0.634
Cataract	7.2	6.4	7.9	0.201
Diabetes	2.6	2.5	2.7	0.798
Angina	8.4	5.0	11.4	<0.001
Chronic lung disease	4.5	4.1	4.8	0.343
Depression	4.5	3.1	5.7	<0.001
Stroke	1.2	1.1	1.3	0.502

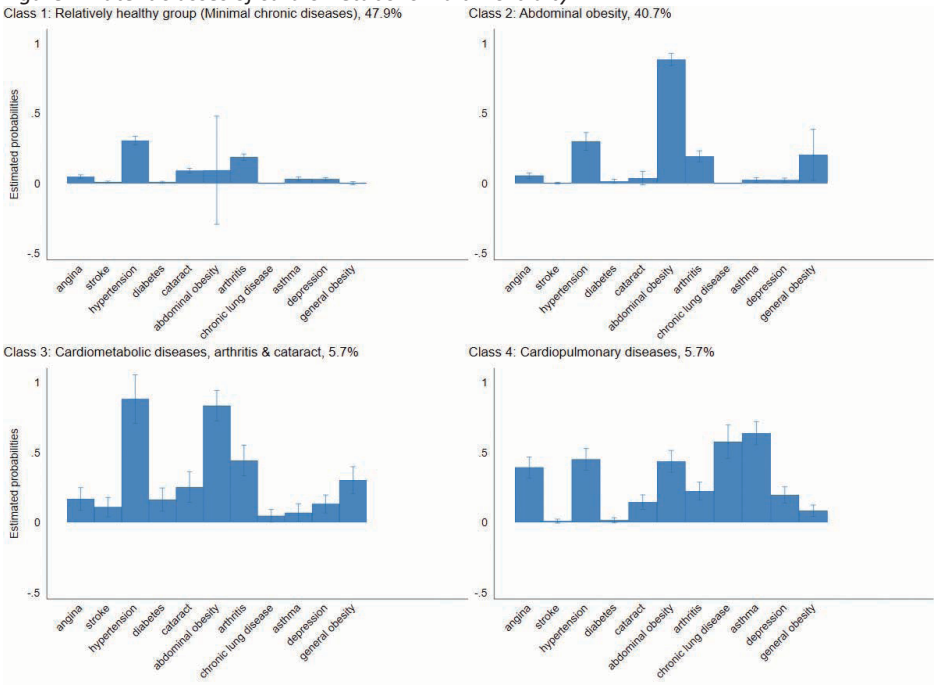
Cells are weighted percentages unless otherwise specified

[†] Other sources of primary care comprise local pharmacies and traditional healers.

Findings of Latent Class Analysis

The multimorbidity classes are shown in Figure 1. We compared LCA models with 1 to 5 classes (online supplementary file 2). The four-class model had the lowest BIC index and thus was selected as the best-fit model. Class one comprised relatively "healthy participants" with no multimorbidity (47.9%). Class two included participants with a high probability of abdominal obesity (40.7%). Class three comprised participants with high probabilities of hypertension, diabetes, stroke, abdominal and general obesity, arthritis and cataract (5.7%). Class four (cardiopulmonary diseases and depression) comprised participants with high probabilities of angina, chronic lung disease, asthma and depression (5.7%).

Figure 1: Latent classes of cardiometabolic multimorbidity

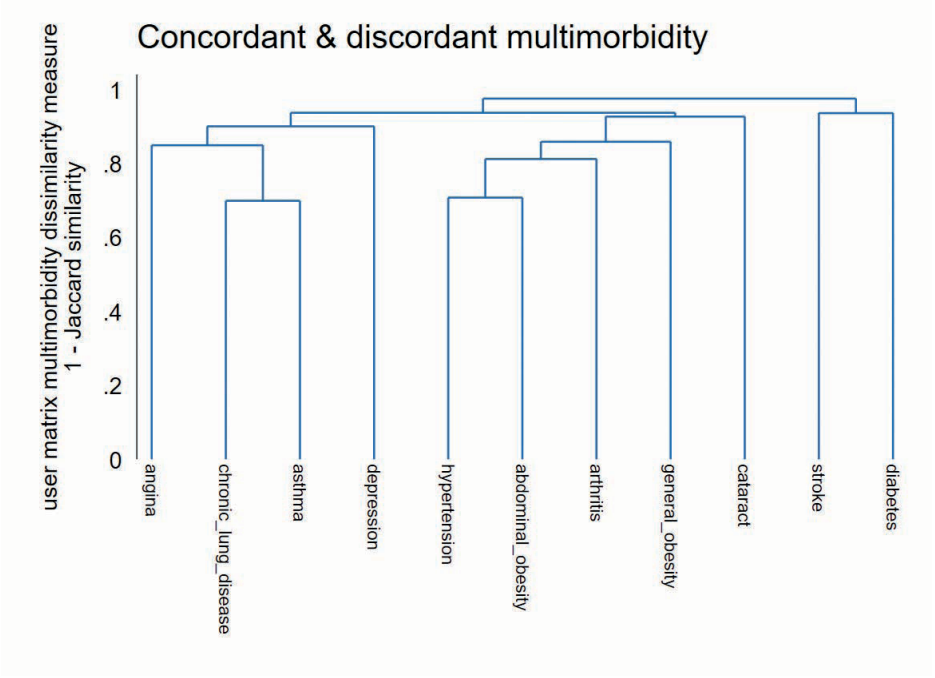


Hierarchical cluster analysis findings

As a supplementary analysis, we used hierarchical cluster analysis with agglomerative algorithms to compute the multimorbidity patterns. Figure 2 shows a dendrogram with a hierarchical tree plot of the multimorbidity clusters. The dendrogram shows a graphical representation of the agglomeration schedules at which multimorbidity clusters are combined. In general, our results were consistent with those obtained using LCA. The hierarchical clustering algorithms revealed distinct groupings of multimorbidity in the study sample. Based on the proximity coefficients, the first cluster comprised angina, chronic lung disease, asthma, and depression (cardiopulmonary and depression class). The second

cluster comprised participants with hypertension, abdominal and general obesity, arthritis, cataract stroke and diabetes (cardiometabolic diseases, arthritis and cataract class).

Figure 2:Dendrogram of concordant and discordant cardiometabolic multimorbidity clusters



Sociodemographic distribution of multimorbidity patterns

The sociodemographic distribution of multimorbidity classes is presented in Table 2. The majority of the participants with abdominal obesity were aged between 50 and 59 years. However, most participants with cardiometabolic and cardiopulmonary multimorbidity were older (aged 60-69 years and 70 years and above). Most participants with abdominal obesity and cardiometabolic multimorbidity resided in urban settings while a majority of those with cardiopulmonary multimorbidity resided in rural settings. In general, most of the participants with abdominal obesity and those with cardiometabolic and cardiopulmonary multimorbidity were females, self-employed, had no formal education nor insurance coverage, and sought care from public facilities.

Table 2: Distribution of multimorbidity by sociodemographic characteristics in Ghana

Characteristics (%)	‡Latent classes of multimorbidity				
Class 1: Relatively healthy/no multimorbidity diseases	Class 2: Abdominal obesity	Class 3: Cardiometabolic diseases, arthritis & cataract	Class 4: Cardiopulmonary diseases & depression		P-value
N	1,482	1,283	166	197	
Age (years)					
50-59	50.1	57.6	31.0	35.5	<0.001
60-69	28.3	24.8	41.0	26.1	
70+	21.7	17.6	28.0	38.4	
Sex					
Male	76.0	18.9	22.5	41.2	<0.001
Female	24.0	81.1	77.5	58.8	
Education					
No formal education	40.2	42.6	33.7	52.3	0.080
Primary	27.6	29.5	34.7	19.1	
Secondary	28.6	23.9	26.5	28.1	
Tertiary	3.7	4.1	5.1	0.6	
Employment					
Public	8.4	7.1	6.9	9.0	<0.001
Private	5.6	2.1	11.5	3.5	
Self-employed	67.1	75.5	58.7	61.1	
Informal employment	17.1	13.9	16.5	25.2	
Unemployed	1.8	1.4	6.4	1.2	
Residence					
Urban	40.8	54.7	69.6	37.8	<0.001
Rural	59.2	45.3	30.4	62.2	
Primary source of care					
Private facility	7.5	9.5	21.5	10.5	<0.001
Public facility	37.9	44.2	48.5	43.8	
Faith-based/ charity hospital	5.0	2.8	1.8	5.4	
†Others	4.2	3.7	0.2	1.1	
Never sought care	45.4	39.8	28.0	39.2	

Table 2: Continued

Characteristics (%)	‡Latent classes of multimorbidity				
Class 1: Relatively healthy/no multimorbidity diseases	Class 2: Abdominal obesity	Class 3: Cardiometabolic diseases, arthritis & cataract	Class 4: Cardiopulmonary diseases & depression		P-value
N	1,482	1,283	166	197	
Health insurance cover					
Yes	23.8	26.8	28.2	26.3	0.490
No	76.2	73.2	71.8	73.7	

Cells are weighted column percentages

† Other sources of primary care comprise local pharmacies and traditional healers

IQR; Interquartile range

‡The multimorbidity clusters included a relatively "healthy class" with no multimorbidity (class 1): abdominal obesity (class 2): cardiometabolic and arthritis class comprising participants with hypertension, abdominal and general obesity, arthritis and cataract (class 3); and cardiopulmonary and depression class including participants with angina, chronic lung disease, asthma, and depression (class 4).

Frequency of healthcare utilization and quality of life

The patterns of healthcare utilization and QoL is presented in Table 3. In general, the participants who visited outpatient clinics frequently and those hospitalized at least once in the previous 12 months were older, women, lived in urban settings, sought primary care from faith-based or charity organizations, and had cardiometabolic and cardiopulmonary multimorbidity. Other participants who visited outpatient clinics frequently mostly comprised those with tertiary-level of education and health insurance coverage and employed in public or informal settings. The QoL score was lowest among older participants, females, unemployed, those with no formal education nor health insurance coverage, living in urban settings, seeking care from faith-based or charity organizations, and participants with cardiometabolic and cardiopulmonary multimorbidity.

Table 3: Healthcare utilization and quality of life in Ghana (n=3,128)

Characteristics	Outpatient visits			Hospitalized		Quality of life		
	Median	IQR	P-Value	Yes	P-value	%	SD	P-value
Age (years)								
50-59	0	1	<0.001	3.6	0.028	76.3	9.5	<0.001
60-69	1	1		4.6		73.8	9.9	
70+	1	1		6.3		68.3	12.1	
Sex								
Male	0	1	<0.001	1.9	0.192	75.5	10.9	<0.001
Female	1	1		2.6		72.4	10.3	

Table 3: Continued

Characteristics	Outpatient visits			Hospitalized		Quality of life		
	Median	IQR	P-Value	Yes	P-value	%	SD	P-value
Education								
No formal education	0	1		1.7	0.826	71.3	10.2	<0.001
Primary	0	1		1.4		74.4	10.8	
Secondary	1	1		1.2		76.5	10.3	
Tertiary	1	2		0.2		80.0	9.7	
Employment								
Public	1	2	<0.001	3.1	0.035	76.9	11.0	<0.001
Private	0	1		0.2		75.2	10.7	
Self-employed	0	1		4.4		74.2	10.3	
Informal employment	1	2		6.2		71.3	11.5	
Unemployed	0	2		6.7		70.0	11.3	
Residence								
Urban	1	2	<0.001	5.3	0.068	74.9	11.1	<0.001
Rural	0	1		3.7		73.0	10.2	
Primary source of care								
Private facility	1	2	<0.001	9.1	<0.001	74.6	9.6	<0.001
Public facility	1	2		7.6		72.1	10.5	
Faith-based/charity hospital	1	3		10.6		70.6	9.9	
†Others	1	1		1.5		70.0	12.2	
Never sought care						76.2	10.5	
Health insurance cover								
Yes	1	1	<0.001	6.0	0.035	73.2	10.2	0.528
No	0	1		3.9		74.1	10.8	
‡Multimorbidity clusters								
Class 1: Relatively healthy class/no multimorbidity	0	1	<0.001	3.8	0.128	74.7	10.4	<0.001
Class 2: Abdominal obesity	1	1		4.6		74.5	10.2	
Class 3: Cardiometabolic diseases, arthritis & cataract	1	3		5.2		68.9	11.3	

Table 3: Continued

Characteristics	Outpatient visits			Hospitalized		Quality of life		
	Median	IQR	P-Value	Yes	P-value	%	SD	P-value
Class 4: Cardiopulmonary diseases & depression	1	2		8.1		67.5	12.4	
Total	0	1		4.5		73.9	10.7	

Cells are weighted column percentages
† Other sources of primary care comprise local pharmacies and traditional healers
IQR; Interquartile range
‡The multimorbidity clusters included a relatively "healthy class" with no multimorbidity (class 1): abdominal obesity (class 2): cardiometabolic and arthritis class comprised participants with hypertension, abdominal and general obesity, arthritis and cataract (class 3); and cardiopulmonary and depression class included participants with angina, chronic lung disease, asthma, and depression (class 4).

Cardiometabolic multimorbidity classes and associated healthcare utilization patterns and QoL in Ghana

Figure 3 shows the association of different multimorbidity combinations with healthcare utilization and QoL. Relative to the class with no multimorbidity, the cardiopulmonary and depression class was associated with a higher frequency of outpatient visits [β=0.3; 95% CI 0.1 to 0.6] and higher odds of hospitalization [aOR=1.9; 95% CI 1.0 to 3.7]. However, cardiometabolic and arthritis class was associated with a higher frequency of outpatient visits [β=0.8; 95% CI 0.3 to 1.2] and not hospitalization [aOR=1.1; 95% CI 0.5 to 2.9]. The mean QoL scores was lowest among participants in the cardiopulmonary and depression class [β=-4.8; 95% CI -7.3 to -2.3] followed by the cardiometabolic and arthritis class [β=-3.9; 95% CI -6.4 to -1.4].

Discussion

In this study, we identified classes of adults with cardiometabolic multimorbidity and assessed the association of different multimorbidity combinations with healthcare utilization and QoL. Our findings show four distinct patterns of multimorbidity: relatively "healthy class" with no multimorbidity : abdominal obesity: cardiometabolic and arthritis class comprising participants with hypertension, diabetes, stroke, abdominal and general obesity, arthritis and cataract; and cardiopulmonary and depression class including participants with angina, chronic lung disease, asthma, and depression cardiopulmonary multimorbidity was associated with a higher frequency of outpatient visits and higher odds of hospitalization compared to those with no multimorbidity . However, multimorbidity of cardiometabolic diseases, cataracts and arthritis was associated with a higher frequency of outpatient visits and not hospitalization. Participants with cardiometabolic and cardiopulmonary multimorbidity had poorer quality of life compared to those with no multimorbidity.

Figure 3: Association of cardiometabolic multimorbidity combinations with healthcare utilization and QoL

The multimorbidity clusters identified in our study are similar to those in previous studies (51, 52). A systematic review of multimorbidity patterns from 39 studies conducted in 12 countries identified hypertension and arthritis as the most frequent multimorbidity combination (52). Another study conducted in South Africa found two distinct multimorbidity clusters comprising hypertension and diabetes and cardiopulmonary diseases such as angina, asthma and chronic lung disease (51). In our study: 47.9% of the participants were classified under a relatively "healthy class" with no multimorbidity: 40.7% under the abdominal obesity class: 5.7% under the cardiometabolic and arthritis class and 5.7% under the cardiopulmonary diseases and depression class. The mechanisms that underlie the clustering of cardiopulmonary diseases and depression are not definitive. However, there is strong evidence linking inflammatory markers to both depression and cardiovascular diseases (53), but why these links exist remains unclear.

Systematic reviews conducted by Mullerova et al. (54) and Prados-Torres et al. (55), identified inflammation, stress processes, hypoxia, and environmental risk factors such as air pollution and smoking as the leading risk factors for the clustering of cardiopulmonary diseases such as hypertension, angina, chronic lung disease and asthma (54, 55). Similarly, our previous study on the patterns of cardiometabolic multimorbidity in sub-Saharan Africa identified the clustering of physical inactivity and obesity as one of the leading risk factors for cardiometabolic multimorbidity. However, the study did not include the clustering of cardiometabolic diseases with unrelated conditions such as arthritis, cataract and chronic respiratory diseases (56). Importantly, the discordant multimorbidity clusters without well-established pathogeneses such as cardiometabolic diseases and arthritis identified in the current study should be studied in the future to elucidate the causal pathways.

Our findings show that the multimorbidity patterns among older adults in Ghana are distinct with important differences with respect to healthcare utilization and QoL. Multimorbidity of cardiometabolic diseases, arthritis and cataract was associated with higher levels of healthcare utilization than cardiopulmonary and depression multimorbidity. However, cardiopulmonary and depression multimorbidity was associated with the highest odds of hospitalization. Nevertheless, both cardiopulmonary and cardiometabolic multimorbidity were positively associated with poor quality of life compared to participants with no multimorbidity. Although these findings are consistent with previous studies conducted in low and middle-income countries (4, 20, 57), it is important to note that the existing studies were based on multimorbidity counts without adequate information on specific disease clusters to guide primary care. Unlike the multimorbidity counts, where all morbidities are equally scored irrespective of their relationships, our approach provides crucial insight into the burden of specific multimorbidity clusters that goes beyond counting the number of coexisting chronic conditions. In line with previous studies (4, 58-60), there is a possibility that QoL may

have deteriorated, partly due to the treatment burden including medication intake, drug management, self-monitoring, lifestyle changes and hospitalization. However, future studies should focus on identifying the underlying causal pathways connecting distinct cardiometabolic multimorbidity clusters, healthcare utilization patterns and QoL.

Strengths and limitations

This study has three main strengths. First, data are from a nationally representative population-based survey using a standardised WHO-SAGE protocol. Thus, the findings are generalizable to the population of persons aged 50 years and above in Ghana. Second, screening for obesity, hypertension, angina pectoris, arthritis, asthma, chronic lung disease, and depression was based on objective measures comprising direct physical measurement of anthropometrics, BP, symptomatology algorithms and self-reports. Third, the use of LCA and agglomerative hierarchical clustering algorithms in the identification of distinct cardiometabolic multimorbidity clusters provides crucial insights into the patterns of non-random co-occurrence of multimorbidity that goes beyond simple counts used in the majority of previous studies.

The current study has some limitations. First, the screening questions particularly for diabetes, stroke and cataract were based on self-reported history of diagnosis. This may have resulted in the underestimation of the true prevalence of chronic diseases. Second, the current study assessed the association of different cardiometabolic multimorbidity combinations with the frequency of outpatient visits and hospitalization in Ghana. However, the nature of outpatient visits or hospitalization such as routine care or emergencies was not explored. Furthermore, the association of multimorbidity clusters with the cost of care were not investigated. Thus future studies on the economic burden of different cardiometabolic multimorbidity combinations are needed. Third, the number of chronic diseases in the LCA was limited to those included in the SAGE survey in Ghana. This may have excluded other common chronic conditions among older persons, such as dementia, cancers chronic kidney disease, resulting in an underestimation of the multimorbidity burden. Future studies need to include more chronic diseases to increase the external validity. Fourth, the cross-sectional design of the data used in this analysis implies a lack of conclusions regarding the temporality or causation between the multimorbidity classes, healthcare utilization patterns and QoL. Further studies based on longitudinal analysis need to estimate the incidence of transitions between latent classes of cardiometabolic multimorbidity and their impact on healthcare utilization patterns and QoL. Finally, The WHO SAGE data used in this analysis were collected in 2015, and rapid changes in health and socioeconomic circumstances in Ghana are likely to have affected the burden of chronic diseases and quality of life in the last 8 years. Nevertheless, our findings are based on the most recent data we could access and act as a baseline with which to compare future studies on the burden of multimorbidity on healthcare utilization and quality of life in Ghana.

This study has two key policy implications. First, we identified distinct multimorbidity combinations comprising cardiometabolic diseases, arthritis and cataract class and cardiopulmonary and depression class. This may inform the design of multimorbidity treatment guidelines and primary care interventions for cardiometabolic diseases. Given that most of the existing guidelines for the management of chronic diseases in Ghana are single-disease-focused (13), there is a need for a policy discourse on integrated care of discordant cardiometabolic multimorbidity to enable patients to benefit from minimally disruptive care. Second, these results are useful for identifying target populations of people living with cardiometabolic diseases at high risk of outpatient visits, hospitalizations and poor QoL. This is important for planning service delivery capacity, optimization of resources and health system response.

Conclusions

Our results provide insight into the cardiometabolic multimorbidity clusters and the associated patterns of healthcare utilization and QoL. The findings of this study show that cardiometabolic multimorbidity among older persons in Ghana cluster together in distinct patterns that differ in healthcare utilization and QoL. This evidence may be used in healthcare planning and development of appropriate clinical guidelines for the management of cardiometabolic multimorbidity. Our findings form the basis for, future research on the aetiology and pathogenesis of discordant multimorbidity clusters, and improved policies to address healthcare access and QoL for older persons living with cardiometabolic multimorbidity in sub-Saharan Africa.

Declarations

Consent for publication

Not required.

Availability of data and materials

Data from SAGE Ghana Wave 2 was used for this study. The necessary permission was obtained from the World Health Organization to use the data. All files were obtained from the World Health Organization Study on global AGEing and adult health (WHO-SAGE). Details on data can be found at http://www.who.int/healthinfo/sage/cohorts/en/. The authors confirm that they had no special access privileges to the data. Interested researchers will have to submit a licensed data request to WHO. Upon approval, the researchers will be granted access to licensed data.

Competing interest

The authors declare that they have no competing interest

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Authors' contributions

PO conceptualized the study, reviewed the literature, and analysed the data. GA, CW, WW, and CA made substantive contributions to the conceptualization of the study, and data analysis and reviewed the manuscript. All authors read and approved the final manuscript.

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Supplementary files

Supplementary file 1: Symptomatology algorithms

Arthritis	
Q1	During the last 12 months, have you experienced, pain, aching, stiffness, or swelling in or around the joints (like arms, hands, legs, or feet)which was not related to an injury and lasted for more than a month?
Q2	During the last 12 months, have you experienced stiffness in the joint in the morning after getting up from bed, or after a long rest of the joint without movement?
Q3	How long did this stiffness last?—1) less than 30 minutes; 2) more than 30 minutes `
Q4	Did this stiffness go away after exercise or movement in the joint?—1) yes; 2) no
Algorithm If the response to Q1 and 2 was "yes" and the response to questions 3 and 4 was the first option, the respondent was said to have arthritis	
Angina	
Q1	During the last 12 months, have you experienced any pain or discomfort in your chest when you walk uphill or hurry?
Q2	During the last 12 months, have you experienced any pain or discomfort in your chest when you walk at an ordinary pace on level ground?
Q3	What do you do if you get the pain or discomfort when you are walking?—1) stop or slow down; 2) carry on after taking a pain-relieving medicine that dissolves in your mouth; 3) carry on walking
Q4	If you stand still, what happens to the pain or discomfort?—1) relieved; 2) not relieved
Q5	Apart from these questions, respondents were asked to identify the points of pain in the upper part of the body (excluding the head) with the help of a picture depicting the upper parts of the body.
Algorithm If the response to Q1 and Q2 was "yes" and the response to Q3 and 4 was the first option, and in Q5 the respondent indicated that the pain was in the upper left part of the body, the person was said to have angina.	
Chronic Lung Disease	
Q1	During the last 12 months, have you experienced any shortness of breath at rest (while awake)?
Q2	During the last 12 months, have you experienced any coughing or wheezing for 10 minutes or more at a time?
Q3	During the last 12 months, have you experienced any coughing up of sputum or phlegm on most days of the month for at least 3 months?
Algorithm A respondent was ascertained to have chronic lung disease if his/her response was "yes" to Q1 or "yes" to both Q2 and Q3.	
Asthma	

Q1 During the last 12 months, have you experienced attacks of wheezing or whistling breathing?

Q2 During the last 12 months, have you experienced an attack of wheezing that came on after you stopped exercising or some other physical activity?

Q3 During the last 12 months, have you had a feeling of tightness in your chest?

Q4 During the last 12 months, have you woken up with a feeling of tightness in your chest in the morning or any other time?

Q5 During the last 12 months, have you had an attack of shortness of breath that came on without an obvious cause when you were not exercising or doing some physical activity?

Algorithm
A respondent was said to suffer from asthma if s/he responded "yes" to Q1 and "yes" to any of the subsequent Q2–Q5.

Depression

Q1 During the last 12 months, have you had a period lasting several days when you felt sad, empty, or depressed?

Q2 During the last 12 months, have you had a period lasting several days when you lost interest in most things you usually enjoy, such as personal relationships, work, or hobbies/ recreation?

Q3 During the last 12 months, have you had a period lasting several days when you have been feeling your energy decreased or that you are tired all the time?

If the response to any of the above 3 questions was "yes," then the following set of questions was asked:

Q4 Did this period (of sadness/loss of interest/low energy) last for more than 2 weeks?

Q5 Was this period (of sadness/loss of interest/low energy) most of the day, nearly every day?

Q6 During this period, did you lose your appetite?

Q7 Did you notice any slowing down in your thinking?

Q8 Did you notice any problems falling asleep?

Q9 Did you notice any problems waking up too early?

Q10 During this period, did you have any difficulties concentrating—for example, listening to others, working, watching television, listening to the radio?

Q11 Did you notice any slowing down in your moving around?

Q12 During this period, did you feel anxious and worried most days?

Q13 During this period, were you so restless or jittery nearly every day that you paced up and down and could not sit still?

Q14 During this period, did you feel negative about yourself or like you had lost confidence?

Q15 Did you frequently feel hopeless—that there was no way to improve things?

Q16 During this period, did your interest in sex decrease?

Q17 Did you think of death, or wish you were dead?

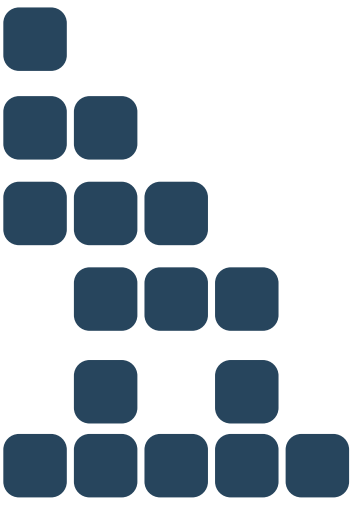
Q18 During this period, did you ever try to end your life?

Algorithm
To ascertain depression from this set of questions, 2 sets of variables were computed. The first set of variables was based on Q1–Q5 and Q16. From this set, 3 variables were computed taking the values 0 and 1, as follows:
1. The first variable takes the value 1 if the response to any of Q1, Q4, and Q5 is "yes."
2. The second variable takes the value 1 if the response to Q2 or Q16 is "yes."
3. The third variable takes the value 1 if the response to Q3 is "yes."
The second set of variables was based on Q6–Q15, Q17, and Q18. From these questions, 7 variables were computed.
1. The first variable takes the value 1 if the response to Q14 or Q15 is "yes."
2. The second variable takes the value 1 if the response to Q12 or Q13 is "yes."
3. The third variable takes the value 1 if the response to Q17 or Q18 is "yes."
4. The fourth variable takes the value 1 if the response to Q7 or Q10 is "yes."
5. The fifth variable takes the value 1 if the response to Q11 is "yes."
6. The sixth variable takes the value 1 if the response to Q8 or Q9 is "yes."
7. The seventh variable takes the value 1 if the response to Q6 is "yes."
These newly created variables from the respective sets were added to obtain 2 new variables, the first consisting of the sum of the first set of variables (maximum value 3) and the second consisting of the sum of the second set of variables (maximum value 7). Based on these 2 variables, a respondent was said to suffer from depression if s/he had a value for the first variable of 2 or more and a value for the second variable of 4 or more

Supplementary file 2: Comparison between latent class models

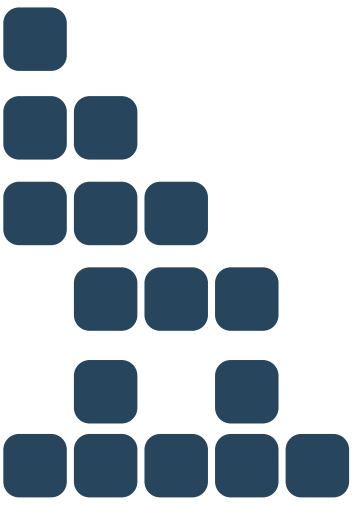
Number of latent classes	CAIC	BIC
1	22909.5	22976.0
2	22498.0	22364.9
3	22043.1	22254.8
4	**21961.0**	**22233.2**
5	21941.3	22280.0

Note: Boldface type indicates the selected model. BIC Bayesian Information Criterion, CAIC consistent Akaike Information Criterion.



PART 2

Chronic care models for Cardiometabolic Multimorbidity in sub-Saharan Africa



5

Effectiveness of integrated chronic care models for cardiometabolic multimorbidity in Sub-Saharan Africa: A systematic review and meta-analysis

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Abstract

Objectives: This review aimed at identifying the elements of integrated care models for cardiometabolic multimorbidity in Sub-Saharan Africa (SSA) and their effects on clinical or mental health outcomes including systolic blood pressure (SBP), blood sugar, depression scores and other patient-reported outcomes such as quality of life, and medication adherence.

Design: Systematic review and meta-analysis using the Grading of Recommendation, Assessment, Development, and Evaluation (GRADE) approach.

Data sources: We systematically searched PubMed, Embase, Scopus, Web of Science, Global Health CINAHL, African Journals Online, Informit, PsycINFO, clinicaltrials.gov, Pan African Clinical Trials Registry and grey literature from OpenSIGLE for studies published between 1999 and 2022.

Eligibility criteria for selecting studies: We included randomized controlled trial studies featuring integrated care models with two or more elements of Wagner's chronic care model.

Data extraction and synthesis: Two independent reviewers used standardised methods to search and screen included studies. Publication bias was assessed using the Doi plot and LFK index. Meta-analysis was conducted using random effects models.

Results: In all, we included 10 randomized controlled trials from 11 publications with 4,864 participants from six SSA countries (South Africa, Kenya, Nigeria, Eswatini, Ghana and Uganda). The overall quality of evidence based on GRADE criteria was moderate. A random-effects meta-analysis of six studies involving 1,754 participants shows that integrated compared to standard care conferred a moderately lower mean SBP (Mean Difference=-4.85mmHg, 95% CI: -7.37 to -2.34) for people with cardiometabolic multimorbidity; Hedges' g effect size (g=-0.25, (-0.39 to -0.11). However, integrated care compared with usual care showed mixed results for HbA1c, depression, medication adherence, and quality of life.

Conclusion: Integrated care improved SBP among patients living with cardiometabolic multimorbidity in SSA. More studies on integrated care are required to improve the evidence pool on chronic care models for multimorbidity in SSA. These include implementation studies and cost-effectiveness studies.

Keywords: Integrated care, chronic care models, multimorbidity, cardiometabolic diseases, Sub-Saharan Africa

PROSPERO registration number: CRD42020187756

Article Summary:

Strengths and limitations of this study

- The inclusion of randomized controlled trials provides more unbiased findings than previous reviews that are mostly based on observational study designs.
- The extraction of important constructs of Wagner's chronic care model from the integrated care models offers deeper insights into the effectiveness of integrated care model elements.
- The review considered both communicable and non-communicable diseases which reflects their converging burdens in Sub-Saharan Africa.
- The varying numbers and types of chronic care model components resulted in heterogeneity in the included studies.
- Since most included studies used multi-component interventions, the absolute effect attributable to a particular element of the chronic care model remains unknown.

Background

Cardiometabolic diseases, including type 2 diabetes and cardiovascular diseases (CVDs), are the leading cause of global mortality (1). People living with cardiometabolic diseases often have multiple rather than a single condition, commonly known as multimorbidity (2). Cardiometabolic multimorbidity occurs against the background of obesity and insulin resistance (3). However, these conditions are also characterised by the simultaneous co-occurrence of other diseases with unrelated pathophysiology or care management profile such as HIV/AIDS, chronic respiratory diseases, cancers, and mental illnesses, a phenomenon referred to as discordant multimorbidity (4-6).

The burden of multimorbidity is highest in low- and middle-income countries (LMICs), which still bear a high burden of infectious diseases while also facing a new threat from non-communicable diseases (7). However, the majority of the chronic care models in Sub-Saharan Africa (SSA) are still built around single disease frameworks (8). Evidence shows that health services delivery based on isolated interventions may derail the value of treatment and preventive measures (9-12). Vertical disease programs result in missed opportunities for early diagnosis and management of multimorbidities (13). Therefore, integrated chronic disease management is recommended to respond to this challenge (14). Singer et al, (2011) (15), define *integrated care* as a set of patient-centred and multidisciplinary care activities coordinated by two or more collaborating service providers within or across the healthcare sector including community and social environments. This definition emphasizes the coordination of care activities and the active involvement of patients in managing their health.

The chronic care model, first identified by McColl Institute for Healthcare Innovation at Group Health Cooperative (11), has been proposed as a solution to improve the

integrated management of chronic diseases. This model identifies six essential elements: community resources and policies, health care organization, self-management support, delivery system design, decision support and clinical information systems. However, what constitutes an integrated chronic care model and how it is implemented and delivered within healthcare services, has continued to evolve with the advent of new interventions. Most of the chronic care models have been developed in HIC with sophisticated health services (16), which may not appropriately apply to SSA.

The untapped capacity of chronic care models for HIV/AIDS care in SSA should be viewed as emerging models for other chronic diseases including cardiometabolic diseases (17). Lessons learned from the implementation of care models for HIV/AIDS and tuberculosis in SSA could be effectively applied to improve care models for cardiometabolic diseases (18). A systematic review by Rohwer et al (19) examined existing integrated care models for diabetes and hypertension in LMICs. However, the included studies did not focus on structured clinical care delivered to persons living with multimorbidity. Furthermore, the integrated care for hypertension and diabetes was based on a 'one-stop-shop' model where all healthcare services are provided under one roof (19). This is just one way of describing integrated care. A comprehensive evaluation of the applicability of the elements of chronic care models for cardiometabolic multimorbidity has not been systematically evaluated in SSA. Therefore, the purpose of this systematic review was to identify elements of integrated chronic care models for cardiometabolic multimorbidity in SSA and their effects on clinical or mental health outcomes including systolic blood pressure (SBP), blood sugar, depression scores and other patient-reported outcomes such as quality of life, and medication adherence.

Methods

Protocol registration

The study protocol was registered in the International Prospective Register for Systematic Reviews (PROSPERO) (CRD42020187756). The findings are reported according to the Preferred Reporting Items for Systematic Reviews (PRISMA) (20).

Eligibility criteria

Participants

We selected studies conducted in SSA among adult patients aged 18 years and over with cardiometabolic multimorbidity receiving care in a primary or community care setting. Cardiometabolic multimorbidity was defined as having two or more chronic conditions; at least one of which is a cardiometabolic disease such as type 2 diabetes, hypertension, hypercholesterolemia, hypertriglyceridemia, dyslipidaemia or CVDs such as stroke. Others included common discordant conditions such as HIV/AIDS, chronic respiratory diseases, cancers and mental illnesses. These conditions constitute over three-quarters of the global burden of chronic diseases (21).

Intervention

We included interventions with integrated chronic care models for persons living with cardiometabolic multimorbidity. In line with previous studies (22-26), we classified the intervention components into six categories based on the elements of Wagner's chronic care model (11). Thus, for the inclusion criterion, the models were considered "integrated care" if they applied at least two of the six chronic care model elements to manage more than one chronic disease (23). This included self-management support, delivery system design, decision support, clinical information system, healthcare organization, and community linkages.

The classification of intervention features and components is shown in Supplementary File 1. Self-management support includes interventions that empower people living with chronic conditions to manage their health. Examples are self-help groups and technological aids for self-care. Delivery system design interventions focus on care delivery efficiency and effectiveness such as patient care planning, coordination, and follow-up. Decision-support interventions promote clinical care that is consistent with scientific evidence and patient preferences. Clinical information systems is the organization of patient data to facilitate efficient and effective care. Healthcare organization interventions focus on creating an organizational culture and mechanisms that promote safe, high-quality care. Community linkages include interventions that mobilize community resources to meet the needs of people living with chronic diseases. Where the chronic care model had multiple components, we defined each element using the Wagner taxonomy (11) and highlighted the predominant components.

Control

The control or comparison group in the included studies received the usual or standard care comprising standalone services for cardiometabolic multimorbidity.

Outcome

We included studies that reported any objective measure of patient clinical or mental health outcomes. For example, SBP (mmHg), glycated haemoglobin ((HbA1c (%)), and depression scores. Others included patient-reported outcomes such as quality of life, and patient behaviour (medication adherence).

Types of studies

We included randomised controlled trials (RCTs) meeting the quality criteria developed by the Cochrane Effective Practice and Organization of Care (EPOC) (27). This is because RCTs provide more unbiased information than other study designs on the differential effects of chronic care models. Studies from SSA published in all languages between 1999 and December 2022 were included. We used 1999 because this was the formal year of inception of the Wagner's chronic care model (28).

Exclusion criteria

We excluded single-disease-focused studies and studies conducted among pregnant women. Interventions with no specified structured clinical care delivered to persons living with cardiometabolic multimorbidity were excluded. Studies with interventions for comorbid conditions where the intervention was targeted solely at one of the conditions rather than integrated care for the co-occurring conditions were also excluded. Studies that assumed multimorbidity to be the norm based on individuals' age without screening and diagnosis by qualified healthcare providers were excluded as the interventions were not being targeted specifically at multimorbidity.

Search strategy

Two reviewers independently searched PubMed, Embase, Scopus, Web of Science, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane library, African Journals Online, Informit, and PsycINFO without language restriction. The search was limited to articles indexed from 1999 up to 15th December 2022 to capture the beginning of the application of the elements of Wagner's chronic care model. The search results were limited by filters for randomized control trials and search concepts for chronic care models, cardiometabolic diseases and multimorbidity (See supplementary file 2). Additional articles were identified by scanning the reference list of relevant studies obtained through the search. Hand-searching of key journals was also conducted. Furthermore, we searched for registered trials in the clinicaltrials.gov, the Pan African Clinical Trials Registry and grey literature from OpenSIGLE.

Data collection and analysis

Selection of studies

The search results were uploaded into the Endnote version 12 reference manager (Clarivate, Philadelphia, USA) and screened for duplicates. Four review authors (EW, MN, PK and DM) independently performed the initial screening of titles and abstracts. Results of screening were recorded against the citation in Excel spreadsheet. The articles selected for full-text review were subsequently assessed for adequacy following the inclusion criteria for patient, intervention, comparator and outcome. Consensus meetings were held between the reviewers and the project coordinator (PO) to resolve disagreements. We used a modified PRISMA flow chart to describe the study selection (Figure 1).

Data extraction and management

Four review authors (EW, MN, PK and DM) abstracted data using a modified version of the EPOC data collection checklist (27). Data were entered in Excel spreadsheets and exported to Stata version 15 (StataCorp LLC). Data quality disagreements were resolved by consensus between the review authors and the project coordinator (PO). Information extracted from the included studies comprised:

1. Participants: type of patients, age, nature of multimorbidity and how it was diagnosed.
2. Study design: randomization, the unit of allocation, and follow-up.
3. Intervention: we extracted a full description of the intervention components and features. This included self-management support, delivery system design, decision support, clinical information system, healthcare organization, and community resources
4. Service providers: specialists, primary care providers, and family members
5. Study setting: primary care and community-based care
6. Patient clinical or mental health outcomes such as SBP, blood glucose control, and depression symptom scores. Others included patient-reported outcomes such as quality of life and medication adherence.
7. Results: We organized results into clinical outcomes, mental health outcomes and patient-reported outcomes.

Assessment of risk of bias

Four review authors (EA, MN, PK and DM) independently assessed the risk of bias in the included studies using standard EPOC criteria (29). The assessment domains included: allocation (sequence generation and concealment); baseline characteristics; incomplete outcome data; contamination; blinding; selective outcome reporting; and other potential sources of bias. The criteria for the assessment were 'low risk', 'high risk' or 'unclear risk' (Figure 2). Loss to follow-up of more than 20% was considered a high risk of bias. We also considered loss to follow-up as a high risk of bias when it was unbalanced between the groups. Published protocols and trial registrations were tracked to assess selective reporting bias. We assessed incomplete reporting for studies that reported different results than the outcomes outlined in the methods sections of selected articles. Any disagreements between the review authors were resolved by consensus, or with the consultation of the project coordinator (PO).

Data analysis

We used a random-effects meta-analysis to estimate the pooled mean effect size of integrated care versus standard care on SBP. The random-effects meta-analysis allows for statistical heterogeneity between studies by assuming that the true effects in the individual studies differ from each other. Six studies with similarities in terms of the patient population, interventions, and outcome assessment, were included in the meta-analysis. Studies with significant heterogeneity were not included in the meta-analysis. Hence, we conducted a structured synthesis of the results. All analyses were performed using *"metan"* command in Stata version 15 (StataCorp LLC).

We calculated the effect size following the methods described by Hedges (30). For each of the included studies, we calculated results in terms of absolute and standardized mean differences with a 95% Confidence Interval (CI). The heterogeneity of the selected

studies were evaluated using χ^2 and I^2 statistics (31). Using the χ^2 test, heterogeneity between studies was considered significant if $p<0.10$ (32). We used I^2 statistics, values of 25%-49%, 50%-74% and >75% to determine low, moderate and high heterogeneity respectively (33). Publication bias was assessed using the Doi plot and Luis Furuya Kanamori (LFK) index (34). The LFK index outside the interval −1 and 1 was considered consistent with asymmetry (35). As Higgins et al. (36) posit, it is justifiable to perform a pooled meta-analysis involving cluster RCTs and individual RCTs. However, sensitivity analyses should be performed to test the robustness of the pooled estimates. (36, 37). We performed sensitivity analyses to assess the robustness of our results by comparing the pooled effect estimates from separate analyses involving RCTs (four studies) and cluster RCTs (two studies).

Certainty of evidence

The certainty of the evidence of included studies was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodological guideline. According to GRADE guidance, RCTs start with high-certainty evidence (38). Our judgements to downgrade the certainty of evidence were based on the assessment of the following five domains: study limitations, inconsistency, imprecision, indirectness and publication bias. For each outcome, we described the certainty of evidence as high, moderate, low or very low. The GRADE criteria also take into consideration the certainty of evidence and the size of the effect (39). We considered a 5 mmHg reduction in SBP to be clinically significant (40). A change of 0.5% for the outcome HbA1c, and 10% for depression scores, medication adherence and quality of life were considered clinically significant (41). For each outcome, we described the certainty of evidence as high, moderate, low or very low (42).

Patient and public involvement

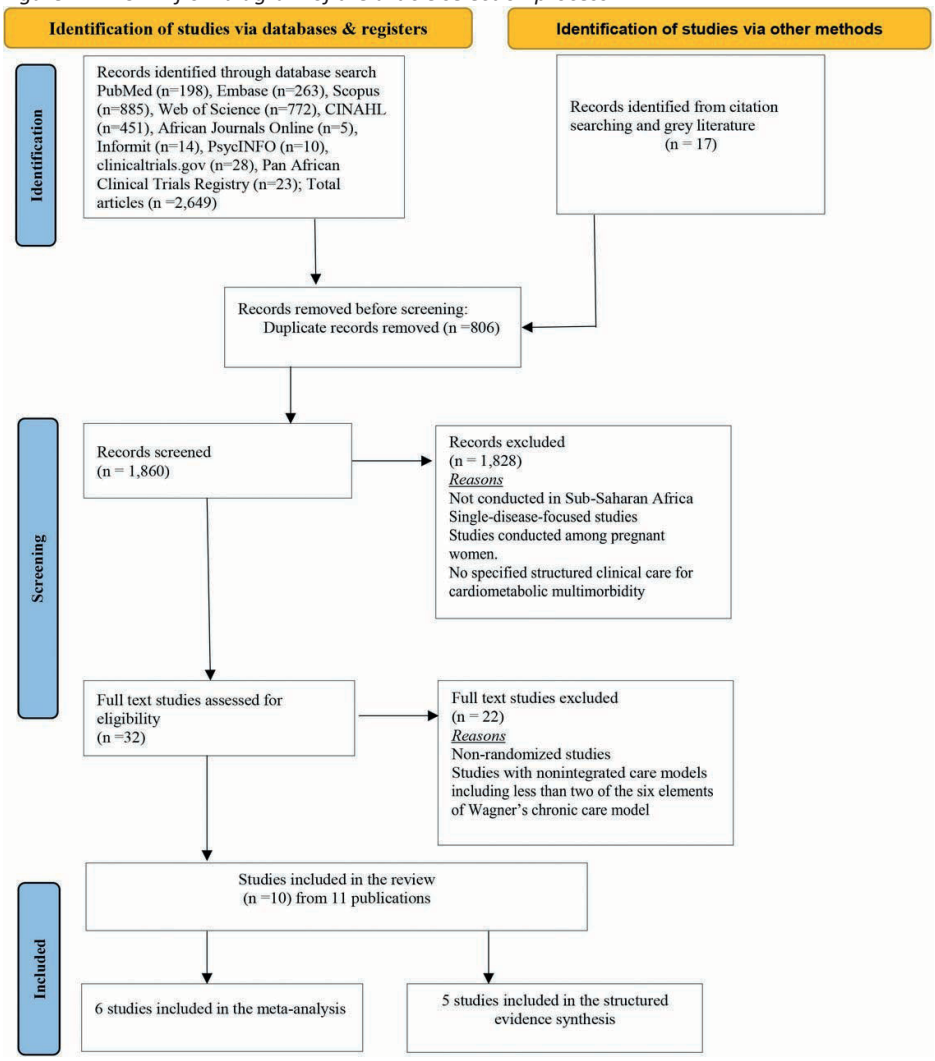
Patients or the public were not involved in the design, conduct, reporting, or dissemination of this research.

Results

Search results

The PRISMA flow diagram of the article selection process is presented in Figure 1. We identified 2,649 studies from our searches. Another 17 studies were included after manually searching the reference list and grey literature. After the removal of 806 duplicate records, we screened the titles and abstracts of 1,860 articles and identified 32 potentially eligible studies. We reviewed the full text of 32 studies and excluded 22 studies. Thus, 10 studies from 11 publications were included in this review (6 randomized controlled trials and 4 cluster randomized trials). Of these 10 studies, 6 were included in the meta-analyses and 4 studies from 5 publications were included in the structured synthesis of the results.

Figure 1: PRISMA flow diagram of the article selection process



Characteristics of included studies

The characteristics of the included studies are presented in Table 1. We included 10 trials from 11 publications (43-53) with a total of 4,864 participants. Sample sizes ranged from 55 to 1,174 participants. Three studies were conducted in South Africa, two in Kenya and Nigeria and one in Eswatini and Ghana, respectively. There was one multi-country study conducted in Uganda and Kenya. Studies mostly took place in primary care settings (n=9) or both community and primary care settings (n=2). Most trials recruited participants with HIV and cardiometabolic diseases (n=9), another two

recruited patients with HIV, type 2 diabetes, hypertension, depression and substance use disorder. Eight studies lasted 12 months or more. In all the included studies, the control group received the usual standard care while the intervention group received structured integrated care with varying elements of chronic care models including self-management support, delivery system design, decision support, clinical information system, healthcare organization, and community resources.

Risk of bias in included studies

The risk of bias summary is presented in Figure 2. All the included studies were RCTs. Hence, all studies had low risk for randomization. Four of the 11 publications had a cluster design that ensured no contamination of control participants (43, 46, 49, 52). The four cluster-randomized controlled trials accounted for clustering effects in their analysis so there was no unit of analysis errors (43, 46, 49, 52). Six studies were appraised as unclear risk due to insufficient information about protection against contamination (44, 47, 48, 50, 51, 53). One study was rated as unclear risk due to lack of sufficient information about allocation concealment. Although it was not feasible to blind the participants and study personnel due to the nature of the interventions, the absence of blinding did not affect the objective outcomes. Hence, all studies were graded as low risk for blinding. Under the reliability of primary outcomes, five studies were rated as high risk due to small sample sizes (48, 51-53) and lack of baseline measurements (43). For selective reporting, all the studies were assessed as low risk, except one that lacked clarity and was assessed as unclear risk (50). Four studies were rated high risk for other biases, mainly short follow-up duration (less than one year) (48, 50, 52, 53). Overall, the certainties of the evidence for SBP, HbA1c, depression, medication adherence and quality of life were downgraded to moderate. This was due to the high risk of bias, imprecision and clinically insignificant effect sizes in the included studies (43-53).

Table 1: Characteristics of included studies

Study	Setting	Study design	Sample size	Age, years	Multimorbidity	Follow-up (months)	Outcome	Intervention
Havlir et al (2019) (43) Uganda and Kenya	Primary and community-based care	Cluster RCT	1,441 patients with hypertension & HIV	≥30	Hypertension and HIV	36	BP control	Multi-disease testing; integrated care for HIV and hypertension; structured follow-up, flexible hours of operation and reduced wait time at clinics; and patient incentives.
Jackson et al (2021) (44) Nigeria	Primary care	RCT	182	18-69	Hypertension & HIV	12	SBP and medication adherence	Pharmaceutical care with structured education and counselling by a pharmacist after seeing a physician on their clinic visit. Education focused on self-monitoring of BP, lifestyle modification, reviewing the date of the next appointment and prescription.
Jackson et al (2022) (45) Nigeria	Primary care	RCT	182	18-69	Hypertension and HIV	12	Health-related quality of life	Structured education and counselling on general self-care, medicines use storage and lifestyle modifications.
Myers et al (2022) (46) South Africa	Primary care	Cluster RCT	1,174	≥18	HIV, Type 2 diabetes, depression and substance use disorder	12	Depression scores	Psychological interventions comprising motivational interviewing and problem-solving therapy delivered by a trained facility-based community health worker.

Table 1: Continued

Study	Setting	Study design	Sample size	Age, years	Multimorbidity	Follow-up (months)	Outcome	Intervention
Okube et al (2022) (47) Kenya	Community-based care	RCT	294	18-64	Metabolic syndrome	12	BP and blood sugar control	Community-based health education on lifestyle modification and face-to-face delivery of verbal and written individualized health recommendations on risk factors for CVDs.
Owolabi et al (2019) (48) Nigeria Primary care RCT			158	≥18	Hypertension and stroke	12	SBP	A culturally appropriate, multipronged intervention comprising patient global risk factor control report card, personalized phone text-messaging, and educational video.
Petersen et al (2021) (49) South Africa	Primary care	Cluster RCT	925	≥18	Hypertension and depression	12	Depression scores	Supplementary training of primary nurses and doctors on mental health and clinical communication skills. Collaborative care model for patients with hypertension and comorbid depressive symptoms including doctors, nurses, clinical psychologists and lay counsellors.
Rabkin et al (2018) (50) Eswatini	Primary care	RCT	236	≥40	HIV, Hypertension, type 2 diabetes, and hyperlipidemia	6	SBP and HbA1c	CVD risk factors screening and structured referrals among patients living with HIV.

Table 1: Continued

Study	Setting	Study design	Sample size	Age, years	Multimorbidity	Follow-up (months)	Outcome	Intervention
Roos et al (2014) (51) South Africa	Primary care	RCT	84	20-65	HIV and metabolic diseases	12	SBP and fasting blood sugar	Pedometer and a physical activity diary with education materials and self-monitoring documents. Structured regular clinic sessions for review of physical activity diary and risk factors for ischemic heart disease. Monthly SMS text motivational messages.
Sarfo et al (2018) (52) Ghana	Primary care	Cluster RCT	55	≥18	Hypertension and stroke	9	BP control and medication adherence	Blue-toothed BP device and smartphone for self-monitoring and reporting BP measurements and medication intake. Tailored motivational text messages delivered based on the levels of adherence to the medication intake protocol.
Thuita et al (2020) Kenya (53)	Primary care	RCT	133	20–79	Metabolic syndrome	6	SBP and HbA1c	Integrated care with nutrition education and peer-to-peer support

*The control group received standard/usual care

Figure 2: Risk of bias in included studies

Components of the chronic care model

Table 2 presents the components of the chronic care model in the included studies. All studies had to include at least two components of the Wagner chronic care model to be defined as "integrated care" for the management of at least two chronic diseases. The number of chronic care elements ranged from two to five. One study included five of the six elements of the chronic care model (43). Three studies included three elements (48, 51, 52) and six enclosed two elements (46, 49, 50, 53-55). All the studies included delivery system design except one. The components of self-delivery included multi-disease screening and treatment, task shifting, structured follow-up, and collaborative care. Seven studies included self-management support such as home-based self-monitoring, lifestyle counselling, post-clinic patient follow-up and patient support groups (43, 44, 48, 51-53, 55). Four studies included decision support components such as supplementary training of healthcare workers and support supervision (43, 46, 49, 50). Three studies included clinical information systems (48, 51, 52). The elements enclosed comprised hospital registries, patient diaries, report cards and electronic platforms for BP monitoring. Two studies included community resource elements to enhance health campaigns (43, 55). One study included the healthcare organization element, mainly quality improvement strategies to enhance access to medication and treatment services (43).

Table 2: Elements of the chronic care model included in the studies

Author (year)	Self-management support	Delivery system design	Decision support	Clinical information system	Healthcare organization	Community resources
Havlir et al (2019) (43)	Enhanced lifestyle modification counselling in primary care centers	Point-of-care multi-disease screening for HIV, hypertension, and diabetes with structured follow-up and care linkages	Telephone and in-person oversight from a senior physician on the services provided by general physicians and nurses.		Quality improvement strategies such as guaranteed access to medication, flexible hours of operations, and reduced wait time at clinics	Multi-disease testing community health campaigns using community resource persons
Jackson et al (2021) (44)	Education on self-monitoring of BP, lifestyle modification, self-care and appropriate use of medicines	Structured pharmaceutical care including prescription review and follow-up				
Myers et al (2022) (45)		Task shifting and empowerment of community health workers to provide basic psychological interventions	Trained community health workers on basic psychological intervention including motivational interviewing and problem-solving therapy			

Table 2: Continued

Author (year)	Self-management support	Delivery system design	Decision support	Clinical information system	Healthcare organization	Community resources
Okube et al (2022) (47)	Individualized health recommendations on CVD risk factors					Community-based health education on lifestyle modification
Owolabi et al 2019 (48)	Post-clinic follow-up phone texts and waiting room educational video	Enhanced follow-up visits and pre-appointment phone texts		Hospital registry and patient report card as part of medical chart		
Petersen et al (2021) (49)		Collaborative care model for patients with hypertension and comorbid depressive symptoms including doctors, nurses, clinical psychologist and lay counsellors	Supplementary training of primary care nurses and doctors on mental health and clinical communication skills			
Rabkin et al (2018) (50)	-	One stop shop for CVD risk factors screening and structured referrals among patients living with HIV	Training of HIV clinic nurses and doctors to conduct CVD risk factors screening during routine clinic appointments of patients			

Table 2: Continued

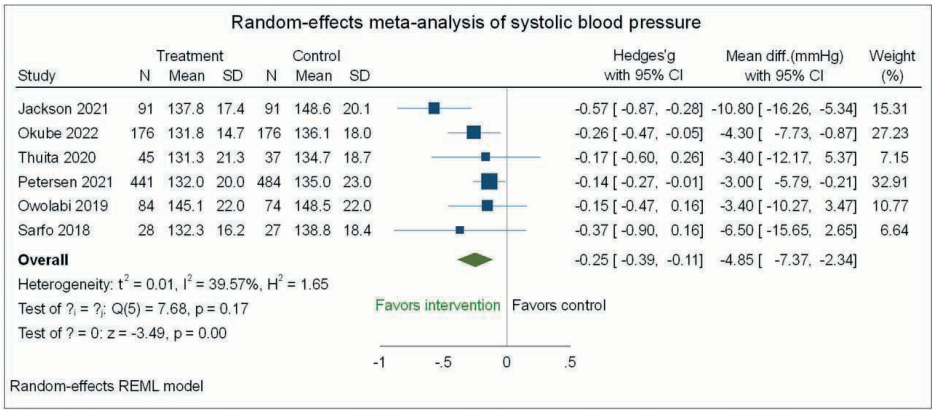
Author (year)	Self-management support	Delivery system design	Decision support	Clinical information system	Healthcare organization	Community resources
Roos et al (2014) (51)	A pedometer and a physical activity diary with education materials and self-monitoring documents. Monthly SMS text motivational messages	Structured regular clinic sessions for review of physical activity diary and risk factors for ischemic heart disease		Patient diary for self-monitoring of risk factors for ischemic heart disease		
Sarfo et al (2018) (52)	Self-monitoring of BP using a blue-toothed device. Tailored motivational text messages delivered based on the levels of adherence to medication	Structured follow-up for BP measurements and medication adherence		Digital platform for tracking BP measurements and medication adherence		
Thuita et al 2020 (53)	Nutrition counselling and peer support group	Monthly follow up visits and structured regular clinic sessions to review patient progress. Facility-based patient support groups.				

Effectiveness of integrated models of care compared with standard care

Systolic blood pressure

Figure 3 presents the random effects meta-analysis of SBP. The pooled results of 6 studies (44, 47-49, 52, 53) involving 1,754 participants show that integrated versus standard care conferred a lower mean SBP (Mean Difference (MD) =-4.85mmHg, 95% CI (-7.37 to -2.34) with a small Hedges' g effect size (g=-0.25, (-0.39 to -0.11). However, the overall quality of evidence based on GRADE criteria was moderate. Moderate heterogeneity (I^2=39.57%) existed in the included studies (Figure 3). The results of the sensitivity analyses separating RCTs from cluster RCTs are consistent with those of the pooled analyses (Supplementary File 3). Integrated care reduced systolic blood pressure in RCTs by (MD=-5.71mmHg, 95% CI -9.32 to -2.09) and by (MD=-3.30mmHg, 95% CI -5.97 to –0.63) for the cluster RCTs. A Doi plot of the random effects meta-analysis of SBP for integrated versus standard care is shown in Supplementary File 4. The presence of publication bias is suggested by the asymmetrical visual inspection of the Doi plot, confirmed by LFK index=-2.37.

Figure 3: *Forest plot of the random effects meta-analysis of the effect of integrated versus standard care on SBP for people with cardiometabolic multimorbidity in Sub-Saharan Africa*



We did not conduct meta-analyses for the four of the included studies in this review (43, 46, 50, 51), as they were too heterogeneous in terms of patient population, interventions, and outcome assessment. Hence, we conducted a structured synthesis of their results. Of the studies included in the structured synthesis of results, the effect of integrated versus standard care on BP were reported in three studies (43, 50, 51). However, the quality of evidence based on GRADE criteria was moderate. The SEARCH trial conducted in Kenya and Uganda found that hypertension control was 22% higher among patients on integrated care versus standard care (relative prevalence=1.22; (95%CI 1.08 to 1.37)) (43). In contrast, a study by Rabkin et al (50) conducted in Eswatini found no significant effect of integrated versus referred management of CVD risk factors on mean SBP. Another study by Roos et al (2014) also found no significant effect of

education and a home-based pedometer walking program on SBP MD=2.50 mmHg, 95% CI (-2.78 to 7.78).

Fasting blood glucose and HbA1c

Two studies included in the structured synthesis of the results assessed the effect of integrated versus standard care on FBS and HbA1c (47, 50). A study by Okube et al (47) found that integrated care conferred a significant ($p < 0.05$) reduction in FBS by -0.5mmol/L versus +0.08 mmol/L among patients on standard care. In a study by Rabkin et al (50), the mean of HbA1c was significantly reduced by -0.7% (95%CI: -1.3 to -0.1) and -1.4% (-2.5 to -0.2) in the integrated and standard care arms, respectively with no statistical difference between arms 0.7% (95%CI -0.4 to 1.8).

Depression

The effect of integrated versus standard care on depression was reported in two studies. A study by Petersen et al (49) found no significant difference in the depression scores in patients on integrated versus standard care (adjusted risk difference = -0.04 (95%CI, -0.19 to 0.11)). By contrast, the results of the study by Myers et al (46) found significant differences in the depression scores in patients on integrated versus standard care (MD = 4.8(95%CI -7.2 to -2.4)).

Medication adherence and quality of life

Two studies assessed the effect of integrated care on hypertension medication adherence (45, 50). One study reported the effect of integrated versus standard care HRQoL (45). In a study by Rabkin et al (50), integrated care conferred a higher likelihood of hypertension medication adherence than standard care (relative risk=1.28 (95%CI 1.10 to 1.47)). A study by Jackson et al (45) found that integrated care led to significant improvements in hypertension medication adherence (Mean Difference in Difference (DiD)= 2.32; $p < 0.001$) and HRQoL (DiD= 6.5%, $P < 0.001$). Two studies assessed the effect of integrated care on hypertension medication adherence (45, 50). One study reported the effect of integrated versus standard care on HRQoL (45). In a study by Rabkin et al (50), integrated care conferred a higher likelihood of hypertension medication adherence than standard care (relative risk=1.28 (95%CI 1.10 to 1.47)). A study by Jackson et al (45) found that integrated care led to significant improvements in hypertension medication adherence (Mean Difference in Difference (DiD)= 2.32; $p < 0.001$) and HRQoL (DiD= 6.5%, $P < 0.001$).

Discussions

This paper presents the results of a systematic review of integrated care models for cardiometabolic multimorbidity and their effects on intermediate health outcomes in SSA. Our results show that, in comparison to usual care, integrated care featuring at least two elements of Wagner's chronic care model conferred moderate improvements in SBP among patients living with cardiometabolic multimorbidity. The overall quality of evidence was moderate. Results of the systematic review suggest that integrated care compared with usual care has mixed results with regards to HbA1c, depression, medication adherence and quality of life, with some studies showing a significant effect and some no effect.

The findings of the current review based on RCTs are broadly consistent with reviews on the effectiveness of the integrated chronic care model from previous observational studies (56, 57). In contrast, one systematic review by Rohwer et al (19) on integrated care models for diabetes and hypertension in LMICs found no evidence of improved blood pressure or diabetes control. However, the evidence presented had very low certainty and the included studies did not focus on care models for persons living with multimorbidity.

Our study used Wagner's chronic care model, a framework for improving the integrated management of chronic diseases through the implementation of its six core elements: community resources and policies, health care organization, self-management support, delivery system design, decision support and clinical information systems (11). A review by Goh et al (56) found greater improvements in HbA1c for care models with more elements over a single element. In the same vein, another systematic review by Ellisen et al [56] reported variations in glycemic control with an increase in the number of elements of the chronic care model. However, most studies included in the current review had two to three chronic care model elements which could partly explain the mixed results with regard to the effect of care integration on intermediate health outcomes such as HbA1c, depression, medication adherence and quality of life, with some studies showing a significant effect and some no effect.

In the current review, delivery system design and self-management support were the most predominant components of the integrated chronic care models while healthcare organization and community resource elements were less common. Nevertheless, the structured synthesis of the results shows no significant differences in health outcomes by the elements of care integration since a majority of studies included two to three elements. Previous studies have shown that intervention intensity including length of implementation and frequency of monitoring, rather than the number of intervention components may have an impact on the direction and magnitude of the health outcomes (57, 58).

Overall, our results have three main implications. First, our findings have great public health significance given that a 5 mmHg reduction of SBP could reduce the risk of major cardiovascular events by about 13% (59). Thus, incorporating integrated care into the implementation of Wagner's chronic care model may partly address the needs of people living with cardiometabolic multimorbidity. Second, this review provides crucial evidence on the applicability of chronic care models in SSA and unearths the components of chronic care models for people living with cardiometabolic multimorbidity. Lastly, most integrated care models sought to support self-management and delivery system design. However, a few included healthcare organizations and community resource elements. More interventions should seek to incorporate these elements to support integrated care.

Strengths and limitations

The current review has three main strengths. First, all the included studies were RCTs. Hence, the findings are more unbiased than previous reviews on integrated care in LMICs that are mostly based on observational study designs (19, 60-62). Second, this study comprehensively extracted important constructs of Wagner's chronic care model, thus offering deeper insights into the effectiveness of its elements and delivering crucial evidence to researchers and health stakeholders for future improvement of integrated care models. The consideration of both communicable and non-communicable diseases in the review is also a strength due to the converging burdens of infectious and non-communicable diseases in SSA (7).

The findings of this review should be interpreted cautiously due to a few limitations. First, the majority of the included studies did not classify the components of chronic care models in the interventions. Although the three reviewers independently classified the type of chronic care model elements in the studies using a standard guide, there is potential for misclassification bias. Second, the varying numbers and types of chronic care model components added to the heterogeneity. Furthermore, the absolute effect attributable to a particular element of the chronic care model remains unknown, as most included studies used multi-component interventions. Third, it may not be possible to have a standard of care that is similar for all the studies included in this review. This resulted in a broad variety of usual care. Lastly, due to the substantial heterogeneity in the studies, in terms of multimorbidity, interventions, follow-up periods, and outcome assessment, only six of the ten studies were included in the meta-analysis, which may have a bearing on the power of the meta-analysis findings. The rest of the studies were included in the structured synthesis of the results.

Conclusions

We found that integrated care may lead to moderate improvements in SBP among patients living with cardiometabolic multimorbidity in SSA. This review highlights the paucity of research on care integration interventions for cardiometabolic multimorbidity

in SSA since the selected RCTs were from only a few SSA countries. In addition, there were fewer studies with outcomes on health-related quality of life, mental health, and medication adherence. The small number of studies addressing healthcare organisation and community resource elements provide less certainty on the benefits associated with these components. More studies are needed on the implementation effectiveness of integrated care models and its impact on cardiometabolic multimorbidity. The relative effectiveness of the different elements of integrated chronic care models and the cost-effectiveness of these models for the management of cardiometabolic multimorbidity should be explored. Other elements that are not well explored such as healthcare organisation and community resource elements should be investigated in future research. Future studies investigating the effectiveness of integrated care should classify the elements in the interventions and standardize the description of each element.

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Data availability statement: All data relevant to the study are included in the article or uploaded as online supplemental information.

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List of supplementary files

Supplementary file 1: Classification of interventions

Intervention component	Feature
Self-management support	• Self-care interventions based on technological aid • Self-help groups • Family-oriented supports • Motivational support • Behaviour therapy
Delivery system design	• Practice team functioning • Patient care planning and follow-up • Coordination between primary care and specialist services
Decision support	• Practice clinical guidelines • Provider education • Involvement of specialists in improving primary care
Clinical information system	• Disease registry • Reminders to providers • Feedback to providers
Healthcare organization	• Organizational goals and resources for chronic disease management • Quality improvement strategies • Incentives
Community linkages	• Linking patients to outside resources • Activities with community-based organizations • Professionals working out in the community

Supplementary file 2: Search strategies for electronic databases

1. **PubMED (Medline) Search strategy**

#1 ("elevated blood pressure"[MeSH Terms] OR "high blood pressure"[MeSH Terms] OR "raised blood pressure"[MeSH Terms] OR "diastolic blood pressure"[MeSH Terms] OR "systolic blood pressure"[MeSH Terms] OR "arterial blood pressure"[MeSH Terms] OR "uncontrolled blood pressure"[MeSH Terms] OR "uncontrolled hypertension"[All Fields] OR "elevated blood pressure"[All Fields] OR "high blood pressure"[All Fields] OR "raised blood pressure"[All Fields] OR "diastolic blood pressure"[All Fields] OR "systolic blood pressure"[All Fields] OR "arterial blood pressure"[All Fields] OR "uncontrolled blood pressure"[All Fields] OR "uncontrolled hypertension"[All Fields])

#2 ("diabetes mellitus"[MeSH Terms] OR "diabetes mellitus, type 2"[MeSH Terms] OR "diabetes type 2"[MeSH Terms] OR "T2DM"[MeSH Terms] OR "diabetes type II"[MeSH Terms] OR "diabetes"[MeSH Terms] OR "glucose intolerance"[MeSH Terms] OR "insulin resistance"[MeSH Terms] OR "hyperglycemia"[MeSH Terms] OR "hyperglycaemia"[MeSH Terms] OR "hypoglycaemia"[MeSH Terms] OR "hypoglycaemia"[MeSH Terms] OR "high blood sugar"[MeSH Terms] OR "elevated

blood sugar"[MeSH Terms] OR "raised blood sugar"[MeSH Terms] OR "high blood glucose"[MeSH Terms] OR "elevated blood glucose"[MeSH Terms] OR "raised blood glucose"[MeSH Terms] OR "diabetes mellitus"[All Fields] OR "diabetes mellitus, type 2"[All Fields] OR "diabetes type 2"[All Fields] OR "T2DM"[All Fields] OR "diabetes type II"[All Fields] OR "diabetes"[All Fields] OR "glucose intolerance"[All Fields] OR "insulin resistance"[All Fields] OR "hyperglycemia"[All Fields] OR "hyperglycaemia"[All Fields] OR "hypoglycemia"[All Fields] OR "hypoglycaemia"[All Fields] OR "high blood sugar"[All Fields] OR "elevated blood sugar"[All Fields] OR "raised blood sugar"[All Fields] OR "high blood glucose"[All Fields] OR "elevated blood glucose"[All Fields] OR "raised blood glucose"[All Fields])

#3 ("stroke"[MeSH Terms] OR "transient ischemic attack"[MeSH Terms] OR "ischemic attack"[MeSH Terms] OR "angina"[MeSH Terms] OR "angina pectoris"[MeSH Terms] OR "heart attack"[MeSH Terms] OR "ischemic heart diseases "[MeSH Terms] OR "transient ischaemic attack"[MeSH Terms] OR "coronary heart disease"[MeSH Terms] OR "coronary disease"[MeSH Terms] OR "heart failure"[MeSH Terms] OR "peripheral vascular disease"[MeSH Terms] OR "Peripheral Vascular diseases"[MeSH Terms] OR "atrial fibrillation"[MeSH Terms] OR "cardiovascular disease"[MeSH Terms] OR "heart disease"[MeSH Terms] OR "stroke"[All Fields] OR "transient ischemic attack"[All Fields] OR "ischemic attack"[All Fields] OR "angina"[All Fields] OR "angina pectoris"[All Fields] OR "heart attack"[All Fields] OR "ischemic heart diseases "[All Fields] OR "transient ischaemic attack"[All Fields] OR "coronary heart disease"[All Fields] OR "coronary disease"[All Fields] OR "heart failure"[All Fields] OR "peripheral vascular disease"[All Fields] OR "Peripheral Vascular diseases"[All Fields] OR "atrial fibrillation"[All Fields] OR "cardiovascular disease"[All Fields] OR "heart disease"[All Fields])

#4 ("Hypercholesterolemia"[MeSH Terms] OR "Dyslipidemias"[MeSH Terms] OR "blood lipid"[MeSH Terms] OR "Cholesterol"[MeSH Terms] OR "high cholesterol"[MeSH Terms] OR "elevated cholesterol"[MeSH Terms] OR "raised cholesterol"[MeSH Terms] OR "low density lipoprotein "[MeSH Terms] OR "high density lipoprotein"[MeSH Terms] OR "Dyslipidemia"[MeSH Terms] OR "Dyslipidaemia"[MeSH Terms] OR "Hypercholesterolemia"[MeSH Terms] OR "hypercholesterolaemia "[MeSH Terms] OR "hypercholesterolimia "[MeSH Terms] OR "Hypertriglyceridemia"[MeSH Terms] OR "Hypertriglyceridemia"[MeSH Terms] OR "Hypertriglyceridaemia"[MeSH Terms] OR "Hyperlipidemia"[MeSH Terms] OR "Hyperlipidemias"[MeSH Terms] OR "Hyperlipidaemia"[MeSH Terms] OR "LDL"[MeSH Terms] OR "HDL"[MeSH Terms] OR "Hypercholesterolemia"[All Fields] OR "Dyslipidemias"[All Fields] OR "blood lipid"[All Fields] OR "Cholesterol"[All Fields] OR "high cholesterol"[All Fields] OR "elevated cholesterol"[All Fields] OR "raised cholesterol"[All Fields] OR "low density lipoprotein "[All Fields] OR "high density lipoprotein"[All Fields] OR "Dyslipidemia"[All Fields] OR "Dyslipidaemia"[All Fields] OR "Hypercholesterolemia"[All Fields] OR "hypercholesterolaemia "[All Fields] OR "hypercholesterolimia "[All

Fields] OR "Hypertriglyceridemia"[All Fields] OR "Hypertriglyceridemia"[All Fields] OR "Hypertriglyceridaemia"[All Fields] OR "Hyperlipidemia"[All Fields] OR "Hyperlipidemias"[All Fields] OR "Hyperlipidaemia"[All Fields] OR "LDL"[All Fields] OR "HDL"[All Fields])

#5 ("Comorbid"[All Fields] OR "co-morbid"[All Fields] OR "co-morbidity"[All Fields] OR "Multimorbidity"[All Fields] OR "multi-morbid"[All Fields] OR "multi morbidity"[All Fields] OR "Multimorbidity"[All Fields] OR "Comorbidity"[All Fields] OR "multi-disease"[All Fields] OR "Multidisease"[All Fields] OR multi disease[All Fields] OR "multiple condition"[All Fields] OR "multi-condition"[All Fields] OR "multi condition"[All Fields] OR "multiple illness"[All Fields] OR "multi-illness"[All Fields] OR "multi illness"[All Fields] OR "multiple syndrome"[All Fields] OR "multi-syndrome"[All Fields] OR "multi syndrome"[All Fields] OR "concurrent condition"[All Fields] OR "concurrent illness"[All Fields] OR "concurrent disease"[All Fields] OR "co-existing disease"[All Fields] OR "coexisting disease"[All Fields] OR "co-existing illness"[All Fields] OR "coexisting illness"[All Fields] OR "co-existing syndrome"[All Fields] OR "coexisting syndrome"[All Fields] OR "co-existing condition"[All Fields] OR "coexisting condition"[All Fields] OR "co-occurring disease"[All Fields] OR "co-occuring disease"[All Fields] OR "co-occuring disease"[All Fields] OR "co-occurring illness"[All Fields] OR "co occurring illness"[All Fields] OR "cooccurring illness"[All Fields] OR "co-occurring syndrome"[All Fields] OR "co occurring syndrome"[All Fields] OR "cooccurring syndrome"[All Fields] OR "co-occurring condition"[All Fields] OR "co occurring condition"[All Fields] OR "cooccurring condition"[All Fields])

#6 ("Wagner model"[All Fields] OR "Wagner* model*"[All Fields] OR "Wagner* chronic care model*"[All Fields] OR "Wagner chronic care model"[All Fields] OR "chronic care model*"[All Fields] OR "model "[All Fields] OR "collaborative care"[All Fields] OR "chronic care framework"[All Fields] OR "chronic disease care"[All Fields] OR "chronic illness care"[All Fields] OR care model[All Fields] OR "model care"[All Fields] OR "Wagner* model*"[All Fields] OR "Wagner* chronic care model*"[All Fields] OR "Wagner chronic care model"[All Fields] OR "theory"[All Fields] OR "concept"[All Fields] OR "framework"[All Fields] OR "model"[All Fields] OR "programme"[All Fields] OR "approach"[All Fields] OR "clinical pathway"[All Fields] OR "care pathway"[All Fields] OR "critical path"[All Fields] OR "vertical integration"[All Fields] OR "virtual integration"[All Fields] OR "physician system integration"[All Fields] OR "provider system integration"[All Fields] OR "functional integration"[All Fields] OR "horizontal integration"[All Fields] OR "clinical integration"[All Fields] OR "case management"[All Fields] OR "delivery of health care, integrated"[All Fields] OR "disease management"[All Fields] OR "patient care management"[All Fields] OR "patient-centred care"[All Fields] OR "accountable care organisations"[All Fields] OR "continuity of patient care"[All Fields] OR "case management"[All Fields] OR "comprehensive health care"[All Fields] OR "delivery of health care, integrated"[All Fields] OR "managed care programmes"[All

Fields] OR “patient-centred care”[All Fields] OR “care delivery”[All Fields] OR “integrated care”[All Fields] OR “comprehensive care”[All Fields] OR “care coordination”[All Fields] OR “managed care”[All Fields] OR “accountable care “[All Fields] OR “accountable care organisations”[All Fields] OR “accountable care organisation”[All Fields] OR “collaborative care”[All Fields] OR “disease management”[All Fields] OR “case-management”[All Fields] OR “case management”[All Fields] OR “shared care”[All Fields] OR “accountable care”[All Fields] OR “patient-centred”[All Fields] OR “patient centred”[All Fields] OR “person-centred”[All Fields] OR “person centred”[All Fields] OR “multidisciplinary care”[All Fields] OR “interdisciplinary care”[All Fields] OR “inter-disciplinary care”[All Fields] OR “cross disciplinary care”[All Fields] OR “cross-disciplinary care”[All Fields] OR “multiple interventions”[All Fields] OR “care chain”[All Fields] OR “care chains”[All Fields] OR “care continuity”[All Fields] OR “care continuation”[All Fields] OR “care transition”[All Fields] OR “care transitions”[All Fields] OR “chain of care”[All Fields] OR “chains of care”[All Fields] OR “continuity of care”[All Fields] OR “cross sectoral care”[All Fields] OR “delivery of health care integrated”[All Fields] OR “integrated medicine”[All Fields] OR “integrated social network”[All Fields] OR “integrated social networks”[All Fields] OR “integration of care”[All Fields] OR “intersectoral care”[All Fields] OR “intrasectoral care”[All Fields] OR “linked care”[All Fields] OR “management model”[All Fields] OR “patient care management”[All Fields] OR “seamless care”[All Fields] OR “service network”[All Fields] OR “service networks”[All Fields] OR “transition of care”[All Fields] OR “transitional care”[All Fields] OR “transmural care”[All Fields] OR “whole system thinking”[All Fields] OR “holistic care”[All Fields])

#7 (“Angola “[All Fields] OR “Benin “[All Fields] OR “Botswana “[All Fields] OR “Burkina Faso”[All Fields] OR “Upper Volta”[All Fields] OR “Burundi “[All Fields] OR “Cameroon “[All Fields] OR “Cameroons “[All Fields] OR “Cape Verde”[All Fields] OR “Central African Republic”[All Fields] OR Chad[All Fields] OR “Comoros “[All Fields] OR “Comoro Islands”[All Fields] OR “Comores”[All Fields] OR “Mayotte “[All Fields] OR “Congo “[All Fields] OR “Zaire “[All Fields] OR “Cote d’Ivoire”[All Fields] OR “Ivory Coast”[All Fields] OR “Democratic Republic of the Congo”[All Fields] OR “Djibouti “[All Fields] OR “French Somaliland”[All Fields] OR “Eritrea “[All Fields] OR “Ethiopia “[All Fields] OR “Gabon “[All Fields] OR “Gabonese Republic”[All Fields] OR “Gambia “[All Fields] OR “Ghana “[All Fields] OR “Gold Coast”[All Fields] OR “Guinea “[All Fields] OR “Kenya “[All Fields] OR “Lesotho”[All Fields] OR “Basutoland”[All Fields] OR “Liberia “[All Fields] OR “Madagascar “[All Fields] OR “Malagasy Republic “[All Fields] OR “Malawi “[All Fields] OR “Nyasaland “[All Fields] OR “Mali “[All Fields] OR “Mauritania “[All Fields] OR “Mauritius “[All Fields] OR “Mozambique”[All Fields] OR “Namibia”[All Fields] OR “Niger”[All Fields] OR “Nigeria”[All Fields] OR “Rwanda”[All Fields] OR “Sao Tome”[All Fields] OR “Seychelles”[All Fields] OR “Senegal “[All Fields] OR “Sierra Leone”[All Fields] OR “Somalia “[All Fields] OR “South Africa”[All Fields] OR “Sudan “[All Fields] OR “Eswatini”[All Fields] OR “Tanzania”[All Fields] OR “Togo “[All Fields] OR “Togolese Republic”[All Fields] OR “Uganda”[All Fields] OR “Zambia”[All Fields] OR “Zimbabwe “[All

Fields] OR "Rhodesia"[All Fields] OR "Sub-Saharan Africa"[All Fields] OR "Africa South of the Sahara"[All Fields])

#8 ((#1 OR #2 OR #3 OR #4 OR #5) AND #6 AND #7) AND Restricted (1999-2022, RCTs)

2. **Web of Science Search Strategy**

#1 elevated blood pressure OR high blood pressure OR raised blood pressure OR diastolic blood pressure OR systolic blood pressure OR arterial blood pressure OR uncontrolled blood pressure OR uncontrolled hypertension OR elevated blood pressure OR high blood pressure OR raised blood pressure OR diastolic blood pressure OR systolic blood pressure OR arterial blood pressure OR uncontrolled blood pressure OR uncontrolled hypertension

#2 diabetes mellitus OR diabetes mellitus, type 2 OR diabetes type 2 OR T2DM OR diabetes type II OR diabetes OR glucose intolerance OR insulin resistance OR hyperglycemia OR hyperglycaemia OR hypoglycaemia OR hypoglycaemia OR high blood sugar OR elevated blood sugar OR raised blood sugar OR high blood glucose OR elevated blood glucose OR raised blood glucose OR diabetes mellitus OR diabetes mellitus, type 2 OR diabetes type 2 OR T2DM OR diabetes type II OR diabetes OR glucose intolerance OR insulin resistance OR hyperglycemia OR hyperglycaemia OR hypoglycemia OR hypoglycaemia OR high blood sugar OR elevated blood sugar OR raised blood sugar OR high blood glucose OR elevated blood glucose OR raised blood glucose

#3 stroke OR transient ischemic attack OR ischemic attack OR angina OR angina pectoris OR heart attack OR ischemic heart diseases OR transient ischaemic attack OR coronary heart disease OR coronary disease OR heart failure OR peripheral vascular disease OR Peripheral Vascular diseases OR atrial fibrillation OR cardiovascular disease OR heart disease OR stroke OR transient ischemic attack OR ischemic attack OR angina OR angina pectoris OR heart attack OR ischemic heart diseases OR transient ischaemic attack OR coronary heart disease OR coronary disease OR heart failure OR peripheral vascular disease OR Peripheral Vascular diseases OR atrial fibrillation OR cardiovascular disease OR heart disease

#4 Hypercholesterolemia OR Dyslipidemias OR blood lipid OR Cholesterol OR high cholesterol OR elevated cholesterol OR raised cholesterol OR low density lipoprotein OR high density lipoprotein OR Dyslipidemia OR Dyslipidaemia OR Hypercholesterolemia OR hypercholesterolaemia OR hypercholesterolimia OR Hypertriglyceridemia OR Hypertriglyceridemia OR Hypertriglyceridaemia OR Hyperlipidemia OR Hyperlipidemias OR Hyperlipidaemia OR LDL OR HDL OR Hypercholesterolemia OR Dyslipidemias OR blood lipid OR Cholesterol OR high cholesterol OR elevated cholesterol OR raised cholesterol OR low density lipoprotein OR high density lipoprotein OR

Dyslipidemia OR Dyslipidaemia OR Hypercholesterolemia OR hypercholesterolaemia OR hypercholesterolimia OR Hypertriglyceridemia OR Hypertriglyceridemia OR Hypertriglyceridaemia OR Hyperlipidemia OR Hyperlipidemias OR Hyperlipidaemia OR LDL OR HDL

#5 Comorbid OR co-morbid OR co-morbidity OR Multimorbidity OR multi-morbid OR multi morbidity OR Multimorbidity OR Comorbidity OR multi-disease OR Multidisease OR multi disease OR multiple condition OR multi-condition OR multi condition OR multiple illness OR multi-illness OR multi illness OR multiple syndrome OR multi-syndrome OR multi syndrome OR concurrent condition OR concurrent illness OR concurrent disease OR co-existing disease OR coexisting disease OR co-existing illness OR coexisting illness OR co-existing syndrome OR coexisting syndrome OR co-existing condition OR coexisting condition OR co-occurring disease OR co-occuring disease OR co-occuring disease OR co-occurring illness OR co occurring illness OR cooccurring illness OR co-occurring syndrome OR co occurring syndrome OR cooccurring syndrome OR co-occurring condition OR co occurring condition OR cooccurring condition

#6 Wagner model OR Wagner* model* OR Wagner* chronic care model* OR Wagner chronic care model OR chronic care model* OR model OR collaborative care OR chronic care framework OR chronic disease care OR chronic illness care OR care model OR model care OR Wagner* model* OR Wagner* chronic care model* OR Wagner chronic care model OR theory OR concept OR framework OR model OR programme OR approach OR clinical pathway OR care pathway OR critical path OR vertical integration OR virtual integration OR physician system integration OR provider system integration OR functional integration OR horizontal integration OR clinical integration OR case management OR delivery of health care, integrated OR disease management OR patient care management OR patient-centred care OR accountable care organisations OR continuity of patient care OR case management OR comprehensive health care OR delivery of health care, integrated OR managed care programmes OR patient-centred care OR care delivery OR integrated care OR comprehensive care OR care coordination OR managed care OR accountable care OR accountable care organisations OR accountable care organisation OR collaborative care OR disease management OR case-management OR case management OR shared care OR accountable care OR patient-centred OR patient centred OR person-centred OR person centred OR multidisciplinary care OR interdisciplinary care OR inter-disciplinary care OR cross disciplinary care OR cross-disciplinary care OR multiple interventions OR care chain OR care chains OR care continuity OR care continuation OR care transition OR care transitions OR chain of care OR chains of care OR continuity of care OR cross sectoral care OR delivery of health care integrated OR integrated medicine OR integrated social network OR integrated social networks OR integration of care OR intersectoral care OR intrasectoral care OR linked care OR management model OR patient care management OR seamless care OR service

network OR service networks OR transition of care OR transitional care OR transmural care OR whole system thinking OR holistic care

#7 Angola OR Benin OR Botswana OR Burkina Faso OR Upper Volta OR Burundi OR Cameroon OR Cameroons OR Cape Verde OR Central African Republic OR Chad OR Comoros OR Comoro Islands OR Comores OR Mayotte OR Congo OR Zaire OR Cote d'Ivoire OR Ivory Coast OR Democratic Republic of the Congo OR Djibouti OR French Somaliland OR Eritrea OR Ethiopia OR Gabon OR Gabonese Republic OR Gambia OR Ghana OR Gold Coast OR Guinea OR Kenya OR Lesotho OR Basutoland OR Liberia OR Madagascar OR Malagasy Republic OR Malawi OR Nyasaland OR Mali OR Mauritania OR Mauritius OR Mozambique OR Namibia OR Niger OR Nigeria OR Rwanda OR Sao Tome OR Seychelles OR Senegal OR Sierra Leone OR Somalia OR South Africa OR Sudan OR Eswatini OR Tanzania OR Togo OR Togolese Republic OR Uganda OR Zambia OR Zimbabwe OR Rhodesia OR Sub-Saharan Africa OR Africa South of the Sahara

#8 trial* OR RCT

#9 ((#1 OR #2 OR #3 OR #4 OR #5) AND #6 AND #7 AND #8) and Clinical Trial (Document Types) and 1999 or 2000 or 2001 or 2002 or 2003 or 2004 or 2005 or 2006 or 2007 or 2008 or 2009 or 2011 or 2010 or 2012 or 2013 or 2014 or 2015 or 2016 or 2017 or 2018 or 2019 or 2020 or 2021 or 2022 (Publication Years)

3. **SCOPUS**

(TITLE-ABS-KEY (trial* OR rct)) AND (((TITLE-ABS-KEY ("wagner model" OR "wagner* model*" OR "wagner* chronic care model*" OR "wagner chronic care model" OR "chronic care model*" OR "model " OR "collaborative care" OR "chronic care framework" OR "chronic disease care" OR "chronic illness care" OR care AND model OR "model care" OR "wagner* model*" OR "wagner* chronic care model*" OR "wagner chronic care model" OR "theory" OR "concept" OR "framework" OR "model" OR "programme" OR "approach" OR "clinical pathway" OR "care pathway" OR "critical path" OR "vertical integration" OR "virtual integration" OR "physician system integration" OR "provider system integration" OR "functional integration" OR "horizontal integration" OR "clinical integration" OR "case management" OR "delivery of health care, integrated" OR "disease management" OR "patient care management" OR "patient-centred care")) OR (TITLE-ABS-KEY ("accountable care organisations" OR "continuity of patient care" OR "case management" OR "comprehensive health care" OR "delivery of health care, integrated" OR "managed care programmes" OR "patient-centred care" OR "care delivery" OR "integrated care" OR "comprehensive care" OR "care coordination" OR "managed care" OR "accountable care " OR "accountable care organisations" OR "accountable care organisation" OR "collaborative care" OR "disease management" OR "case-management" OR "case management" OR "shared care" OR "accountable

care" OR "patient-centred" OR "patient centred" OR "person-centred" OR "person centred" OR "multidisciplinary care" OR "interdisciplinary care" OR "inter-disciplinary care" OR "cross disciplinary care" OR "cross-disciplinary care" OR "multiple interventions" OR "care chain" OR "care chains" OR "care continuity" OR "care continuation" OR "care transition")) OR (TITLE-ABS-KEY ("care transitions" OR "chain of care" OR "chains of care" OR "continuity of care" OR "cross sectoral care" OR "delivery of health care integrated" OR "integrated medicine" OR "integrated social network" OR "integrated social networks" OR "integration of care" OR "intersectoral care" OR "intrasectoral care" OR "linked care" OR "management model" OR "patient care management" OR "seamless care" OR "service network" OR "service networks" OR "transition of care" OR "transitional care" OR "transmural care" OR "whole system thinking" OR "holistic care"))) AND ((TITLE-ABS-KEY (("elevated blood pressure" OR "high blood pressure" OR "raised blood pressure" OR "diastolic blood pressure" OR "systolic blood pressure" OR "arterial blood pressure" OR "uncontrolled blood pressure" OR "uncontrolled hypertension" OR "elevated blood pressure" OR "high blood pressure" OR "raised blood pressure" OR "diastolic blood pressure" OR "systolic blood pressure" OR "arterial blood pressure" OR "uncontrolled blood pressure" OR "uncontrolled hypertension"))) OR (TITLE-ABS-KEY (("diabetes mellitus" OR "diabetes mellitus, type 2" OR "diabetes type 2" OR "t2dm" OR "diabetes type ii" OR "diabetes" OR "glucose intolerance" OR "insulin resistance" OR "hyperglycemia" OR "hyperglycaemia" OR "hypoglycaemia" OR "hypoglycaemia" OR "high blood sugar" OR "elevated blood sugar" OR "raised blood sugar" OR "high blood glucose" OR "elevated blood glucose" OR "raised blood glucose" OR "diabetes mellitus" OR "diabetes mellitus, type 2" OR "diabetes type 2" OR "t2dm" OR "diabetes type ii" OR "diabetes" OR "glucose intolerance" OR "insulin resistance" OR "hyperglycemia" OR "hyperglycaemia" OR "hypoglycemia" OR "hypoglycaemia" OR "high blood sugar" OR "elevated blood sugar" OR "raised blood sugar" OR "high blood glucose" OR "elevated blood glucose" OR "raised blood glucose"))) OR (TITLE-ABS-KEY (("stroke" OR "transient ischemic attack" OR "ischemic attack" OR "angina" OR "angina pectoris" OR "heart attack" OR "ischemic heart diseases " OR "transient ischaemic attack" OR "coronary heart disease" OR "coronary disease" OR "heart failure" OR "peripheral vascular disease" OR "peripheral vascular diseases" OR "atrial fibrillation" OR "cardiovascular disease" OR "heart disease" OR "stroke" OR "transient ischemic attack" OR "ischemic attack" OR "angina" OR "angina pectoris" OR "heart attack" OR "ischemic heart diseases " OR "transient ischaemic attack" OR "coronary heart disease" OR "coronary disease" OR "heart failure" OR "peripheral vascular disease" OR "peripheral vascular diseases" OR "atrial fibrillation" OR "cardiovascular disease" OR "heart disease"))) OR (TITLE-ABS-KEY (("hypercholesterolemia" OR "dyslipidemias" OR "blood lipid" OR "cholesterol" OR "high cholesterol" OR "elevated cholesterol" OR "raised cholesterol" OR "low density lipoprotein " OR "high density lipoprotein" OR "dyslipidemia" OR "dyslipidaemia" OR "hypercholesterolemia" OR "hypercholesterolaemia " OR "hypercholesterolimia

" OR "hypertriglyceridemia" OR "hypertriglyceridemia" OR "hypertriglyceridaemia" OR "hyperlipidemia" OR "hyperlipidemias" OR "hyperlipidaemia" OR "ldl" OR "hdl" OR "hypercholesterolemia" OR "dyslipidemias" OR "blood lipid" OR "cholesterol" OR "high cholesterol" OR "elevated cholesterol" OR "raised cholesterol" OR "low density lipoprotein " OR "high density lipoprotein" OR "dyslipidemia" OR "dyslipidaemia" OR "hypercholesterolemia" OR "hypercholesterolaemia " OR "hypercholesterolimia " OR "hypertriglyceridemia" OR "hypertriglyceridemia" OR "hypertriglyceridaemia" OR "hyperlipidemia" OR "hyperlipidemias" OR "hyperlipidaemia" OR "ldl" OR "hdl"))) OR (TITLE-ABS-KEY (("comorbid" OR "co-morbid" OR "co-morbidity" OR "multimorbidity" OR "multi-morbid" OR "multi morbidity" OR "multimorbidity" OR "comorbidity" OR "multi-disease" OR "multidisease" OR multi AND disease OR "multiple condition" OR "multi-condition" OR "multi condition" OR "multiple illness" OR "multi-illness" OR "multi illness" OR "multiple syndrome" OR "multi-syndrome" OR "multi syndrome" OR "concurrent condition" OR "concurrent illness" OR "concurrent disease" OR "co-existing disease" OR "coexisting disease" OR "co-existing illness" OR "coexisting illness" OR "co-existing syndrome" OR "coexisting syndrome" OR "co-existing condition" OR "coexisting condition" OR "co-occurring disease" OR "co-occuring disease" OR "co-occuring disease" OR "co-occurring illness" OR "co occurring illness" OR "cooccurring illness" OR "co-occurring syndrome" OR "co occurring syndrome" OR "cooccurring syndrome" OR "co-occurring condition" OR "co occurring condition" OR "cooccurring condition")))) AND (TITLE-ABS-KEY (("angola " OR "benin " OR "botswana " OR "burkina faso" OR "upper volta" OR "burundi " OR "cameroon " OR "cameroons " OR "cape verde" OR "central african republic" OR chad OR "comoros " OR "comoro islands" OR "comores" OR "mayotte " OR "congo " OR "zaire " OR "cote d'ivoire" OR "ivory coast" OR "democratic republic of the congo" OR "djibouti " OR "french somaliland" OR "eritrea " OR "ethiopia " OR "gabon " OR "gabonese republic" OR "gambia " OR "ghana " OR "gold coast" OR "guinea " OR "kenya " OR "lesotho" OR "basutoland" OR "liberia " OR "madagascar " OR "malagasy republic " OR "malawi " OR "nyasaland " OR "mali " OR "mauritania " OR "mauritius " OR "mozambique" OR "namibia" OR "niger" OR "nigeria" OR "rwanda" OR "sao tome" OR "seychelles" OR "senegal " OR "sierra leone" OR "somalia " OR "south africa" OR "sudan " OR "Eswatini" OR "tanzania" OR "togo " OR "Togolese republic" OR "uganda" OR "zambia" OR "zimbabwe " OR "rhodesia" OR "sub-saharan africa" OR "africa south of the sahara")))) AND (LIMIT-TO (PUBYEAR , 2022) OR LIMIT-TO (PUBYEAR , 2021) OR LIMIT-TO (PUBYEAR , 2020) OR LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010) OR LIMIT-TO (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR , 2007) OR LIMIT-TO (PUBYEAR , 2006) OR LIMIT-TO (PUBYEAR , 2005) OR LIMIT-TO (PUB-

YEAR , 2004) OR LIMIT-TO (PUBYEAR , 2003) OR LIMIT-TO (PUBYEAR , 2002) OR LIMIT-TO (PUBYEAR , 2001) OR LIMIT-TO (PUBYEAR , 2000) OR LIMIT-TO (PUBYEAR , 1999))

4. **Embase**

#1 ("elevated blood pressure"/ OR "high blood pressure"/ OR "raised blood pressure"/ OR "diastolic blood pressure"/ OR "systolic blood pressure"/ OR "arterial blood pressure"/ OR "uncontrolled blood pressure"/ OR "uncontrolled hypertension" OR "elevated blood pressure" OR "high blood pressure" OR "raised blood pressure" OR "diastolic blood pressure" OR "systolic blood pressure" OR "arterial blood pressure" OR "uncontrolled blood pressure" OR "uncontrolled hypertension")

#2 ("diabetes mellitus"/ OR "diabetes mellitus, type 2"/ OR "diabetes type 2"/ OR "T2DM"/ OR "diabetes type II"/ OR "diabetes"/ OR "glucose intolerance"/ OR "insulin resistance"/ OR "hyperglycemia"/ OR "hyperglycaemia"/ OR "hypoglycaemia"/ OR "hypoglycaemia"/ OR "high blood sugar"/ OR "elevated blood sugar"/ OR "raised blood sugar"/ OR "high blood glucose"/ OR "elevated blood glucose"/ OR "raised blood glucose"/ OR "diabetes mellitus" OR "diabetes mellitus, type 2" OR "diabetes type 2" OR "T2DM" OR "diabetes type II" OR "diabetes" OR "glucose intolerance" OR "insulin resistance" OR "hyperglycemia" OR "hyperglycaemia" OR "hypoglycemia" OR "hypoglycaemia" OR "high blood sugar" OR "elevated blood sugar" OR "raised blood sugar" OR "high blood glucose" OR "elevated blood glucose" OR "raised blood glucose")

#3 ("stroke"/ OR "transient ischemic attack"/ OR "ischemic attack"/ OR "angina"/ OR "angina pectoris"/ OR "heart attack"/ OR "ischemic heart diseases "/ OR "transient ischaemic attack"/ OR "coronary heart disease"/ OR "coronary disease"/ OR "heart failure"/ OR "peripheral vascular disease"/ OR "Peripheral Vascular diseases"/ OR "atrial fibrillation"/ OR "cardiovascular disease"/ OR "heart disease"/ OR "stroke" OR "transient ischemic attack" OR "ischemic attack" OR "angina" OR "angina pectoris" OR "heart attack" OR "ischemic heart diseases " OR "transient ischaemic attack" OR "coronary heart disease" OR "coronary disease" OR "heart failure" OR "peripheral vascular disease" OR "Peripheral Vascular diseases" OR "atrial fibrillation" OR "cardiovascular disease" OR "heart disease")

#4 ("Hypercholesterolemia"/ OR "Dyslipidemias"/ OR "blood lipid"/ OR "Cholesterol"/ OR "high cholesterol"/ OR "elevated cholesterol"/ OR "raised cholesterol"/ OR "low density lipoprotein "/ OR "high density lipoprotein"/ OR "Dyslipidemia"/ OR "Dyslipidaemia"/ OR "Hypercholesterolemia"/ OR "hypercholesterolaemia "/ OR "hypercholesterolimia "/ OR "Hypertriglyceridemia"/ OR "Hypertriglyceridemia"/ OR "Hypertriglyceridaemia"/ OR "Hyperlipidemia"/ OR "Hyperlipidemias"/ OR "Hyperlipidaemia"/ OR "LDL"/ OR "HDL"/ OR "Hypercholesterolemia" OR "Dyslipidemias" OR "blood lipid" OR "Cholesterol" OR "high cholesterol" OR "elevated

cholesterol" OR "raised cholesterol" OR "low density lipoprotein " OR "high density lipoprotein" OR "Dyslipidemia" OR "Dyslipidaemia" OR "Hypercholesterolemia" OR "hypercholesterolaemia " OR "hypercholesterolimia " OR "Hypertriglyceridemia" OR "Hypertriglyceridemia" OR "Hypertriglyceridaemia" OR "Hyperlipidemia" OR "Hyperlipidemias" OR "Hyperlipidaemia" OR "LDL" OR "HDL")

#5 ("Comorbid" OR "co-morbid" OR "co-morbidity" OR "Multimorbidity" OR "multi-morbid" OR "multi morbidity" OR "Multimorbidity" OR "Comorbidity" OR "multi-disease" OR "Multidisease" OR multi disease OR "multiple condition" OR "multi-condition" OR "multi condition" OR "multiple illness" OR "multi-illness" OR "multi illness" OR "multiple syndrome" OR "multi-syndrome" OR "multi syndrome" OR "concurrent condition" OR "concurrent illness" OR "concurrent disease" OR "co-existing disease" OR "coexisting disease" OR "co-existing illness" OR "coexisting illness" OR "co-existing syndrome" OR "coexisting syndrome" OR "co-existing condition" OR "coexisting condition" OR "co-occurring disease" OR "co-occuring disease" OR "co-occuring disease" OR "co-occurring illness" OR "co occurring illness" OR "cooccurring illness" OR "co-occurring syndrome" OR "co occurring syndrome" OR "cooccurring syndrome" OR "co-occurring condition" OR "co occurring condition" OR "cooccurring condition")

#6 ("Wagner model" OR "Wagner* model*" OR "Wagner* chronic care model*" OR "Wagner chronic care model" OR "chronic care model*" OR "model " OR "collaborative care" OR "chronic care framework" OR "chronic disease care" OR "chronic illness care" OR care model OR "model care" OR "Wagner* model*" OR "Wagner* chronic care model*" OR "Wagner chronic care model" OR "theory" OR "concept" OR "framework" OR "model" OR "programme" OR "approach" OR "clinical pathway" OR "care pathway" OR "critical path" OR "vertical integration" OR "virtual integration" OR "physician system integration" OR "provider system integration" OR "functional integration" OR "horizontal integration" OR "clinical integration" OR "case management" OR "delivery of health care, integrated" OR "disease management" OR "patient care management" OR "patient-centred care" OR "accountable care organisations" OR "continuity of patient care" OR "case management" OR "comprehensive health care" OR "delivery of health care, integrated" OR "managed care programmes" OR "patient-centred care" OR "care delivery" OR "integrated care" OR "comprehensive care" OR "care coordination" OR "managed care" OR "accountable care " OR "accountable care organisations" OR "accountable care organisation" OR "collaborative care" OR "disease management" OR "case-management" OR "case management" OR "shared care" OR "accountable care" OR "patient-centred" OR "patient centred" OR "person-centred" OR "person centred" OR "multidisciplinary care" OR "interdisciplinary care" OR "inter-disciplinary care" OR "cross disciplinary care" OR "cross-disciplinary care" OR "multiple interventions" OR "care chain" OR "care chains" OR "care continuity" OR "care continuation" OR "care transition" OR "care transitions" OR "chain of care" OR "chains

of care" OR "continuity of care" OR "cross sectoral care" OR "delivery of health care integrated" OR "integrated medicine" OR "integrated social network" OR "integrated social networks" OR "integration of care" OR "intersectoral care" OR "intrasectoral care" OR "linked care" OR "management model" OR "patient care management" OR "seamless care" OR "service network" OR "service networks" OR "transition of care" OR "transitional care" OR "transmural care" OR "whole system thinking" OR "holistic care")

#7 ("Angola " OR "Benin " OR "Botswana " OR "Burkina Faso" OR "Upper Volta" OR "Burundi " OR "Cameroon " OR "Cameroons " OR "Cape Verde" OR "Central African Republic" OR Chad OR "Comoros " OR "Comoro Islands" OR "Comores" OR "Mayotte " OR "Congo " OR "Zaire " OR "Cote d'Ivoire" OR "Ivory Coast" OR "Democratic Republic of the Congo" OR "Djibouti " OR "French Somaliland" OR "Eritrea " OR "Ethiopia " OR "Gabon " OR "Gabonese Republic" OR "Gambia " OR "Ghana " OR "Gold Coast" OR "Guinea " OR "Kenya " OR "Lesotho" OR "Basutoland" OR "Liberia " OR "Madagascar " OR "Malagasy Republic " OR "Malawi " OR "Nyasaland " OR "Mali " OR "Mauritania " OR "Mauritius " OR "Mozambique" OR "Namibia" OR "Niger" OR "Nigeria" OR "Rwanda" OR "Sao Tome" OR "Seychelles" OR "Senegal " OR "Sierra Leone" OR "Somalia " OR "South Africa" OR "Sudan " OR "Eswatini" OR "Tanzania" OR "Togo " OR "Togolese Republic" OR "Uganda" OR "Zambia" OR "Zimbabwe " OR "Rhodesia" OR "Sub-Saharan Africa" OR "Africa South of the Sahara")

#8 ((#1 OR #2 OR #3 OR #4 OR #5) AND #6 AND #7) & 1999 - 2022 & RCTs

5. **Cochrane Library**

#1 (("elevated blood pressure"(MeSH Terms) OR "high blood pressure"(MeSH Terms) OR "raised blood pressure"(MeSH Terms) OR "diastolic blood pressure"(MeSH Terms) OR "systolic blood pressure"(MeSH Terms) OR "arterial blood pressure"(MeSH Terms) OR "uncontrolled blood pressure"(MeSH Terms) OR "uncontrolled hypertension" OR "elevated blood pressure" OR "high blood pressure" OR "raised blood pressure" OR "diastolic blood pressure" OR "systolic blood pressure" OR "arterial blood pressure" OR "uncontrolled blood pressure" OR "uncontrolled hypertension")):ti,ab,kw (Word variations have been searched)

#2 (("diabetes mellitus"(MeSH Terms) OR "diabetes mellitus, type 2"(MeSH Terms) OR "diabetes type 2"(MeSH Terms) OR "T2DM"(MeSH Terms) OR "diabetes type II"(MeSH Terms) OR "diabetes"(MeSH Terms) OR "glucose intolerance"(MeSH Terms) OR "insulin resistance"(MeSH Terms) OR "hyperglycemia"(MeSH Terms) OR "hyperglycaemia"(MeSH Terms) OR "hypoglycaemia"(MeSH Terms) OR "hypoglycaemia"(MeSH Terms) OR "high blood sugar"(MeSH Terms) OR "elevated blood sugar"(MeSH Terms) OR "raised blood sugar"(MeSH Terms) OR "high blood glucose"(MeSH Terms) OR "elevated blood glucose"(MeSH Terms) OR "raised blood glucose"(MeSH Terms) OR "diabetes mellitus"

OR “diabetes mellitus, type 2” OR “diabetes type 2” OR “T2DM” OR “diabetes type II” OR “diabetes” OR “glucose intolerance” OR “insulin resistance” OR “hyperglycemia” OR “hyperglycaemia” OR “hypoglycemia” OR “hypoglycaemia” OR “high blood sugar” OR “elevated blood sugar” OR “raised blood sugar” OR “high blood glucose” OR “elevated blood glucose” OR “raised blood glucose”)):ti,ab,kw (Word variations have been searched)

#3 (((“stroke”(MeSH Terms) OR “transient ischemic attack”(MeSH Terms) OR “ischemic attack”(MeSH Terms) OR “angina”(MeSH Terms) OR “angina pectoris”(MeSH Terms) OR “heart attack”(MeSH Terms) OR “ischemic heart diseases “(MeSH Terms) OR “transient ischaemic attack”(MeSH Terms) OR “coronary heart disease”(MeSH Terms) OR “coronary disease”(MeSH Terms) OR “heart failure”(MeSH Terms) OR “peripheral vascular disease”(MeSH Terms) OR “Peripheral Vascular diseases”(MeSH Terms) OR “atrial fibrillation”(MeSH Terms) OR “cardiovascular disease”(MeSH Terms) OR “heart disease”(MeSH Terms) OR “stroke” OR “transient ischemic attack” OR “ischemic attack” OR “angina” OR “angina pectoris” OR “heart attack” OR “ischemic heart diseases “ OR “transient ischaemic attack” OR “coronary heart disease” OR “coronary disease” OR “heart failure” OR “peripheral vascular disease” OR “Peripheral Vascular diseases” OR “atrial fibrillation” OR “cardiovascular disease” OR “heart disease”)):ti,ab,kw (Word variations have been searched)

#4 (((“Hypercholesterolemia”(MeSH Terms) OR “Dyslipidemias”(MeSH Terms) OR “blood lipid”(MeSH Terms) OR “Cholesterol”(MeSH Terms) OR “high cholesterol”(MeSH Terms) OR “elevated cholesterol”(MeSH Terms) OR “raised cholesterol”(MeSH Terms) OR “low density lipoprotein “(MeSH Terms) OR “high density lipoprotein”(MeSH Terms) OR “Dyslipidemia”(MeSH Terms) OR “Dyslipidaemia”(MeSH Terms) OR “Hypercholesterolemia”(MeSH Terms) OR “hypercholesterolaemia “(MeSH Terms) OR “hypercholesterolimia “(MeSH Terms) OR “Hypertriglyceridemia”(MeSH Terms) OR “Hypertriglyceridemia”(MeSH Terms) OR “Hypertriglyceridaemia”(MeSH Terms) OR “Hyperlipidemia”(MeSH Terms) OR “Hyperlipidemias”(MeSH Terms) OR “Hyperlipidaemia”(MeSH Terms) OR “LDL”(MeSH Terms) OR “HDL”(MeSH Terms) OR “Hypercholesterolemia” OR “Dyslipidemias” OR “blood lipid” OR “Cholesterol” OR “high cholesterol” OR “elevated cholesterol” OR “raised cholesterol” OR “low density lipoprotein “ OR “high density lipoprotein” OR “Dyslipidemia” OR “Dyslipidaemia” OR “Hypercholesterolemia” OR “hypercholesterolaemia “ OR “hypercholesterolimia “ OR “Hypertriglyceridemia” OR “Hypertriglyceridemia” OR “Hypertriglyceridaemia” OR “Hyperlipidemia” OR “Hyperlipidemias” OR “Hyperlipidaemia” OR “LDL” OR “HDL”)):ti,ab,kw (Word variations have been searched)

#5 ((“Comorbid” OR “co-morbid” OR “co-morbidity” OR “Multimorbidity” OR “multi-morbid” OR “multi morbidity” OR “Multimorbidity” OR “Comorbidity” OR “multi-disease” OR “Multidisease” OR multi disease OR “multiple condition” OR

"multi-condition" OR "multi condition" OR "multiple illness" OR "multi-illness" OR "multi illness" OR "multiple syndrome" OR "multi-syndrome" OR "multi syndrome" OR "concurrent condition" OR "concurrent illness" OR "concurrent disease" OR "co-existing disease" OR "coexisting disease" OR "co-existing illness" OR "coexisting illness" OR "co-existing syndrome" OR "coexisting syndrome" OR "co-existing condition" OR "coexisting condition" OR "co-occurring disease" OR "co-occuring disease" OR "co-occuring disease" OR "co-occurring illness" OR "co occurring illness" OR "cooccurring illness" OR "co-occurring syndrome" OR "co occurring syndrome" OR "cooccurring syndrome" OR "co-occurring condition" OR "co occurring condition" OR "cooccurring condition")):ti,ab,kw (Word variations have been searched)

#6 (("Wagner model" OR "Wagner* model*" OR "Wagner* chronic care model*" OR "Wagner chronic care model" OR "chronic care model*" OR "model " OR "collaborative care" OR "chronic care framework" OR "chronic disease care" OR "chronic illness care" OR care model OR "model care" OR "Wagner* model*" OR "Wagner* chronic care model*" OR "Wagner chronic care model" OR "theory" OR "concept" OR "framework" OR "model" OR "programme" OR "approach" OR "clinical pathway" OR "care pathway" OR "critical path" OR "vertical integration" OR "virtual integration" OR "physician system integration" OR "provider system integration" OR "functional integration" OR "horizontal integration" OR "clinical integration" OR "case management" OR "delivery of health care, integrated" OR "disease management" OR "patient care management" OR "patient-centred care" OR "accountable care organisations" OR "continuity of patient care" OR "case management" OR "comprehensive health care" OR "delivery of health care, integrated" OR "managed care programmes" OR "patient-centred care" OR "care delivery" OR "integrated care" OR "comprehensive care" OR "care coordination" OR "managed care" OR "accountable care " OR "accountable care organisations" OR "accountable care organisation" OR "collaborative care" OR "disease management" OR "case-management" OR "case management" OR "shared care" OR "accountable care" OR "patient-centred" OR "patient centred" OR "person-centred" OR "person centred" OR "multidisciplinary care" OR "interdisciplinary care" OR "inter-disciplinary care" OR "cross disciplinary care" OR "cross-disciplinary care" OR "multiple interventions" OR "care chain" OR "care chains" OR "care continuity" OR "care continuation" OR "care transition" OR "care transitions" OR "chain of care" OR "chains of care" OR "continuity of care" OR "cross sectoral care" OR "delivery of health care integrated" OR "integrated medicine" OR "integrated social network" OR "integrated social networks" OR "integration of care" OR "intersectoral care" OR "intrasectoral care" OR "linked care" OR "management model" OR "patient care management" OR "seamless care" OR "service network" OR "service networks" OR "transition of care" OR "transitional care" OR "transmural care" OR "whole system thinking" OR "holistic care")):ti,ab,kw (Word variations have been searched)

#7 (("Angola " OR "Benin " OR "Botswana " OR "Burkina Faso" OR "Upper Volta" OR "Burundi " OR "Cameroon " OR "Cameroons " OR "Cape Verde" OR "Central African Republic" OR Chad OR "Comoros " OR "Comoro Islands" OR "Comores" OR "Mayotte " OR "Congo " OR "Zaire " OR "Cote d'Ivoire" OR "Ivory Coast" OR "Democratic Republic of the Congo" OR "Djibouti " OR "French Somaliland" OR "Eritrea " OR "Ethiopia " OR "Gabon " OR "Gabonese Republic" OR "Gambia " OR "Ghana " OR "Gold Coast" OR "Guinea " OR "Kenya " OR "Lesotho" OR "Basutoland" OR "Liberia " OR "Madagascar " OR "Malagasy Republic " OR "Malawi " OR "Nyasaland " OR "Mali " OR "Mauritania " OR "Mauritius " OR "Mozambique" OR "Namibia" OR "Niger" OR "Nigeria" OR "Rwanda" OR "Sao Tome" OR "Seychelles" OR "Senegal " OR "Sierra Leone" OR "Somalia " OR "South Africa" OR "Sudan " OR "Eswatini" OR "Tanzania" OR "Togo " OR "Togolese Republic" OR "Uganda" OR "Zambia" OR "Zimbabwe " OR "Rhodesia" OR "Sub-Saharan Africa" OR "Africa South of the Sahara")):ti,ab,kw (Word variations have been searched)

#8 ((#1 OR #2 OR #3 OR #4 OR #5) AND #6 AND #7) AND Restricted (1999-2022, RCTs)

6. **Psycinfo via Ovid**

#1 ("elevated blood pressure"/ OR "high blood pressure"/ OR "raised blood pressure"/ OR "diastolic blood pressure"/ OR "systolic blood pressure"/ OR "arterial blood pressure"/ OR "uncontrolled blood pressure"/ OR "uncontrolled hypertension" OR "elevated blood pressure" OR "high blood pressure" OR "raised blood pressure" OR "diastolic blood pressure" OR "systolic blood pressure" OR "arterial blood pressure" OR "uncontrolled blood pressure" OR "uncontrolled hypertension")

#2 ("diabetes mellitus"/ OR "diabetes mellitus, type 2"/ OR "diabetes type 2"/ OR "T2DM"/ OR "diabetes type II"/ OR "diabetes"/ OR "glucose intolerance"/ OR "insulin resistance"/ OR "hyperglycemia"/ OR "hyperglycaemia"/ OR "hypoglycaemia"/ OR "hypoglycaemia"/ OR "high blood sugar"/ OR "elevated blood sugar"/ OR "raised blood sugar"/ OR "high blood glucose"/ OR "elevated blood glucose"/ OR "raised blood glucose"/ OR "diabetes mellitus" OR "diabetes mellitus, type 2" OR "diabetes type 2" OR "T2DM" OR "diabetes type II" OR "diabetes" OR "glucose intolerance" OR "insulin resistance" OR "hyperglycemia" OR "hyperglycaemia" OR "hypoglycemia" OR "hypoglycaemia" OR "high blood sugar" OR "elevated blood sugar" OR "raised blood sugar" OR "high blood glucose" OR "elevated blood glucose" OR "raised blood glucose")

#3 ("stroke"/ OR "transient ischemic attack"/ OR "ischemic attack"/ OR "angina"/ OR "angina pectoris"/ OR "heart attack"/ OR "ischemic heart diseases "/ OR "transient ischaemic attack"/ OR "coronary heart disease"/ OR "coronary disease"/ OR "heart failure"/ OR "peripheral vascular disease"/ OR "Peripheral Vascular diseases"/ OR "atrial fibrillation"/ OR "cardiovascular disease"/ OR "heart disease"/ OR "stroke" OR "transient ischemic attack" OR "ischemic attack" OR "angina" OR "angina pectoris" OR "heart

attack" OR "ischemic heart diseases " OR "transient ischaemic attack" OR "coronary heart disease" OR "coronary disease" OR "heart failure" OR "peripheral vascular disease" OR "Peripheral Vascular diseases" OR "atrial fibrillation" OR "cardiovascular disease" OR "heart disease")

#4 ("Hypercholesterolemia"/ OR "Dyslipidemias"/ OR "blood lipid"/ OR "Cholesterol"/ OR "high cholesterol"/ OR "elevated cholesterol"/ OR "raised cholesterol"/ OR "low density lipoprotein "/ OR "high density lipoprotein"/ OR "Dyslipidemia"/ OR "Dyslipidaemia"/ OR "Hypercholesterolemia"/ OR "hypercholesterolaemia "/ OR "hypercholesterolimia "/ OR "Hypertriglyceridemia"/ OR "Hypertriglyceridemia"/ OR "Hypertriglyceridaemia"/ OR "Hyperlipidemia"/ OR "Hyperlipidemias"/ OR "Hyperlipidaemia"/ OR "LDL"/ OR "HDL"/ OR "Hypercholesterolemia" OR "Dyslipidemias" OR "blood lipid" OR "Cholesterol" OR "high cholesterol" OR "elevated cholesterol" OR "raised cholesterol" OR "low density lipoprotein " OR "high density lipoprotein" OR "Dyslipidemia" OR "Dyslipidaemia" OR "Hypercholesterolemia" OR "hypercholesterolaemia " OR "hypercholesterolimia " OR "Hypertriglyceridemia" OR "Hypertriglyceridemia" OR "Hypertriglyceridaemia" OR "Hyperlipidemia" OR "Hyperlipidemias" OR "Hyperlipidaemia" OR "LDL" OR "HDL")

#5 ("Comorbid" OR "co-morbid" OR "co-morbidity" OR "Multimorbidity" OR "multi-morbid" OR "multi morbidity" OR "Multimorbidity" OR "Comorbidity" OR "multi-disease" OR "Multidisease" OR multi disease OR "multiple condition" OR "multi-condition" OR "multi condition" OR "multiple illness" OR "multi-illness" OR "multi illness" OR "multiple syndrome" OR "multi-syndrome" OR "multi syndrome" OR "concurrent condition" OR "concurrent illness" OR "concurrent disease" OR "co-existing disease" OR "coexisting disease" OR "co-existing illness" OR "coexisting illness" OR "co-existing syndrome" OR "coexisting syndrome" OR "co-existing condition" OR "coexisting condition" OR "co-occurring disease" OR "co-occuring disease" OR "co-occuring disease" OR "co-occurring illness" OR "co occurring illness" OR "cooccurring illness" OR "co-occurring syndrome" OR "co occurring syndrome" OR "cooccurring syndrome" OR "co-occurring condition" OR "co occurring condition" OR "cooccurring condition")

#6 ("Wagner model" OR "Wagner* model*" OR "Wagner* chronic care model*" OR "Wagner chronic care model" OR "chronic care model*" OR "model " OR "collaborative care" OR "chronic care framework" OR "chronic disease care" OR "chronic illness care" OR care model OR "model care" OR "Wagner* model*" OR "Wagner* chronic care model*" OR "Wagner chronic care model" OR "theory" OR "concept" OR "framework" OR "model" OR "programme" OR "approach" OR "clinical pathway" OR "care pathway" OR "critical path" OR "vertical integration" OR "virtual integration" OR "physician system integration" OR "provider system integration" OR "functional integration" OR "horizontal integration" OR "clinical integration" OR "case management"

OR “delivery of health care, integrated” OR “disease management” OR “patient care management” OR “patient-centred care” OR “accountable care organisations” OR “continuity of patient care” OR “case management” OR “comprehensive health care” OR “delivery of health care, integrated” OR “managed care programmes” OR “patient-centred care” OR “care delivery” OR “integrated care” OR “comprehensive care” OR “care coordination” OR “managed care” OR “accountable care “ OR “accountable care organisations” OR “accountable care organisation” OR “collaborative care” OR “disease management” OR “case-management” OR “case management” OR “shared care” OR “accountable care” OR “patient-centred” OR “patient centred” OR “person-centred” OR “person centred” OR “multidisciplinary care” OR “interdisciplinary care” OR “inter-disciplinary care” OR “cross disciplinary care” OR “cross-disciplinary care” OR “multiple interventions” OR “care chain” OR “care chains” OR “care continuity” OR “care continuation” OR “care transition” OR “care transitions” OR “chain of care” OR “chains of care” OR “continuity of care” OR “cross sectoral care” OR “delivery of health care integrated” OR “integrated medicine” OR “integrated social network” OR “integrated social networks” OR “integration of care” OR “intersectoral care” OR “intrasectoral care” OR “linked care” OR “management model” OR “patient care management” OR “seamless care” OR “service network” OR “service networks” OR “transition of care” OR “transitional care” OR “transmural care” OR “whole system thinking” OR “holistic care”)

#7 (“Angola “ OR “Benin “ OR “Botswana “ OR “Burkina Faso” OR “Upper Volta” OR “Burundi “ OR “Cameroon “ OR “Cameroons “ OR “Cape Verde” OR “Central African Republic” OR Chad OR “Comoros “ OR “Comoro Islands” OR “Comores” OR “Mayotte “ OR “Congo “ OR “Zaire “ OR “Cote d’Ivoire” OR “Ivory Coast” OR “Democratic Republic of the Congo” OR “Djibouti “ OR “French Somaliland” OR “Eritrea “ OR “Ethiopia “ OR “Gabon “ OR “Gabonese Republic” OR “Gambia “ OR “Ghana “ OR “Gold Coast” OR “Guinea “ OR “Kenya “ OR “Lesotho” OR “Basutoland” OR “Liberia “ OR “Madagascar “ OR “Malagasy Republic “ OR “Malawi “ OR “Nyasaland “ OR “Mali “ OR “Mauritania “ OR “Mauritius “ OR “Mozambique” OR “Namibia” OR “Niger” OR “Nigeria” OR “Rwanda” OR “Sao Tome” OR “Seychelles” OR “Senegal “ OR “Sierra Leone” OR “Somalia “ OR “South Africa” OR “Sudan “ OR “Eswatini” OR “Tanzania” OR “Togo “ OR “Togolese Republic” OR “Uganda” OR “Zambia” OR “Zimbabwe “ OR “Rhodesia” OR “Sub-Saharan Africa” OR “Africa South of the Sahara”)

8 ((#1 OR #2 OR #3 OR #4 OR #5) AND #6 AND #7)

9 limit 8 to (“0300 clinical trial” and yr=”1999 - 2022”)

7. **CINAHL**

#1 (“elevated blood pressure” OR “high blood pressure” OR “raised blood pressure” OR “diastolic blood pressure” OR “systolic blood pressure” OR “arterial

blood pressure" OR "uncontrolled blood pressure" OR "uncontrolled hypertension" OR "elevated blood pressure" OR "high blood pressure" OR "raised blood pressure" OR "diastolic blood pressure" OR "systolic blood pressure" OR "arterial blood pressure" OR "uncontrolled blood pressure" OR "uncontrolled hypertension")

#2 ("diabetes mellitus" OR "diabetes mellitus, type 2" OR "diabetes type 2" OR "T2DM" OR "diabetes type II" OR "diabetes" OR "glucose intolerance" OR "insulin resistance" OR "hyperglycemia" OR "hyperglycaemia" OR "hypoglycaemia" OR "hypoglycaemia" OR "high blood sugar" OR "elevated blood sugar" OR "raised blood sugar" OR "high blood glucose" OR "elevated blood glucose" OR "raised blood glucose" OR "diabetes mellitus" OR "diabetes mellitus, type 2" OR "diabetes type 2" OR "T2DM" OR "diabetes type II" OR "diabetes" OR "glucose intolerance" OR "insulin resistance" OR "hyperglycemia" OR "hyperglycaemia" OR "hypoglycemia" OR "hypoglycaemia" OR "high blood sugar" OR "elevated blood sugar" OR "raised blood sugar" OR "high blood glucose" OR "elevated blood glucose" OR "raised blood glucose")

#3 ("stroke" OR "transient ischemic attack" OR "ischemic attack" OR "angina" OR "angina pectoris" OR "heart attack" OR "ischemic heart diseases " OR "transient ischaemic attack" OR "coronary heart disease" OR "coronary disease" OR "heart failure" OR "peripheral vascular disease" OR "Peripheral Vascular diseases" OR "atrial fibrillation" OR "cardiovascular disease" OR "heart disease" OR "stroke" OR "transient ischemic attack" OR "ischemic attack" OR "angina" OR "angina pectoris" OR "heart attack" OR "ischemic heart diseases " OR "transient ischaemic attack" OR "coronary heart disease" OR "coronary disease" OR "heart failure" OR "peripheral vascular disease" OR "Peripheral Vascular diseases" OR "atrial fibrillation" OR "cardiovascular disease" OR "heart disease")

#4 ("Hypercholesterolemia" OR "Dyslipidemias" OR "blood lipid" OR "Cholesterol" OR "high cholesterol" OR "elevated cholesterol" OR "raised cholesterol" OR "low density lipoprotein " OR "high density lipoprotein" OR "Dyslipidemia" OR "Dyslipidaemia" OR "Hypercholesterolemia" OR "hypercholesterolaemia " OR "hypercholesterolimia " OR "Hypertriglyceridemia" OR "Hypertriglyceridemia" OR "Hypertriglyceridaemia" OR "Hyperlipidemia" OR "Hyperlipidemias" OR "Hyperlipidaemia" OR "LDL" OR "HDL" OR "Hypercholesterolemia" OR "Dyslipidemias" OR "blood lipid" OR "Cholesterol" OR "high cholesterol" OR "elevated cholesterol" OR "raised cholesterol" OR "low density lipoprotein " OR "high density lipoprotein" OR "Dyslipidemia" OR "Dyslipidaemia" OR "Hypercholesterolemia" OR "hypercholesterolaemia " OR "hypercholesterolimia " OR "Hypertriglyceridemia" OR "Hypertriglyceridemia" OR "Hypertriglyceridaemia" OR "Hyperlipidemia" OR "Hyperlipidemias" OR "Hyperlipidaemia" OR "LDL" OR "HDL")

#5 ("Comorbid" OR "co-morbid" OR "co-morbidity" OR "Multimorbidity" OR "multi-morbid" OR "multi morbidity" OR "Multimorbidity" OR "Comorbidity" OR

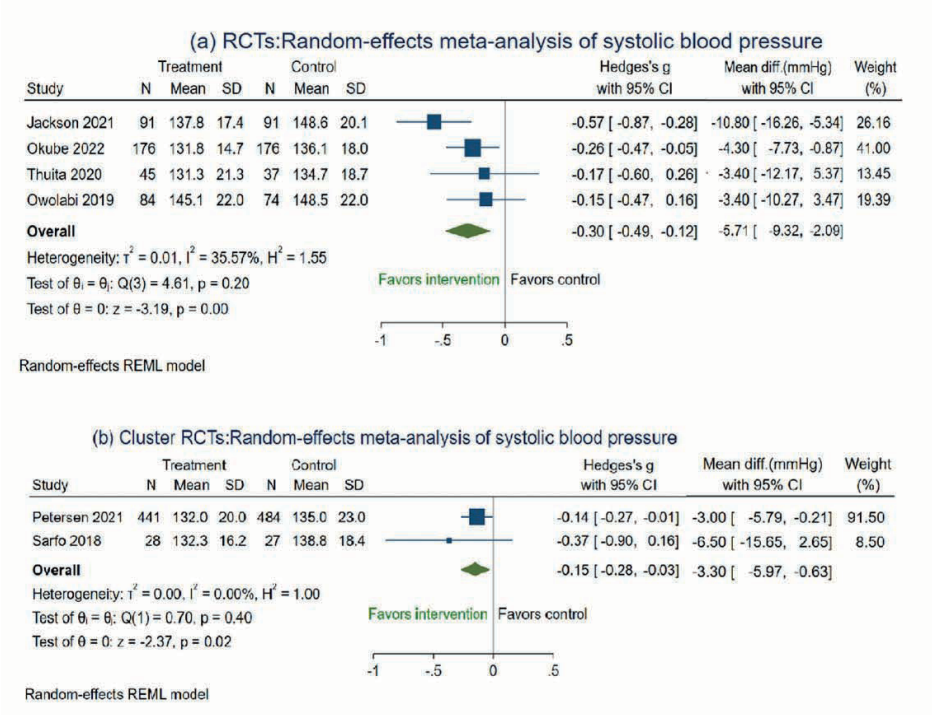
"multi-disease" OR "Multidisease" OR multi disease OR "multiple condition" OR "multi-condition" OR "multi condition" OR "multiple illness" OR "multi-illness" OR "multi illness" OR "multiple syndrome" OR "multi-syndrome" OR "multi syndrome" OR "concurrent condition" OR "concurrent illness" OR "concurrent disease" OR "co-existing disease" OR "coexisting disease" OR "co-existing illness" OR "coexisting illness" OR "co-existing syndrome" OR "coexisting syndrome" OR "co-existing condition" OR "coexisting condition" OR "co-occurring disease" OR "co-occuring disease" OR "co-occuring disease" OR "co-occurring illness" OR "co occurring illness" OR "cooccurring illness" OR "co-occurring syndrome" OR "co occurring syndrome" OR "cooccurring syndrome" OR "co-occurring condition" OR "co occurring condition" OR "cooccurring condition")

#6 ("Wagner model" OR "Wagner* model*" OR "Wagner* chronic care model*" OR "Wagner chronic care model" OR "chronic care model*" OR "model " OR "collaborative care" OR "chronic care framework" OR "chronic disease care" OR "chronic illness care" OR care model OR "model care" OR "Wagner* model*" OR "Wagner* chronic care model*" OR "Wagner chronic care model" OR "theory" OR "concept" OR "framework" OR "model" OR "programme" OR "approach" OR "clinical pathway" OR "care pathway" OR "critical path" OR "vertical integration" OR "virtual integration" OR "physician system integration" OR "provider system integration" OR "functional integration" OR "horizontal integration" OR "clinical integration" OR "case management" OR "delivery of health care, integrated" OR "disease management" OR "patient care management" OR "patient-centred care" OR "accountable care organisations" OR "continuity of patient care" OR "case management" OR "comprehensive health care" OR "delivery of health care, integrated" OR "managed care programmes" OR "patient-centred care" OR "care delivery" OR "integrated care" OR "comprehensive care" OR "care coordination" OR "managed care" OR "accountable care " OR "accountable care organisations" OR "accountable care organisation" OR "collaborative care" OR "disease management" OR "case-management" OR "case management" OR "shared care" OR "accountable care" OR "patient-centred" OR "patient centred" OR "person-centred" OR "person centred" OR "multidisciplinary care" OR "interdisciplinary care" OR "inter-disciplinary care" OR "cross disciplinary care" OR "cross-disciplinary care" OR "multiple interventions" OR "care chain" OR "care chains" OR "care continuity" OR "care continuation" OR "care transition" OR "care transitions" OR "chain of care" OR "chains of care" OR "continuity of care" OR "cross sectoral care" OR "delivery of health care integrated" OR "integrated medicine" OR "integrated social network" OR "integrated social networks" OR "integration of care" OR "intersectoral care" OR "intrasectoral care" OR "linked care" OR "management model" OR "patient care management" OR "seamless care" OR "service network" OR "service networks" OR "transition of care" OR "transitional care" OR "transmural care" OR "whole system thinking" OR "holistic care")

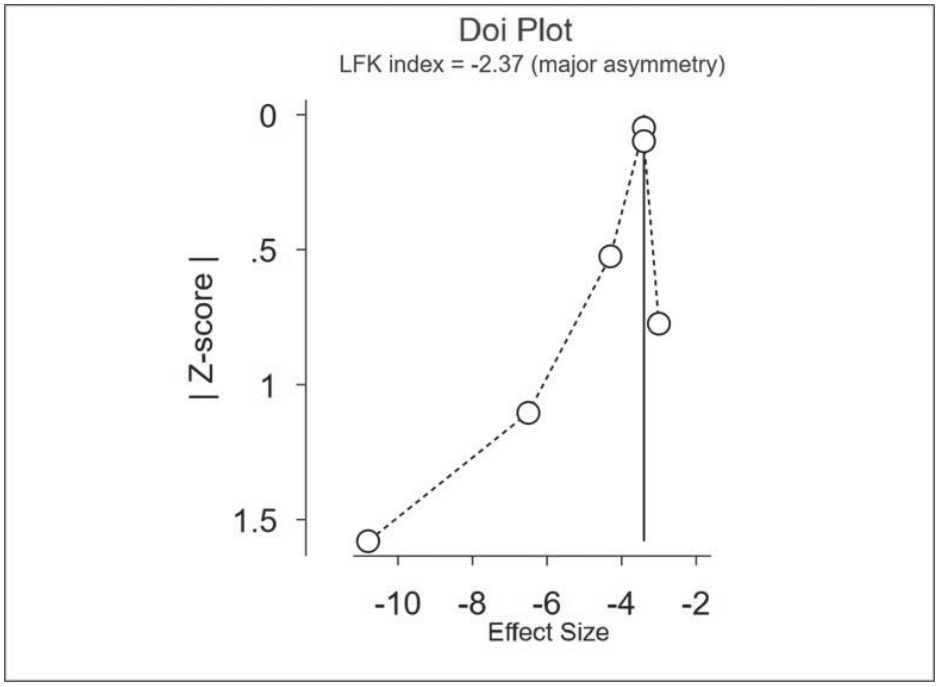
#7 ("Angola " OR "Benin " OR "Botswana " OR "Burkina Faso" OR "Upper Volta" OR "Burundi " OR "Cameroon " OR "Cameroons " OR "Cape Verde" OR "Central African Republic" OR Chad OR "Comoros " OR "Comoro Islands" OR "Comores" OR "Mayotte " OR "Congo " OR "Zaire " OR "Cote d'Ivoire" OR "Ivory Coast" OR "Democratic Republic of the Congo" OR "Djibouti " OR "French Somaliland" OR "Eritrea " OR "Ethiopia " OR "Gabon " OR "Gabonese Republic" OR "Gambia " OR "Ghana " OR "Gold Coast" OR "Guinea " OR "Kenya " OR "Lesotho" OR "Basutoland" OR "Liberia " OR "Madagascar " OR "Malagasy Republic " OR "Malawi " OR "Nyasaland " OR "Mali " OR "Mauritania " OR "Mauritius " OR "Mozambique" OR "Namibia" OR "Niger" OR "Nigeria" OR "Rwanda" OR "Sao Tome" OR "Seychelles" OR "Senegal " OR "Sierra Leone" OR "Somalia " OR "South Africa" OR "Sudan " OR "Eswatini" OR "Tanzania" OR "Togo " OR "Togolese Republic" OR "Uganda" OR "Zambia" OR "Zimbabwe " OR "Rhodesia" OR "Sub-Saharan Africa" OR "Africa South of the Sahara")

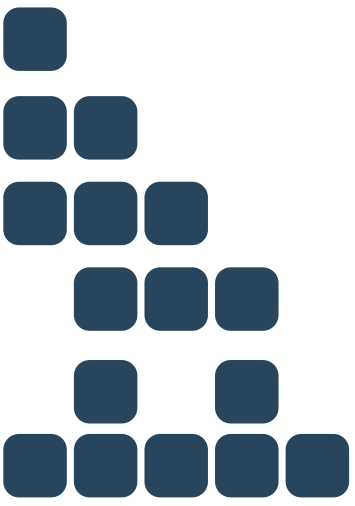
#8 ((S1 OR S2 OR S3 OR S4 OR S5) AND S6 AND S7) & 1999-2022 & research article& peer-reviewed

Supplementary file 3: Sensitivity analysis of RCTs and cluster RCTs



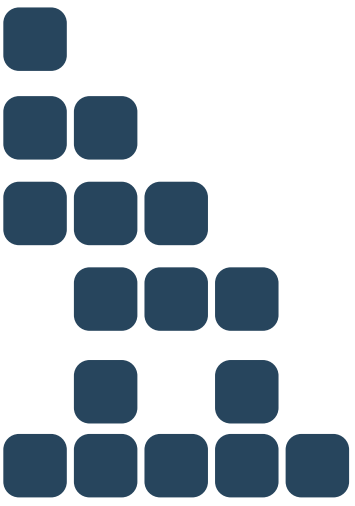
Supplementary file 4: DOI plot of the random effects meta-analysis of SBP for integrated versus standard care for cardiometabolic multimorbidity in Sub-Saharan Africa





PART 3

The readiness of healthcare facilities to provide integrated chronic disease management in sub-Saharan Africa



6

Assessing the Readiness to Provide Integrated Management of Cardiovascular Diseases and Type 2 Diabetes in Kenya: Results from a National Survey

Peter Otieno, Charles Agyemang, Welcome Wami, Calistus Wilunda, Richard E Sanya, Gershim Asiki

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DOI: https://doi.org/10.5334/gh.1213

Abstract

Introduction: Integrated chronic disease management is the desired core function of a responsive healthcare system. However, many challenges surround its implementation in Sub-Saharan Africa. The current study assessed the readiness of healthcare facilities to provide integrated management of cardiovascular diseases (CVDs) and type 2 diabetes in Kenya.

Methods: We used data from a nationally representative cross-sectional survey of 258 public and private health facilities conducted in Kenya between 2019 and 2020. Data were collected using a standardised facility assessment questionnaire and observation checklists modified from the World Health Organization Package of Essential Non-communicable Diseases. The primary outcome was the readiness to provide integrated care for CVDs and diabetes—defined as the mean availability of tracer items comprising trained staff and clinical guidelines, diagnostic equipment, essential medicines, diagnosis, treatment and follow-up. A cut-off threshold of ≥70% was used to classify facilities as 'ready'. Gardner-Altman plots and modified Poisson regression were used to examine the facility characteristics associated with care integration readiness.

Results: Of the surveyed facilities, only a quarter (24.1%) were ready to provide integrated care for CVDs and type 2 diabetes. Care integration readiness was lower in public versus private facilities [aPR=0.6; 95% CI 0.4 to 0.9], and primary healthcare facilities were less likely to be ready compared to hospitals [aPR=0.2; 95% CI 0.1 to 0.4]. Facilities located in Central Kenya [aPR=0.3; 95% CI 0.1 to 0.9], and the Rift Valley region [aPR=0.4; 95% CI 0.1 to 0.9], were less likely to be ready compared to the capital Nairobi.

Conclusions: There are gaps in the readiness of healthcare facilities particularly primary healthcare facilities in Kenya to provide integrated care services for CVDs and diabetes. Our findings inform the review of current supply-side interventions for integrated management of CVDs and type 2 diabetes, especially in lower-level public health facilities in Kenya.

Key Words: integrated care, cardiovascular diseases, type 2 diabetes, readiness assessment

Background

Cardiovascular diseases (CVDs) and type 2 diabetes are the leading contributors to the global burden of morbidity and mortality (1, 2). Three-quarters of CVDs and diabetes-related mortalities occur in low and middle-income countries (LMICs) (3). In Kenya, CVDs are responsible for 50% of hospital admissions and 40% of hospital mortalities (4). Complications of hypertension remain the most prevalent among all CVDs (5). One in four adults in Kenya has hypertension, and 3% have type 2 diabetes (6, 7). Half of the patients with type 2 diabetes in Kenya also have hypertension (8). From the 2015 nationwide non-communicable diseases (NCD) STEPS survey, only 15.6% and 43.7% of people living with hypertension and diabetes were aware that they had hypertension and type 2 diabetes, respectively (6, 7). Only 26.9% of individuals with hypertension and 20.0% of those with type 2 diabetes were on treatment, with more than half of those on treatment having poor control (6, 7).

The rising global burden of CVDs and type 2 diabetes requires a shift from vertical disease management programs toward integrated care (9). Healthcare services are 'integrated' when services for two or more diseases are offered at the same facility during the same visit, and the provider of one service encourages patients to consider using the other service during the visit (10). Previous studies show that access to integrated healthcare services has the potential to elicit positive health outcomes, including improved prognosis, clinical outcomes, and overall quality of life (11-15). However, many challenges surround its design and implementation (16, 17). People living with CVDs and type 2 diabetes often have multimorbidities (multiple conditions) (18). In 2019, about one-third of adults in the world lived with multimorbidities, typically including CVDs and type 2 diabetes (19).

The United Nation's sustainable development goal of universal health coverage envisages access to high-quality integrated healthcare services (20). Kenya has set out several measures to curb the burden of CVDs and diabetes (21-23). At the policy level, chronic disease prevention and management has been prioritised as one of the key objectives of the Kenya Health Policy 2014–2030 (24). Kenya established national guidelines for preventing and managing diabetes and CVDs in 2010 and 2018, respectively (25, 26). These guidelines follow the WHO HEARTS technical package for CVD management in primary health care (25, 27). One of the major policy directions toward addressing the burden of CVD and type 2 diabetes is to provide integrated care (25). Consequently, the Kenya Expanded Program on Health has included care for CVDs and type 2 diabetes in the essential package of primary healthcare (28).

Despite these policy initiatives, little is known about the extent to which the healthcare facilities in Kenya apply the elements of care integration envisioned in the national policy guidelines. A readiness assessment of care integration capacity is crucial for

benchmarking the health system response to the burden of CVDs and type 2 diabetes and supporting policy-makers in planning sustainable chronic care models. To respond to this need, this study assessed the readiness of public and private healthcare facilities in Kenya to provide integrated management of CVDs and type 2 diabetes.

Methods

Study design and setting

We analysed secondary data from a nationally representative cross-sectional study conducted between 2019 and 2020 investigating Kenya's healthcare system response to chronic disease management (29). The overarching aim of the study was to strengthen the health system's responsiveness to managing chronic diseases in Kenya. The health service delivery in Kenya is structured in a six-tiered system ranging from levels 1 to 6 (30). Level 1 comprises community services with no physical infrastructure while level 2 are small clinics and dispensaries. Level 3 consists of small maternity clinics and community health centres. The sub-county hospitals and the county teaching and referral hospitals are classified as levels 4 and 5, respectively, while level 6 includes the national teaching and referral hospitals. The county governments are responsible for the first five levels of care while the national government is responsible for the sixth level.

Sample size

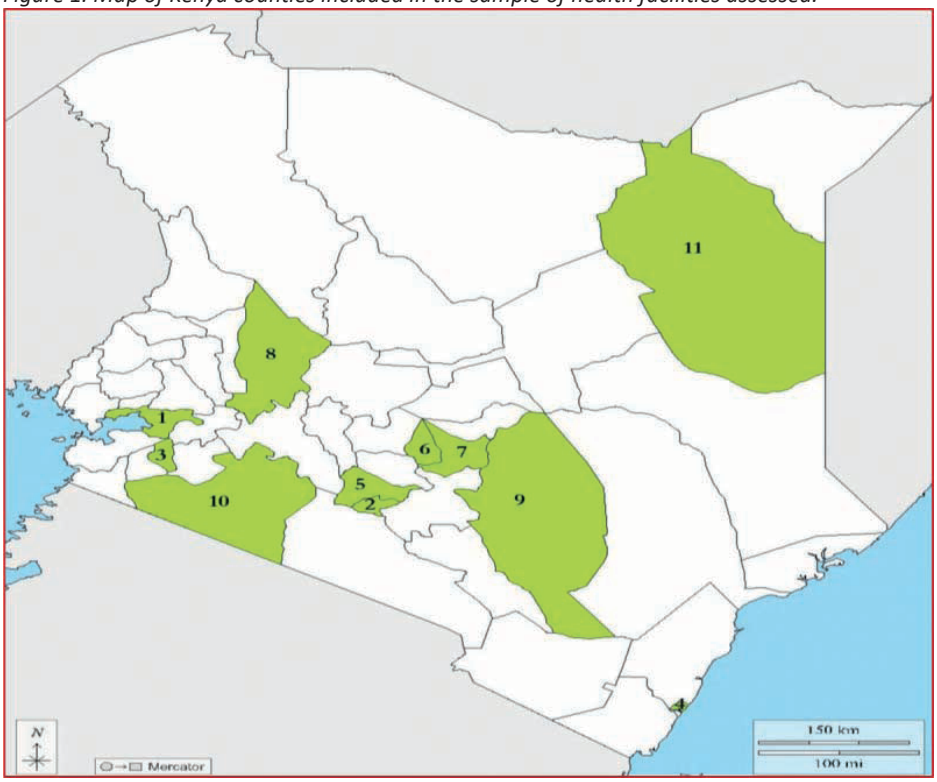
The process of sample size estimation is explained in detail elsewhere (29). The sample size for the study was calculated using the formula commonly used for Service Availability and Readiness Assessment Mapping (SARAM) surveys. The SARAM surveys are nationally representative systematic surveys designed by the WHO to generate reliable and regular information on a set of tracer indicators of service availability and readiness (31). These include the availability of human resources, infrastructure, equipment, essential medicines, diagnostic capacities and the readiness of health facilities to provide primary healthcare interventions for infectious and non-communicable diseases (31). Based on a pilot study conducted in Machakos and Nairobi counties in 2016–2017, 40% of the facilities in Kenya were assumed to be ready to deliver some aspects of chronic disease management [23]. A design effect of 1.2 and 15% margin of error were used in the sample size calculation, with adjustment for a non-response rate of 10%. Thus, the final sample was 301 health facilities (29).

Selection of facilities

Figure 1 shows the geographical distribution of the study counties. The study facilities were randomly selected using a multistage stratified sampling method. Kenya was first stratified into six geo-political regions: Nairobi, Central, Coast and North-Eastern, Eastern, Nyanza and Western, and Rift Valley. In the first stage, two counties (sub-counties in the case of Nairobi) were randomly sampled in each region by probability proportional to size, with size being the total number of healthcare facilities in the

county. The 12 randomly selected study counties comprised Kisumu, Nyamira, Mombasa, Wajir, Baringo, Narok, Kitui, Embu, Kirinyaga, Kiambu and two sub-counties in Nairobi (Dagoretti and Starehe). The second stage involved sampling healthcare facilities in each county. A sampling frame consisting of healthcare facilities in each county was drawn from the Kenya Health Master Facility List of 2019 (32). The healthcare facilities were stratified by levels (levels 2 to 6) and type of ownership (private or public). Stratified simple random sampling was then used to select 301 healthcare facilities from the 12 study counties. However, data were successfully collected in 258 out of the 301 sampled facilities (response rate of 86%).

Figure 1: Map of Kenya counties included in the sample of health facilities assessed.



1 = Kisumu, 2 = Nairobi, 3 = Nyamira, 4 = Mombasa, 5 = Kiambu, 6 = Kirinyaga, 7 = Embu, 8 = Baringo, 9 = Kitui, 10 = Narok, 11 = Wajir. Blank map retrieved and adapted from: https://d-maps.com/ [Accessed: 16 May 2022].

Data collection

Data were collected using an interviewer-administered structured facility assessment questionnaire and observation checklists modified from the WHO Package of Essential Non-communicable Disease Interventions for Primary Health Care (WHO-PEN). The respondents were facility in-charges and heads of clinical departments. In some

higher-level facilities, more than one health service provider participated in the study because some of the tracer items assessed were located in different departments. The data collected comprised facility characteristics including the level of care (levels 2 to 6), type of managing authority (private or public), setting (urban or rural) and region in Kenya. Other data comprised equipment, service availability, human resources, clinical guidelines, essential medicines, medical record system, nutrition monitoring and self-management support. The interview responses were confirmed by direct observation using a checklist for all services where it was potentially feasible. Details of the measurements of the variables used in the current analysis are shown in Table 1.

Table 1: Tracer indicator items for service availability and readiness

Domains	Resources
Trained staff, and clinical guidelines,	• Trained staff on cardiovascular disease diagnosis and treatment • Trained staff on diabetes diagnosis and treatment • Clinical guidelines for the management of cardiovascular diseases • Clinical guidelines for the management of diabetes
Basic diagnostic equipment	• Blood pressure apparatus • Weighing machine • Stethoscope • Blood glucose test • Urine dipstick-protein • Urine dipstick-ketones • Blood analyzer for cholesterol screening (Level 3–6) facilities • Electrocardiogram (ECG) (Level 3–6) facilities • X-ray machine (Level 3–6) facilities
Essential medicines	• ACE inhibitor (enalapril) • Thiazide • Beta-blocker (atenolol) • Calcium channel blocker (amlodipine) • Aspirin (acetylsalicylic acid) capsules/tablets • Metformin capsules/tablets • Hydrochlorothiazide tablet or other thiazide diuretic tablet • Furosemide • Statins • Aspirin • Glibenclamide capsules/tablets • Insulin regular injectable • Gliclazide tablet or glipizide tablet

Table 1: Continued

Domains	Resources
Diagnosis, treatment, follow-up & self-management support	• Diagnosis & treatment of cardiovascular diseases • Diagnosis & treatment of diabetes • Referral services • Nutrition monitoring services • Counseling services on lifestyle risk factors • Hypertension and diabetes self-management counselling • Electronic medical records systems on patient information, symptoms, examination, diagnosis and prescription

Definition of variables

The outcome variable was the readiness of a healthcare facility to provide integrated care services for CVD and type 2 diabetes. In line with the WHO (33), we defined and operationalised integration readiness as 'a one-stop center' with essential resources for comprehensive management of CVDs and type 2 diabetes following the Kenya national guidelines for CVDs and diabetes management requirements for levels 2 to 6 facilities (25). Integration readiness requires a trained workforce, essential drug supplies, treatment and diagnostic resources and structural improvements to support comprehensive management of CVDs and diabetes (33, 34). Hence, the assessment for care integration capacity and readiness in the present study was based on the availability of tracer items across four domains: trained staff and clinical guidelines, basic diagnostic equipment, essential medicines, diagnosis, treatment and follow-up. Details of the tracer items for each domain is shown in Table 1. For each of domain, we calculated an index as the mean score of items expressed as a percentage. The facility readiness index was then calculated as the average of domain indices expressed as a percentage. Service readiness scores ranging from 70% to 100% reflect better preparedness (35). Hence, health facilities that scored ≥70% were classified as 'ready'. The explanatory variables included facility characteristics: level of care, type of managing authority (private or public), setting (urban or rural) and region in Kenya.

Data analysis

Sample weights

The sample facilities were weighted using the probability of selection at each sampling stage. The sampling strata comprised region, county, healthcare level and facility type. Thus, a facility's weight was equal to the inverse of the product of the probability of the selection at each sampling stage.

Descriptive analysis

Descriptive statistics comprising frequencies and percentages or means and standard deviations were used to summarise the characteristics of the study facilities. We used the Gardner-Altman estimation plots to determine the differences in the mean care

integration readiness by facility characteristic (36, 37). The biases in the confidence intervals of the Gardner-Altman estimation plots were corrected using 5,000 accelerated bootstraps resamples [26].

Regression analysis

Modified Poisson regression analysis with robust error variances was used to determine the association of care integration capacity and readiness with facility characteristics. Generally, since using a P-value threshold to select variables can fail to identify important covariates (38), we included all the facility characteristics in the multivariable model. Bayesian Information criterion was used to determine changes in the overall fit of the bivariable and multivariable models. The strength of association was assessed using adjusted prevalence rate ratios (PR) and 95% confidence intervals (CI).

Data analysis was carried out using Stata version 17 (StataCorp, College Station, TX, USA). Estimation statistics and the Gardner-Altman plots (36) were performed using R Statistical Software (version 4.1.0; R Foundation for Statistical Computing, Vienna, Austria).

Results

Health facility profiles

The health facility characteristics are presented in Table 2. Most facilities were level 2 (54.6%) and 3 (34.1%), publicly owned (67.8%), and located in urban settings (53.5%). In addition, three of the five national hospitals (level 6) in Kenya were included in the sample. The facilities were proportionately distributed across the six geo-political regions in Kenya (Nairobi, Central, Coast and North-Eastern, Eastern, Nyanza and Western, and Rift Valley).

Table 2: Health facilities profiles

Characteristics		N = 258
Level		n (%)
	Level 2	140 [54.3]
	Level 3	88 [34.1]
	Level 4	19 [7.4]
	Level 5	8 [3.1]
	Level 6	3 [1.2]
Type		
	Private	83 [32.2]
	Public	175 [67.8]

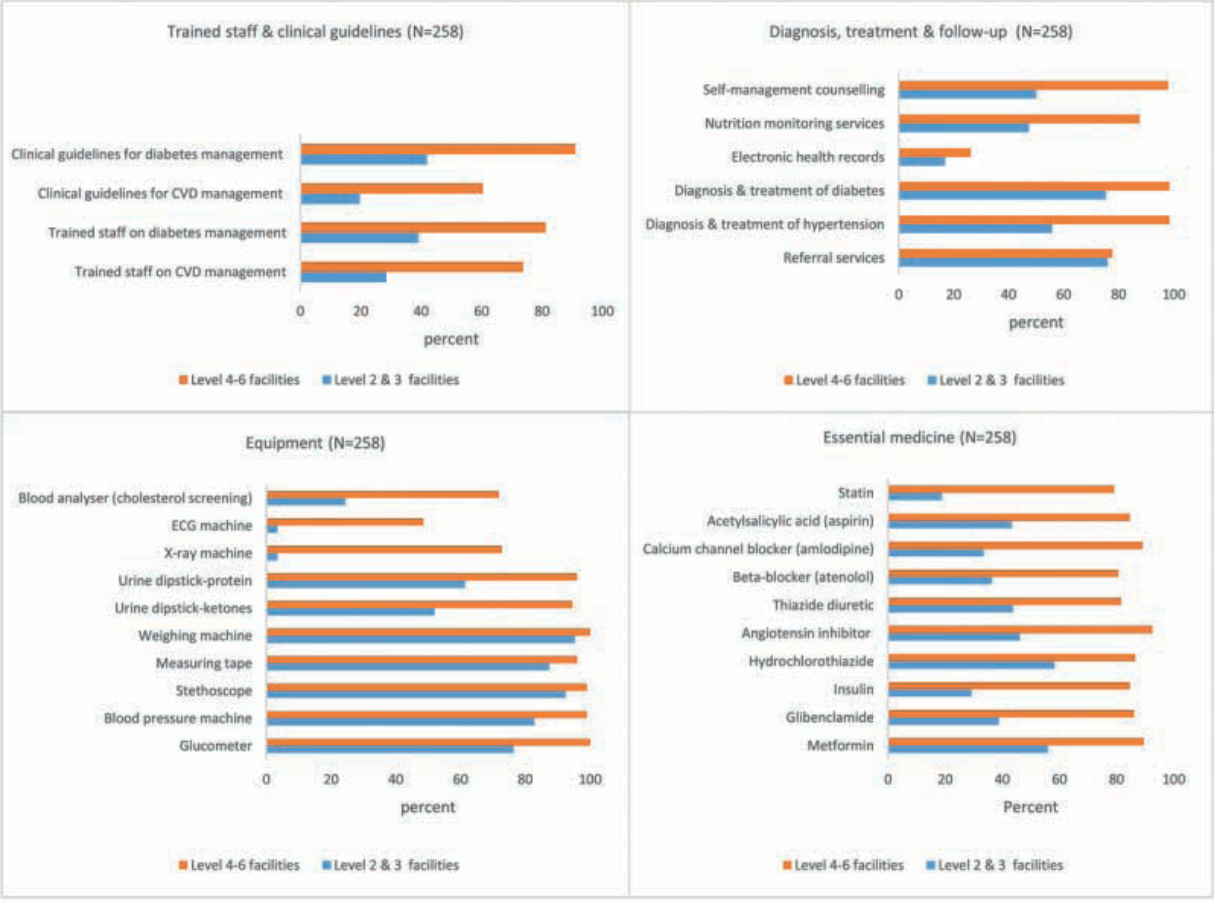
Table 2: Continued

Characteristics		N = 258
Setting		
	Urban	138 [53.5]
	Rural	120 [46.5]
Region		
	Central	39 [15.1]
	Coast and North-Eastern	45 [17.4]
	Eastern	45 [17.4]
	Nairobi	36 [14.0]
	Rift Valley	46 [17.8]
	Western and Nyanza	47 [18.2]

Healthcare services availability and readiness

The availability of tracer items for the management of CVDs and diabetes is shown in Figure 2. Trained staff, clinical guidelines and essential medicines were generally unavailable in most level 2 and 3 facilities but available in level 4 to 6 facilities. Under the domain of basic equipment, weighing machines, measuring tapes, stethoscopes, glucometers and blood pressure machines were generally available across most facilities. Urine dipsticks for ketones and proteins were available in most level 4–6 facilities (94.6% and 96.0%), respectively, and only available in 51.9% and 61.4% of level 2 and 3 facilities, respectively. Blood analysers were available in a quarter of level 2 and 3 facilities compared to 71.8% in level 4 to 6 facilities. X-ray and ECG machines were only available in 3.4% of level 2 and 3 facilities compared to 72.8%, and 48.5% in level 4 to 6 facilities. Diagnosis, treatment, referral and preventive services for CVD and diabetes were generally available across all the facilities except hypertension diagnosis and treatment, which was only available in 58.9% of level 2 and 3 facilities compared to 98.5% of level 4–6 facilities. Electronic health records systems were available in 26.4% of level 2–3 facilities and 16.9% of level 4–6 facilities.

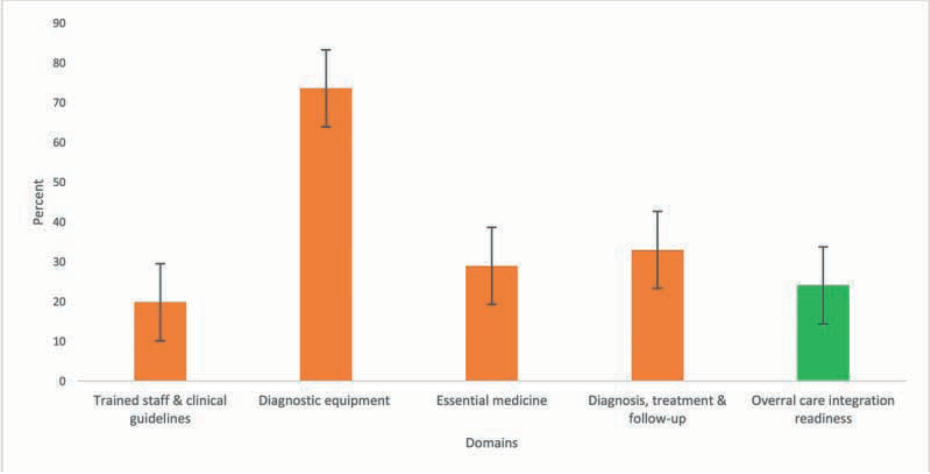
Figure 2: Healthcare services availability and readiness



Care integration readiness for CVD and type 2 diabetes

The average domain score for care integration readiness items is shown in Figure 3. Overall, only a quarter (24.1%) of the healthcare facilities were ready to provide integrated care for CVDs and type 2 diabetes. About three-quarters of the facilities had diagnostic equipment for CVDs and diabetes while less than a third had the minimum threshold for 'trained staff and clinical guidelines', 'equipment', 'essential medicines' and 'diagnosis, treatment and follow-up'.

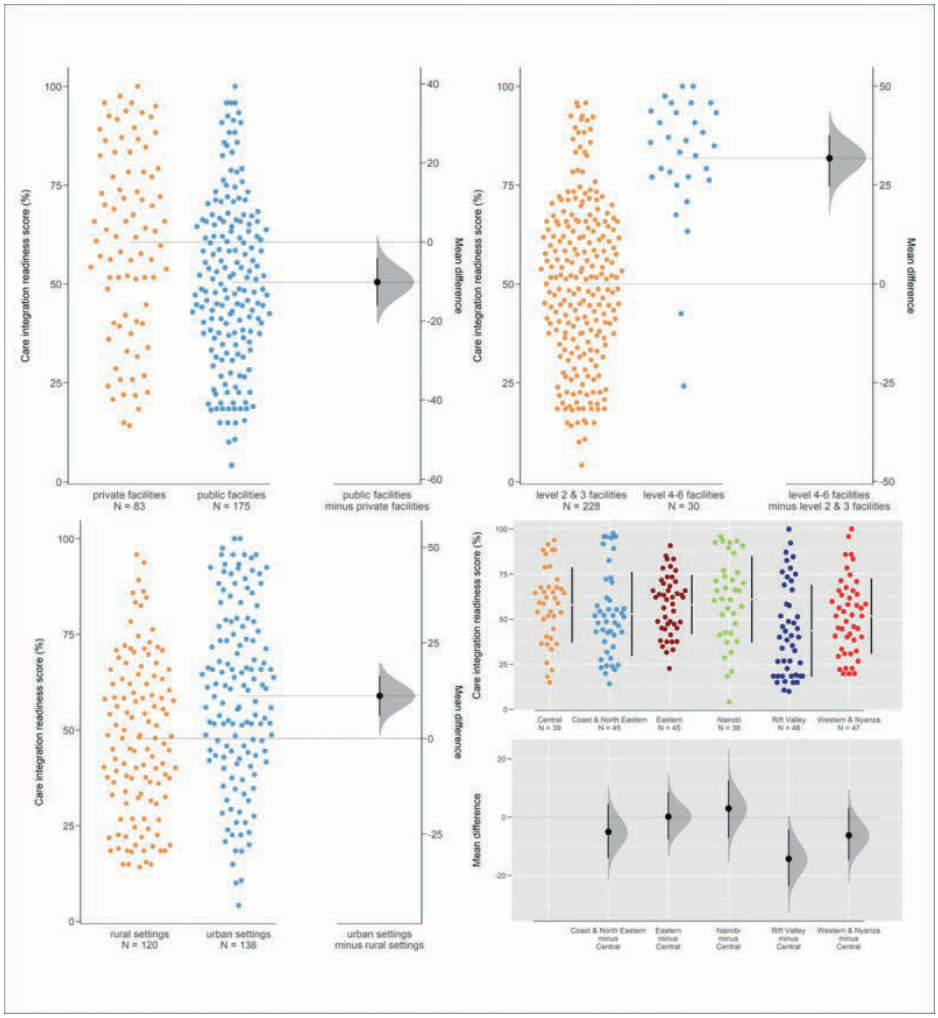
Figure 3: Care integration readiness for management CVD and type 2 diabetes



Comparison of care integration readiness scores and facility characteristics

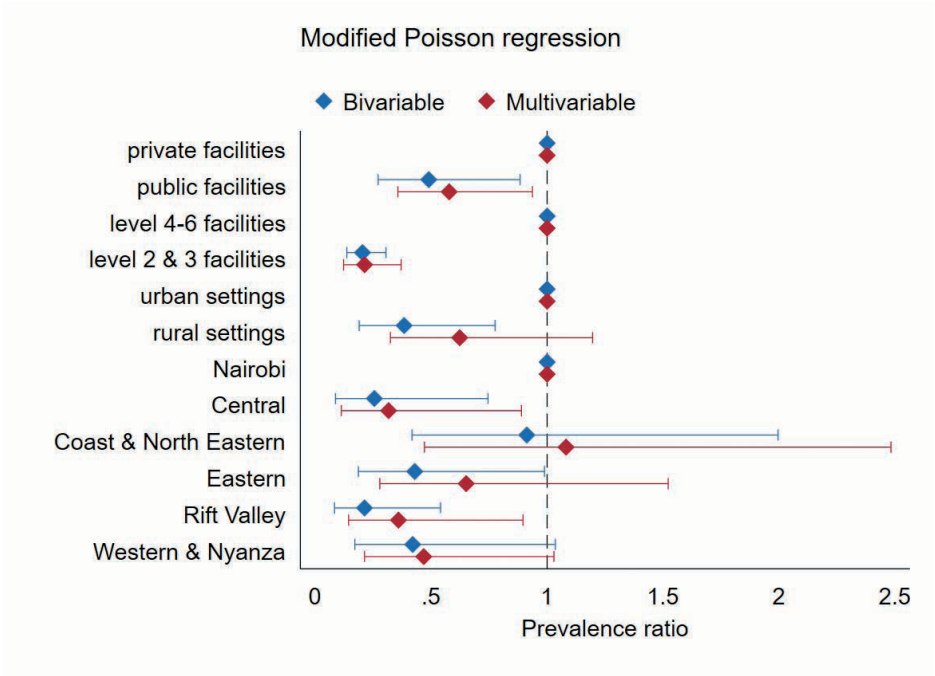
The Gardner-Altman comparisons plots of care integration readiness scores and facility characteristics is shown in Figure 4. The mean difference and 95% CI are represented by the bold black dot and line, respectively. The results show significant differences in the mean care integration readiness index across facility type, level of care, rural-urban settings and geographical regions. Level 4–6 facilities, private facilities and healthcare facilities in urban settings had higher mean care integration readiness index than level 2 and 3 facilities, public facilities and healthcare facilities in rural settings, respectively. Similar patterns were observed across regions. The mean care integration readiness index was highest in Nairobi and lowest in Rift Valley. The magnitude of the facility level differences in the mean care integration readiness index was higher compared to those observed by type of facility, rural-urban setting and geographical region.

Figure 4: Gardner-Altman comparisons plots of care integration readiness scores and facility characteristics



Facility characteristics associated with CVD and type 2 diabetes care integration readiness.

The results of the modified Poisson regression are shown in Figure 5. In the adjusted model, care integration readiness was lower in public versus private facilities [aPR=0.6; 95% CI 0.4 to 0.9], and primary healthcare facilities were less likely to be ready compared to hospitals [aPR=0.2; 95% CI 0.1 to 0.4]. Facilities located in Central Kenya [aPR=0.3; 95% CI 0.1 to 0.9], and the Rift Valley region [aPR=0.4; 95% CI 0.1 to 0.9], were less likely to be ready compared to the capital Nairobi.



Discussion

We examined the readiness of health facilities to provide integrated management of CVDs and type 2 diabetes and the associated facility characteristics in Kenya. Overall, only a quarter of the healthcare facilities were ready to provide integrated care for CVDs and type 2 diabetes. Care integration readiness was lower in public versus private facilities, level 2 and 3 versus level 4–6 facilities and facilities located in the study counties in Central and Rift Valley regions versus Nairobi. Most of the facilities included in the current study failed to reach the minimum threshold for 'trained staff and clinical guidelines', 'essential medicines', and 'diagnosis, treatment and follow-up'. However, basic medical equipment including weighing machines, measuring tapes, blood pressure machines, stethoscopes and glucometers were generally available in most facilities.

Our findings show gaps in the readiness of Kenyan healthcare facilities to provide integrated care services for CVDs and type 2 diabetes. This finding aligns with previous studies from Kenya and other LMICs (39-43). The 2013 SARAM study conducted in Kenya also found that only a third of healthcare facilities were ready to manage (NCDs) (44). Other SARAM surveys performed in sub-Saharan African countries showed that less than half of healthcare facilities were ready to manage type 2 diabetes and CVDs in Sierra Leone, Tanzania, Zambia and Uganda (45-48). However, it is important to note that the definition of readiness in the SARAM surveys differed from the one used in our study. The SARAM surveys take into account single morbidities (49), while the present

study focused on care integration readiness for CVDs and type 2 diabetes. The gaps in the availability of integrated healthcare services for CVDs and type 2 diabetes in our study may partly explain the high burden of unmet needs for hypertension and type 2 diabetes in Kenya (6, 7).

Our results indicate progress in the availability of basic diagnostic equipment, as the 2008–2012 strategic report by the Ministry of Public Health and Sanitation outlined a general lack of basic diagnostic equipment to support healthcare service delivery for NCDs in Kenya (50). The shortage of trained staff and essential medicines for diabetes and CVDs in the current study is in tandem with the SARAM survey conducted in Kenya in 2013 (44). Indeed, shortage of medication, trained staff and clinical guidelines are among the major health system challenges affecting the control of CVDs and diabetes in LMICs (51, 52). In, Kenya less than a quarter of people on medication for hypertension and diabetes are controlled (6, 7). The high burden of uncontrolled hypertension and diabetes could be partly due to the non-availability of medicines. Consistent with previous studies conducted in SSA (53, 54), our results show low uptake of the treatment guidelines for diabetes and CVDs, particularly at a primary healthcare level, where most patients with diabetes and CVDs are likely to seek care. In particular, the shortage of physicians in most primary healthcare settings in Kenya (55), calls for new task-shifting strategies to improve the training of nurses and clinical officers on the treatment guidelines for diabetes CVDs.

Similar to previous studies (56-58), our results show significant disparities in CVDs and type 2 diabetes care integration readiness across facility types, levels of care and geographical settings. The disparities in the care integration readiness across facility levels were not unexpected, as the Kenyan health system is deliberately structured in a tier system with varying levels of care, from level 2 (small clinics and dispensaries) to level 6 (national referral hospitals) (59, 60). However, the substantial variation found within facility types could be partly due to the fact that private health facilities may be more efficient and responsive to patient needs than public facilities (61). A possible explanation for the observed regional differences in care integration readiness for CVDs and type 2 diabetes may be due to, in part, the rapid urbanisation in the capital Nairobi that has increased the influx of people and high concentration of human resources for health, thereby creating the need to expand and improve health services for chronic diseases (62). However, the healthcare service delivery for diabetes and CVDs in facilities located the study counties in Rift valley and Central region may not have received the needed attention. Similar findings of regional disparities in healthcare service readiness for chronic disease have been reported in Ghana, Nigeria and Nepal (63-65).

Overall, this study has two key policy implications for the integrated management of CVDs and type 2 diabetes in Kenya and extends to other countries in SSA. First, the results point to gaps in implementing the national guidelines for managing CVDs and

type 2 diabetes in Kenya. The widespread unavailability of essential resources and capacity in most primary care facilities exemplifies this gap. Incorporating these findings into programmatic interventions and resource allocations may improve equity in access to healthcare services for CVDs and type 2 diabetes. Second, the service availability and readiness for the management of CVDs and type 2 diabetes were remarkably heterogeneous across facility types, locations, and ownership, and this phenomenon is likely to evolve. This highlights the need for continuous and timely assessment of the health system's capacity and readiness for timely identification of gaps and areas of successful implementation.

Strengths and limitations

This study assessed the capacity and readiness to provide integrated management of CVDs and type 2 diabetes in a nationally representative sample of public and private health facilities in Kenya, which increases the generalisability of the findings in the country. The data were collected using a standardised facility assessment questionnaire and observation checklists modified from the WHO Package of Essential Noncommunicable Disease Interventions for primary healthcare. Therefore, the results are comparable to those of other studies conducted in LMICs.

The results of this study should be interpreted in light of a few limitations. First, some of the domain tracer items used in the assessment of care integration capacity and readiness could not be verified by visual observation. Hence, there is a possibility of information bias and underestimation of the gaps. Second, this being a cross-sectional study means causality cannot be inferred. Lastly, the care integration capacity and readiness indicator was constructed without taking into account the patient-perceived perspectives on the quality of healthcare services. We acknowledge the importance of patient perceptions on the quality of healthcare services (66). However, studies have shown a higher likelihood of social-desirability bias from perceived quality than objective assessments (67-69). Despite these limitations, the findings of this study provide crucial insights on the overall readiness of Kenya's healthcare system to provide integrated management of CVDs and type 2 diabetes and identified gaps that require targeted interventions.

Conclusions

This study provides an in-depth assessment of health facility capacity and readiness for integrated management of CVDs and diabetes. The findings indicate that Kenya is far behind in being ready to provide integrated management of CVDs and type 2 diabetes, especially in public facilities and lower-level tiers. This evidence could potentially inform the review of current supply-side interventions for integrated management of CVDs and type 2 diabetes. The findings highlight the need for multifaceted primary care strengthening approaches for improving the equitable supply of essential equipment and first-line medicines, guidelines, counselling and education for patients, and regular

training of healthcare workers in lower lower-level facilities. Further studies on the health system facilitators and barriers to the integrated management of CVDs and type 2 diabetes are needed to inform the design of contextually appropriate care models in Kenya.

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Competing interests: None declared.

Data sharing statement: The datasets used in this study are available upon a reasonable request to the African Population and Health Research Center (APHRC) through its Microdata portal (https:// microdataportal.aphrc.org/index.php/catalog/124).

Ethics approval: The original health service provision assessment in Kenya was approved by the Amref Health Africa Ethics and Scientific Review Committee based in Nairobi, Kenya (ref: DOR/2019/017). All participants were fully informed during the consent process that their participation was voluntary with the freedom to decline any question or withdraw from the study at any point in time and that no harm would occur to them or anyone in their family regardless of their participation decisions.

Author contributions: PO conceptualised the study, reviewed literature and analysed the data. CA, WW, CW, RS and GA made substantive contributions to the conceptualisation of the study and data analysis and reviewed the manuscript. All authors read and approved the final manuscript.

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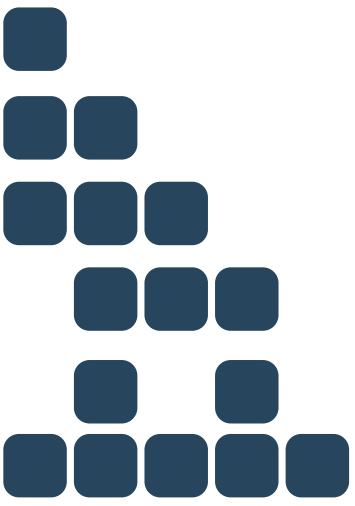

7

Perceived health system facilitators and barriers to integrated management of hypertension and type 2 diabetes in Kenya: a qualitative study

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Abstract

Objective: Understanding the facilitators and barriers to managing hypertension and type 2 diabetes will inform the design of a contextually appropriate integrated chronic care model in Kenya. We explored the perceived facilitators and barriers to the integrated management of hypertension and type 2 diabetes in Kenya using the Rainbow Model of Integrated Care.

Design: This was a qualitative study using data from a larger mixed methods study on the health system response to chronic disease management in Kenya, conducted between July 2019 and February 2020. Data were collected through 44 key informant interviews (KIIs) and 8 focus group discussions (FGDs).

Setting: Multistage sampling procedures were used to select a random sample of 12 study counties in Kenya.

Participants: The participants for the KIIs comprised purposively selected healthcare providers, county health managers, policy experts and representatives from non-state organizations. The participants for the FGDs included patients with hypertension and type 2 diabetes.

Outcome measures: Patients' and providers' perspectives of the health system facilitators and barriers to the integrated management of hypertension and type 2 diabetes in Kenya.

Results: The clinical integration facilitators included patient peer support groups for hypertension and type 2 diabetes. The major professional integration facilitators included task shifting, continuous medical education, and integration of community resource persons. The national referral system, hospital insurance fund, and health management information system emerged as the major facilitators for organizational and functional integration. The system integration facilitators included decentralization of services and multi-sectoral partnerships. The major barriers comprised vertical healthcare services characterized by service unavailability, unresponsiveness, and unaffordability. Others included a shortage of skilled personnel, a lack of interoperable e-health platforms, and care integration policy implementation gaps.

Conclusions: Our study identified barriers and facilitators that may be harnessed to improve the integrated management of hypertension and type 2 diabetes. The facilitators should be strengthened, and barriers to care integration redressed.

Keywords: Integrated care, facilitators and barriers, hypertension, type 2 diabetes, multimorbidity.

Article Summary:

Strengths and limitations of this study

- This study triangulated perspectives from multiple stakeholders including healthcare providers, patients, and policymakers to understand the barriers and facilitators to the integrated management of hypertension and type 2 diabetes in Kenya.
- The use of the Rainbow Model of Integrated Care enabled the identification of the facilitators and barriers of integrated care for hypertension and type 2 diabetes at different levels of the health system in Kenya.
- Our results cannot be generalized to all patients with hypertension and type 2 diabetes but may generate hypotheses for further research on integrated care in Kenya.
- The findings are based on self-reports and may therefore differ from actual health service delivery for hypertension and type 2 diabetes in Kenya.

Background

Hypertension and type 2 diabetes are the leading global risk factors for cardiovascular diseases (1). In Kenya, 3% of adults have impaired fasting glycemia and 25% live with hypertension (2). People living with hypertension and type 2 diabetes often have multiple rather than a single condition, commonly referred to as multimorbidity (3). This implies a shift in primary healthcare services away from single disease-focused, towards integrated care (4). The World Health Organization (WHO) defines integrated chronic disease management as the delivery of a continuum of patient-centered services that are based on promotive, preventive, therapeutic, rehabilitative, and palliative interventions coordinated within and beyond different health sectors throughout the life course (5). The aim of integrated care is to promote collaboration and coordination among different healthcare providers such as primary care physicians, specialists, nurses, and allied health professionals, to deliver seamless and continuous care across different care settings (6, 7).

Several integrated care frameworks exist in the global literature (5, 8-10). However, the conceptual ambiguity of integrated care poses a significant challenge in understanding the gaps in the implementation of integrated care. Developed and validated through systematic reviews and the Delphi method (11-13), the Rainbow Model of Integrated (RMIC) care provides a detailed description of integrated care that emphasizes on consolidation of various healthcare components into a single 'one-stop-shop' setting, where individuals with chronic conditions can receive comprehensive care that includes medical, behavioral, and social support. Broadly, the RMIC cover three main domains including macro, meso, and micro-environment (5, 8-10). The macro-environment comprises legislative, policies, governance, and financial structures. The meso-environment involves collaboration among multifunctional and interdisciplinary teams

or organizations in delivering integrated care. The micro-environment consists of the frontline health service delivery elements including the design, clinical practices, and chronic care models. Although the macro, meso, and micro-environment are crucial elements of the integrated care framework, they have not been considered extensively by previous studies.

The key challenges to the management of hypertension and type 2 diabetes comorbidity in sub-Saharan Africa (SSA) include high treatment burden, polypharmacy, poor coordination, linkage and continuity in care, inadequate access to essential medicines, and poor adherence to treatment (14-16). Most studies on the integrated management of hypertension and type 2 diabetes in Kenya have focused on aggregated output measures such as service delivery indices (17-19). However, such measures may not provide information on the practice of health service providers and patient experiences. In line with the WHO and the RMIC, we defined and operationalized integration as a 'one-stop-shop' model where people living with hypertension and type 2 diabetes receive all essential healthcare services under one roof by one or more service providers. This included prevention, diagnosis, treatment and follow-up. Our 2019 nationwide services availability and readiness assessment survey revealed the low readiness of public primary health facilities in Kenya to provide integrated care services for hypertension and type 2 diabetes (20). Thus, understanding the facilitators and barriers to the management of hypertension and type 2 diabetes will inform the design of a contextually appropriate integrated chronic care model in Kenya. In this study, we explored the facilitators and barriers to the integrated management of hypertension and type 2 diabetes in Kenya using the RMIC.

Methods

Study design

Data reported in this study are part of a larger mixed methods study on the health system response to chronic disease management in Kenya, conducted between July 2019 and February 2020 (21). A qualitative approach, based on phenomenological study design (22) was used to gather participants' views and experiences on integrated management of hypertension and type 2 diabetes. A phenomenological approach is a type of qualitative enquiry that focus on lived experiences of individuals by exploring the meaning of a phenomenon while gaining a deeper understanding of the phenomenon (23). The main goal of the phenomenological approach is to identify a phenomenon by how it is perceived by those with lived experiences (22) .

Research participants.

The research participants comprised frontline health workers such as medical doctors, clinical officers, nurses, pharmacists, and laboratory technologists. The following criteria had to be met for participation: (i) the healthcare professionals should have worked

for at least one year in a health facility with a good understanding of the facility's capacity and chronic diseases-related services provided by the facility; (ii) the healthcare professionals should have voluntarily been willing to participate in the study and able to provide information related to the management of hypertension and type 2 diabetes. Other participants included patients with hypertension and type 2 diabetes who sought care for at least one year in the facilities located in the study counties. County health managers, NCD policy experts and representatives from non-state service delivery organizations were also interviewed. The rationale for interviewing diverse stakeholders at multiple levels was to allow for an exploration of multiple perspectives on the availability and challenges of implementing integrated management of hypertension and type 2 diabetes defined as a "one-stop-shop" model with all essential healthcare services under one roof.

Sampling and recruitment procedures

Multistage sampling procedures (24) were used to select a total of 12 study counties in Kenya from six main regions namely Nairobi, Central, Coast & North Eastern, Eastern, Nyanza & Western, and Rift Valley. (See online supplementary file 1). In the first stage, two counties (sub-counties in the case of Nairobi) were selected in each region. The counties were then sampled with probability proportional to size, with size being the total number of healthcare facilities. The 12 randomly selected study counties included Kisumu, Nyamira, Mombasa, Wajir, Baringo, Narok, Kitui, Embu, Kirinyaga, Kiambu and two sub-counties in Nairobi (Dagoretti and Starehe). However, Wajir, a county neighbouring the conflict-prone Kenya-Somali border was excluded from the qualitative interviews due to insecurity. More details of the sampling methods have been published elsewhere (21). In total, 11 health managers from each of the participating counties were purposively selected to participate in the key informant interviews (KIIs). In addition, 24 healthcare workers from each level of health facility in the participating counties were also purposively selected to participate in the KIIs. Details of the facility levels have been published elsewhere (20). Other study participants for the KIIs comprised five purposively selected policymakers from the non-communicable disease (NCD) division of the Ministry of Health, Kenya and four key persons from non-governmental organisations (NGOs) implementing programs on hypertension and type 2 diabetes at the national level. Five focus group discussions (FGDs) were also conducted among purposively selected patients with hypertension and type 2 diabetes in the study counties (one FGD per region) and an additional three FGDs with patient support groups for hypertension and type 2 diabetes in Nairobi County.

Data collection methods

Data were collected via key KIIs and FGDs. The participants discussed the facilitators and barriers in delivering and accessing integrated management of hypertension and type 2 diabetes in Kenya. The key informants were selected for their expertise in primary health care service for hypertension and type 2 diabetes . The FGDs were used to

supplement the KIIs because they give participants an opportunity to reflect on other participants' views while building on their views (25). The interviews were facilitated by 11 qualitative research assistants from the respective study counties. The research assistants were trained for five days before conducting the interviews. The training covered the objectives of the study, question-by-question explanation of the contents of the interview guides, and standard operating procedures during field interviews. The training also comprised practical sessions involving role-playing in which the research assistants practiced interview sessions with each other as expert respondents.

The FGDs were moderated by a trained qualitative research assistant alongside a note-taker. Each session included 8-10 participants and lasted between one to two hours. Sessions began with brief introductions followed by a discussion on the facilitators and barriers in accessing integrated management of hypertension and type 2 diabetes in Kenya. The discussants expressed their ideas, beliefs, personal experiences and concerns about access to integrated healthcare services for hypertension and type 2 diabetes. All the interviews were held at venues chosen in consultation with the participants. The KIIs with frontline health workers, county health managers, policy experts and representatives from non-state service delivery organizations were conducted in English and lasted about one hour. The FGDs with patients living with hypertension and type 2 diabetes were conducted in Kiswahili or a local language depending on the participant's preference to minimize the language barrier.

Research instruments

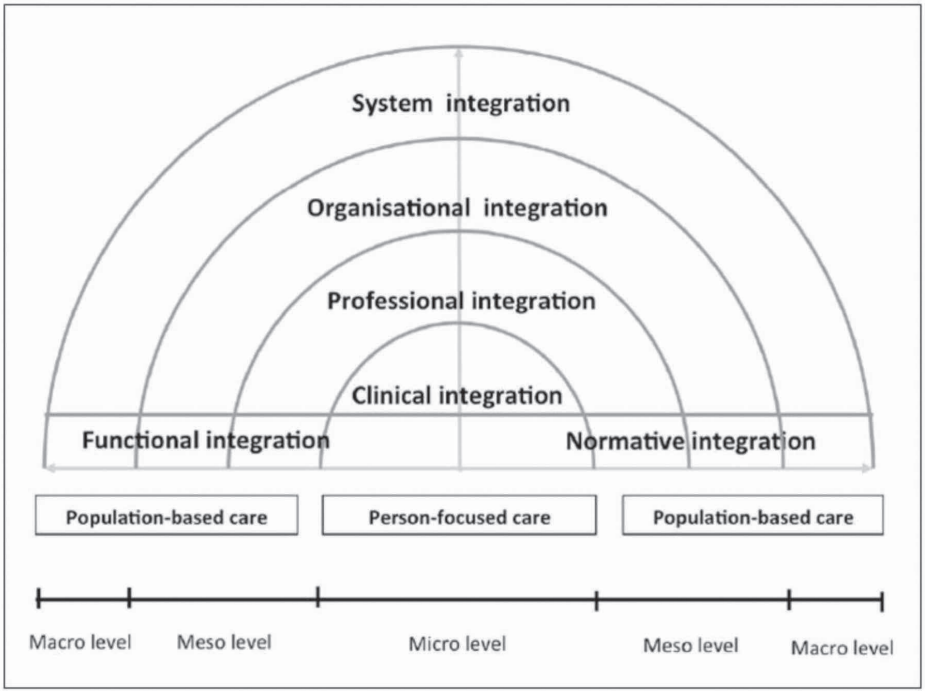
Open-ended thematic interview guides were used for all the KIIs and FGDs (See supplementary file 2). The design of the instruments ensured coverage of similar themes with in-built flexibility for the flow of questions to allow probing of the pertinent issues during the interviews. The interviews consisted of questions**,** aiming to understand the gaps, barriers, enabling, and reinforcing factors in delivering integrated care for hypertension and type 2 diabetes at the primary care level. The items in the KIIs and FGDs were developed based on the concepts of WHO building blocks for health systems (26). The questions focused on the elements of care integration following RMIC (27) and the routine management of hypertension and type 2 diabetes based on the six building blocks of primary healthcare, namely health service delivery, health workforce, health information systems, access to essential medicines, health systems financing, leadership, and governance.

Conceptual framework

The elements of care integration were identified and presented following the Rainbow Model of Integrated Care (RMIC) (27) shown in Figure 1. The RMIC is a validated framework that enables a comprehensive evaluation of care integration elements across the micro, meso, and macro levels of a healthcare system (27). The micro-level focuses on clinical integration comprising coordination of care activities across

conditions, health service providers, and primary care settings. The meso-level is based on organizational and professional integration such as collaboration by health service providers and sharing of roles, responsibilities, and competencies. The macro-level focuses on systems integration comprising healthcare services linkages through rules and policies. The three levels of care integration are linked together by functional and normative integration. Functional integration refers to support functions such as financial, and information management systems. Normative integration comprises a common shared vision, values, mission, and culture that promote care integration.

Figure 1: Rainbow Model of Integrated Care



Adapted from Valentijn et al. 2015 (27) .

Data analysis

The audio-taped recordings were transcribed verbatim alongside handwritten notes. The transcriptions of interviews conducted in languages other than English were translated into English. Data verification for accuracy and completeness was done by reading and rereading the interview transcripts and listening to the audio for clarity. The interview transcripts were reviewed and exported to Nvivo version 12 software for coding. Deductive and inductive thematic analysis were used to deduce the overreaching themes based on the core elements of the RMIC(28). First, three research team members (PO, EOAW, JO) conducted the coding of the transcripts to identify themes,

messages, and patterns emerging from the data. Codes were developed and matched to ensure integrity and similarity between the researchers. A codebook was developed after the integration and collation of the identified codes. Two similar transcripts were coded with constant comparison of the data among the researchers and then discussed to establish agreement before coding all the transcripts (29). Coding of the transcripts was an iterative process among the researchers and refining of the codebook was done during the process to maintain data accuracy. From the codebook, broader themes and subthemes that emerged from the data were identified and reviewed to ensure they were appropriate for the interpretation.

Patient and public involvement

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

Results

Distribution of the study participants

Table 1 shows the characteristics of the study participants. In total, 44 participants comprising of 27 males and 17 females participated in the KIIs. The participants for the KIIs comprised frontline healthcare workers (medical doctors, clinical officers, nurses, pharmacists, and laboratory technologists) and county health managers. Other study participants included national policymakers and key persons from NGOs implementing hypertension and type 2 diabetes programs at the national level. The participants for the FGDs comprised 57 male and 25 female patients with hypertension and type 2 diabetes comorbidity.

Table 1: Characteristics of the study participants

	Male	Female	N
KIIs, n=44			
National policymakers	4	1	5
County health managers	8	3	11
County health service providers	12	12	24
Directors of NGOs implementing hypertension and type 2 diabetes programs	3	1	4
Total	27	17	44
FGDs, n=8			
Patients with hypertension and type 2 diabetes (5 FGDs)	20	37	57
Patient support groups (3 FGDs)	5	20	25
Total	25	57	82

Facilitators and barriers to integrated management hypertension and type 2 diabetes

Various facilitators and barriers to the integrated management of hypertension and type 2 diabetes were identified and presented in Table 2. The results have been presented separately for each dimension of care integration: the micro (clinical integration), meso (professional and organizational integration), macro (system integration), and functional and normative integration (connecting all the levels of integration).

Table 2: Facilitators and barriers in delivering integrated management of hypertension and type 2 diabetes in Kenya.

Health system level	Dimension of care integration	Facilitators (+)	Barriers (-)
Micro level	Clinical integration	• Patient peer support groups for hypertension and type 2 diabetes • Health education & promotion on shared risk factors for cardiovascular diseases	• Vertical healthcare services for hypertension and type 2 diabetes • Lack of basic screening, diagnostic & treatment services for hypertension and type 2 diabetes in primary care facilities • Unavailability of medication for hypertension & type 2 diabetes
Meso level	Professional integration	• Task shifting • Continuous medical education • Integration of community resource persons such as CHVs	• Shortage of skilled personnel • Inadequate budgetary allocations for in-service training • High attrition rate & poor replacement mechanisms • Shortage of specialists • Unqualified healthcare providers • Inadequate training curricula skewed toward therapeutic interventions
	Organizational integration	• Well-established referral systems in public facilities	• Corruption • Conflict of interest

Table 2: Continued

Health system level	Dimension of care integration	Facilitators (+)	Barriers (-)
Macro level	System integration	• Decentralization of healthcare services for hypertension & type 2 diabetes • Multi-sectoral partnerships • Interdependency in the delivery of integrated management of hypertension & type 2 diabetes	• Care integration policy implementation gaps • Challenges with the devolution of healthcare services for hypertension & type 2 diabetes. • Inadequate monitoring and evaluation frameworks for care integration programs
Connecting all the levels of integration	Functional integration	• National health management information system (HMIS) • National health insurance fund (NHIF)	• Inadequate budgetary allocations • Lack of NHIF accreditation of most primary care facilities. • Unaffordability of healthcare services • Coverage limits for hypertension and type 2 diabetes by NHIF • Lack of interoperable e-health platforms
	Normative integration	• Political goodwill for universal health coverage & integrated care	• Poor leadership

Micro level: clinical integration

Clinical integration refers to the extent to which person-centered care services are coordinated in primary care settings. In the current study, the clinical integration facilitators broadly included patient-centered care models such as peer support groups and health education and promotion on shared risk factors for cardiovascular diseases. The peer support groups were considered by the patients interviewed as important avenues for addressing psychosocial needs and raising awareness of shared lifestyle risk factors for hypertension and type 2 diabetes. One patient living with hypertension and type 2 diabetes stated,

> *"When I was diagnosed with hypertension and diabetes, I was overweight and never used to care about what I eat. However, I have acted on the health information I received in this facility from the patient support group sessions, especially on the shared risk factors for hypertension and type 2 diabetes such as diet, exercise and*

medication adherence and my sugar levels and blood pressure are now controlled within the normal range". (Patient FGD participant).

The support group forums provided a platform for sharing experiences and dealing with similar types of health and personal issues and emotional distress. One of the patients living with both hypertension and type 2 diabetes stated,

"I have benefited from the support groups in the sense that I do not have the feeling of being sick alone. We always share our experiences to the point you feel your situation might be even better. When you are alone you can suffer from a lot of psychological problems". (Patient FGD participant).

The patients also acknowledged feeling more motivated and able to improve their self-care. A sense of self-confidence empowered the patients to take responsibility for their health, with one remarking that,

"Being in the support group has enabled me to accept my condition and I am also always free to disclose it to anyone. I am also motivated to adhere to my medication". ((Patient FGD participant).

The major clinical integration barriers identified by the patients and other health stakeholders interviewed comprised vertical and unresponsive healthcare services. One of the NCD experts stated,

"The primary care for hypertension and type 2 diabetes are offered as standalone services in primary care settings even if the patient is living with comorbidities. This results in fragmentation of services that threaten the holistic perspective of healthcare services." (NCD policy expert).

Unresponsive healthcare services were cited by the patients interviewed as a major limitation for the integrated management of hypertension and type 2 diabetes. This was characterized by the unavailability of medication for hypertension and type 2 diabetes, and lack of basic screening, diagnosis, and treatment services for hypertension and type 2 diabetes in primary care facilities. One county health manager stated,

"A majority of primary care facilities in our county offer basic screening for hypertension and screening for risk factors such as body mass index, and basic health education and promotion. However, only a few higher-level facilities might be able to provide blood sugar tests and treatment for type 2 diabetes". (County health manager).

According to one primary care facility in-charge interviewed, the supply-side gaps in essential medicine for hypertension and type 2 diabetes had perceived cross-cutting effects at the patient level such as poor medication adherence. This was exemplified in the following excerpts:

> *"Poor medication adherence is a major challenge among patients with hypertension and type 2 diabetes comorbidities. We have some patients who are chronic defaulters. Some patients do not take medicine and prefer to come to the health facility when they are in a critical stage with serious complications". […] "Sometimes we run out of stock for essential drugs for hypertension and type 2 diabetes since it takes longer for drugs to be restocked in the facility. This leaves us with no choice but to prescribe drugs for patients to buy from private pharmacies". (Primary care facility in charge).*

The vast market for medical products and the relaxed legal status for the medicine trade were identified by the primary care facility in-charges interviewed as major facilitators for inappropriate polypharmacy and irrational use of medicines for the treatment of hypertension and type 2 diabetes in patients with multimorbidities. According to one primary care facility in charge, the drug regulatory authorities are not very effective in enforcing the laws on the trade of medicine. The market is dominated by several drug shops managed by quacks who sell prescription drugs for hypertension and type 2 diabetes over the counter thereby endangering the lives of the patients. This was noted by one of the patients interviewed who said,

> *"There is a time I went to a chemist for refills and I was told by the pharmacist that despite the difference in the brands the drugs were the same. However, my condition deteriorated after using those drugs and I had to come with them here in the facility and the doctor ordered me not to take them again". (Patient FGD participant).).*

Meso level: professional integration

Professional integration refers to the extent to which healthcare professionals delivering care for hypertension and type 2 diabetes coordinate services across various disciplines. In this study, inter-professional partnerships and shared competencies were classified under the overarching theme of professional integration. The facilitators of professional integration included task shifting and continuous medical education (CMEs) on new guidelines for integrated management of hypertension and type 2 diabetes care. The integration of community resource persons such as community health volunteers (CHVs) enabled nurses and clinical officers to delegate healthcare responsibilities such as screening for blood pressure and anthropometrics to the CHVs. According to one County health manager, CHVs played an increasingly important role in the identification, linkage, and retention of patients living with hypertension and type 2 diabetes in care.

One nurse stated that the facility-based CMEs enabled her to upgrade her professional skills and competence in the face of advances in medical science and the ever-changing clinical guidelines for the integrated management of hypertension and type 2 diabetes.

The county health managers and the frontline healthcare workers interviewed identified several gaps in professional integration. These included a shortage of skilled personnel, inadequate budgetary allocations for in-service training, a high attrition rate, poor replacement mechanisms, a shortage of specialists, and a rising number of unqualified healthcare providers. Inadequate curricula were cited by the County health managers interviewed as a major gap in the training of healthcare workers for integrated hypertension and type 2 diabetes care. The training curricula for hypertension and type 2 diabetes management were perceived by the doctors and nurses interviewed to be skewed toward therapeutic interventions with minimal focus on preventive measures. Voicing a general sentiment in response to a question regarding the healthcare workforce for hypertension and type 2 diabetes management, one of the county directors of health interviewed stated,

> *"There is an assumption that training of healthcare workers is a function of the national government and not county government and therefore the approved budget always has zero allocation for training and yet the capacity building has to continue". […] "Most of our curriculums in the colleges used for training our personnel are just focused on therapeutic interventions with little emphasis on how we can integrate prevention programs considering that prevention is more cost-effective than treatment, especially for diseases such as hypertension and type 2 diabetes that require early detection" (County health director).*

Meso level: organisational integration

Organizational integration refers to the extent to which healthcare facilities coordinate services for hypertension and type 2 diabetes across different facilities. In the current study, referral systems for hypertension and type 2 diabetes emerged as a dominant theme under the overarching theme of organizational integration. Our findings show that public facilities had well-established referral systems. Voicing a general sentiment in response to a question regarding the referral systems for hypertension and type 2 diabetes, one of the NCD policy experts stated,

> *"The referrals for hypertension and type 2 diabetes are structured across a four-tiered system comprising community health centers, primary care centers, county referral hospitals, and national hospitals and CHV led community-based demand creation activities such as screening for blood pressure and blood glucose, and identification of cases for referrals at higher levels of care". (NCD policy expert)*

However, there were significant gaps in the referral systems as noted by one FGD patient:

> **"***Some of the doctors in the referral hospitals requests to have the test outside the facility yet they can offer those services and the reason is that they are collaborating with the owners of those facilities to make extra money from some of the services such as X-rays". (Patient FGD participant).*

The macro level: system integration

Systems integration refers to the alignment of regulations and policies on care integration. Two themes emerged under system integration facilitators: decentralization of services and multi-sectoral partnerships and interdependency.

Decentralization of services

The decentralization of healthcare services was cited by the County health managers interviewed as a major facilitator for the development of integrated care models for hypertension and type 2 diabetes that suit the unique primary care needs of the county governments. The decentralization also promotes the autonomy of decisions regarding resource mobilization, allocation, expenditures, and other administrative issues as was noted by a County health manager. The County governments are in charge of the management of secondary and primary care facilities including the county public sector health services such as ambulances and primary healthcare services while the national government is in charge of the national referral facilities and health policy.

Multi-sectoral partnerships and interdependency

Multi-sectoral partnerships and interdependency were reported as one of the drivers for the sustainability of integrated care for hypertension and type 2 diabetes. The NCD policymakers interviewed preferred a people-centered approach rather than an output-oriented one in delivering healthcare services for hypertension and type 2 diabetes. According to one NCD policymaker, putting people-centered core health services in the spotlight was crucial in removing health system bottlenecks that limit coverage of essential healthcare services for hypertension and type 2 diabetes. Some of the key health stakeholders identified included county governments, the Ministry of health, NGOs, civil societies, the private sector, and other government agencies such as the Ministry of education, and public service. These stakeholders formed national and county-based technical working groups whose primary role is policy formulation, advocacy, and coordination of management activities for hypertension and activities at the national and county levels.

The barriers to system integration identified from the interviews were disintegrated into three major domains including policy implementation gaps, devolution challenges, and inadequate monitoring and evaluation frameworks.

Policy implementation gaps

The NCD policy experts interviewed indicated that, despite the wide adoption of policies and guidelines on integrated management of hypertension and type 2 diabetes, there was a widespread consensus that a majority of the policies had not been implemented as envisioned resulting in modest success. The implementation barriers are rooted in factors such as ineffective enforcement, inadequate allocation of human or financial resources, poor coordination, and conflicting roles and responsibilities of the national and county governments. One of the NCD policy experts interviewed stated,

> *"I can confidently say that Kenya has good policy experts who have developed a good policy framework for care integration of hypertension and type 2 diabetes with good indicators, but what we are still grappling with is the implementation. (NCD policy expert).*

Devolution challenges

The county health managers interviewed narrated that the health sector is bedeviled with conflictual relationships between the county and the national governments. The transition of the functions from the national to county governments has been marred by administrative issues and poor coordination of functions that presented resource allocation and utilization challenges as captured in the following response:

> *"The implementation of the devolution has been characterized by challenges on the transition of the functions of the national to the county government resulting in conflicts of interest, especially with regards to the budgetary allocations" (County health manager).*

Inadequate monitoring and evaluation frameworks

Inadequate monitoring and evaluation frameworks for hypertension and type 2 diabetes programs were cited by the NCD experts interviewed as a major barrier to the integrated management of hypertension and type 2 diabetes. According to one NCD expert interviewed, the national HMIS, commonly known as District Health Information System, prioritizes reporting on communicable diseases such as HIV/AIDS, tuberculosis, and malaria, with a limited focus on hypertension and type 2 diabetes. Furthermore, hypertension and type 2 diabetes indicators covered in the annual work plans for the national and county governments are very few compared to the communicable diseases and reproductive health programs. The paucity of data on hypertension and type 2 diabetes results in difficulties to analyze the progress of implementation of integrated care programs and the overall health systems performance.

Functional integration

Functional integration refers to the extent to which support functions such as financial, and information management systems are coordinated to promote integrated

management of hypertension and type 2 diabetes . In this study, the functional integration facilitators included the national health management information system (HMIS) and the National health insurance fund (NHIF).

National health management information system

The HMIS framework provides access to a free web-based open-source health management data platform. One of the County HMIS experts interviewed indicated that the availability of an HMIS was a major facilitating factor for the efficiency of integrated healthcare service delivery for hypertension and type 2 diabetes. According to one HMIS expert, data reporting for hypertension and type 2 diabetes is a requirement by the Ministry of Health in Kenya. Therefore, all public health facilities are mandated to submit healthcare utilization data for hypertension and type 2 diabetes on the District Health Management Information system. This enables easy access to patient data and enhanced decision-making. The high mobile phone coverage in Kenya and internet connectivity especially in urban settings were also cited by the HMIS experts as major facilitators for the adoption of e-health technologies in hypertension and diabetes care.

National health insurance fund

The NHIF emerged as a major facilitator for healthcare financing. The patients interviewed explained how having an NHIF card was key in facilitating their access to health services for hypertension and type 2 diabetes comorbidities:

> *"In this facility, primary healthcare services are free as long as you have an NHIF card. I have benefited from free consultation, treatment, medication, and drugs under the Universal Health Coverage (UHC) initiative" (Patient FGD participant).*

As highlighted in the quote, patients with health insurance coverage were able to access basic outpatient and inpatient services for hypertension and type 2 diabetes , including consultation, tests and scans, treatment and medicine (except when the drugs prescribed are not listed in the coverage). This according to the patients would help them in making a timely decision to seek care, as money is no longer a barrier. Other financial support the patients reported included county-based public health insurance plans, donor funding support and free or subsidized services.

The functional integration barriers emerged along two broad domains including lack of interoperable e-health platforms for hypertension and type 2 diabetes, health system-wide and individual financing barriers. The health system-wide financing barriers comprised; inadequate budgetary allocations to the health sector in general and hypertension and type 2 diabetes health services in particular, lack of NHIF accreditation of most primary care facilities. The individual financing barriers comprised; unaffordability of healthcare services, catastrophic out-of-pocket expenditures, lack of

a health insurance plan, and coverage limits for hypertension and type 2 diabetes by insurance plans.

Lack of interoperable e-health platforms for hypertension and type 2 diabetes

The lack of interoperable e-health platforms emerged from the HMIS experts interviewed as a major obstacle to the integrated management of hypertension and type 2 diabetes. Patient data are dispersed over multiple systems making it impossible to make decisions for individuals or populations. Other barriers included; poor internet connectivity, poor technology, and lack of provider-patient interaction e-health platforms. One of the HMIS experts interviewed stated,

> *"The lack of technological advancement to ensure interoperability is a major challenge for integrated management of hypertension and type 2 diabetes. There is a lot of competition between different stakeholders in the profession of HMIS, but I think we should consider something universal so that when a patient goes to another facility, a unique code can be used to retrieve their information" (HMIS expert).*

Inadequate budgetary allocation

According to one of the County health managers interviewed, the national and county budget investments on health in general and integrated management of hypertension and type 2 diabetes in particular is woefully small with more allocations on recurrent expenditures such as wages and salaries. Furthermore, most donor funds target communicable diseases such as HIV, tuberculosis and malaria despite the growing burden of hypertension and type 2 diabetes as exemplified in the following response:

> *"We have very little budgetary allocation for preventive and promotive healthcare services for hypertension and type 2 diabetes since a lot of our budget goes to salaries and acute illness. For example in the last financial year, a third of our health budget was spent on salaries and wages" (County health manager).*

Lack of accreditation by NHIF

The NHIF is a national priority under Sustainable Development Goal 3 to remove cost barriers to accessing healthcare services for hypertension and type 2 diabetes. However, the lack of NHIF accreditation of most primary facilities by the Ministry of Health was cited by the county health managers interviewed as a major healthcare-financing obstacle. The NHIF subscribers living with hypertension and type 2 diabetes mostly pay out of pocket for services accessed in some primary care facilities. One county health manager reported that only a few of the public primary healthcare facilities are accredited by NHIF. Most facilities rely on the collection of user fees and funding from the county government.

Unaffordability and perceived financial catastrophe

The cost of treatment for hypertension and type 2 diabetes comorbidity was perceived by the patients to be very high causing most patients to not only forego essential therapeutic interventions but also endure the physical, economic, and psychosocial effects of high out-of-pocket expenditures. The user fees and co-payments for health services for hypertension and type 2 diabetes were perceived by the patients to be so high in relation to their incomes resulting in a financial catastrophe for the patients and their households. This situation forced them to cut down on necessities such as food and clothing. These sentiments were also confirmed by the facility in charge interviewed as explained in the following excerpts:

> *"The diagnosis and treatment cost for type 2 diabetes and hypertension is very high, especially for patients living with comorbidities. Some patients are forced to wait until they raise the money for essential lifesaving intervention, which is time-consuming, and may result in reduced prognosis and improve the disease severity. […] Approximately over sixty percent of the income of patients with hypertension and type 2 diabetes goes towards financing health since most of the drugs are not covered by the NHIF". (Primary care facility in charge)*

Poor health insurance coverage

The NHIF does not offer comprehensive coverage for hypertension and type 2 diabetes and most patients are often forced to pay out of pocket for healthcare services despite having health insurance coverage. One patient explained how she pays for drugs for hypertension:

> *"I do not see any direct benefit even with my NHIF card. When I come to this facility, it cannot cover the cost me drugs for hypertension and diabetes and I have to pay out of pocket". (Patient FGD participant).*

Such experiences frustrate patients to pay out of pocket for healthcare services at the point of care, which seemingly, impedes access to the needed healthcare services as further captured in an interview with a primary care facility in charge. This was also noted by one of the primary care facility in charge interviewed, who reported that,

> *"Over seventy percent of patients seeking care for hypertension and type 2 diabetes in this facility pay out of pocket for access to healthcare and this serves as a major barrier to access since most patients are often unable to afford the cost services such as medication and forego essential healthcare services" (Primary care facility in charge)*

Normative integration

Normative integration refers to the extent to which vision and work values that promote integrated management of hypertension and type 2 diabetes are shared within the healthcare system. According to one of the NCD experts, the Kenyan government has prioritized UHC as one of the agendas for socio-economic transformation in line with Kenya's Vision 2030. The subsequent integration of chronic disease management activities in the UHC package was considered by the NCD expert interviewed as crucial in accelerating access to integrated care services for hypertension and type 2 diabetes . However, the patients interviewed blamed corruption for the poor state of health service delivery for hypertension and type 2 diabetes. Corruption is evidenced when some rogue doctors in public health facilities refer patients to their privately owned facilities for services available in the public facilities. One FGD patient narrated,

> *"The problem we have in this facility is that the doctors who attend to us have their privately owned facilities where they spend more hours than in the public facilities. Therefore, they always refer us to their privately owned facilities where they overcharge the services for hypertension and type 2 diabetes care". (Patient FGD participant)*

Discussions

In this study, we explored the perceived health system facilitators and barriers to the integrated management of hypertension and type 2 diabetes in Kenya. Our findings follow the RMIC framework for monitoring and evaluation of integrated care. The results highlight the facilitators and barriers that are intrinsic to the RMIC domains including macro, meso, and micro-environment. The major facilitators included patient-centered care models such as peer support groups, task shifting and integration of CHVs in primary care, and a national referral system. Others included a national health management information system, decentralization of services, multi-sectoral partnerships, and political will for UHC. The major health system barriers identified included vertical and unresponsive healthcare services, unavailability and unaffordability of medication, poor treatment adherence and irrational polypharmacy. Others included a shortage of skilled personnel, a lack of interoperable e-health platforms, care integration policy implementation gaps, and inadequate monitoring and evaluation frameworks.

This study shows that patient-centered care models such as peer support groups are potentially important adjuncts to clinical care for addressing patients' unique challenges. The WHO also proposes patients support groups, as an intervention to promote patients' coping behaviour and psychosocial functioning, medication adherence, and retention in care (30). The groups also, serve the purpose of sharing experiences, providing a safe learning environment which reduces stigma and discrimination, and improves self-esteem (31). However, further studies and operational lessons are needed

to maximize the benefits of the support groups among patients living with hypertension and type 2 diabetes comorbidities.

Our results show that the healthcare services for hypertension and type 2 diabetes were primarily offered as standalone services. This results in the fragmentation of services that threatens the holistic perspective of primary healthcare services. A possible explanation for this observation is the fact that the current chronic disease management guidelines were developed at a period when single chronic disease frameworks were common and have routinely focused on a single disease rather than a more holistic approach (4). The findings of the current study are consistent with the results of the 2015 nationwide NCD survey in Kenya where only 15.6% of individuals with hypertension were aware of their elevated blood pressure and only 26.9% of hypertensive patients were on treatment with 48% of those on treatment having poor control (2). Previous studies have also shown that essential primary care services for hypertension and type 2 diabetes are not readily available in low-income and middle-income countries (32, 33). This decreased healthcare access to primary care is partly attributable to the decline in the overall well-being of people living with hypertension and type 2 diabetes comorbidity in SSA (34).

The NHIF emerged as a major facilitator for access to integrated healthcare services for hypertension and type 2 diabetes. The lack of access to essential medicines has been identified by previous studies as one of the major health system challenges affecting the management of hypertension and type 2 diabetes in SSA (32, 33). The high costs of medications for hypertension and type 2 diabetes are unaffordable to the majority of the patients who have to meet these expenses out of pocket payments. This situation is made worse by the long-term treatment and comorbidities that impose a lifetime financial burden on poor households, strained family support and leads to poor adherence to medication (35). A study in Malawi estimated that a 1-month course of medication for a patient with hypertension could cost as much as 18-days' daily wage (33). In Kenya, public health facilities offer treatment for hypertension and type 2 diabetes services only at the sub-county and county referral hospital levels and most patients have to pay user fees to access medicines. These high treatment costs inevitably constrain the success of long-term treatment. A great proportion of patients are lost to follow-up and many who attend their visits adhere less to treatment due to the high economic burden of purchasing drugs. Deficient procurement and distribution process of essential drugs for the treatment of diseases such as hypertension and type 2 diabetes leads to frequent stock-outs of medications, thus affecting the compliance of patients to medications and overall prognosis.

Our findings on limited skilled personnel at healthcare facilities concur with the 2018 report on Human Resources for Health by the WHO that revealed an acute global shortage of health personnel in SSA (36). The critical shortage of skilled healthcare

workforce in SSA, including Kenya, is partly attributable to several factors such as low investment in training and recruitment, poor incentive structures, systems, and mechanisms for healthcare workers and brain drain (37). Efforts need to be made to ensure the availability, retention, and capacity building of skilled healthcare personnel and specialist and efficient use of the existing health workforce such as task shifting.

Our results show that the national HMIS framework, high mobile phone penetration, and HMIS pilot experiences facilitated the health information systems while the barriers included lack of interoperable platforms, poor internet connectivity, and lack of provider-patient interaction. Previous studies have also shown that in urban settings of African countries, there is the availability of basic information, communication and technology (ICT) infrastructure that supports electronic HMIS such as electricity, high penetration of mobile telecommunication and network, ICT human resources, and higher population literacy rates (38-40). However, the availability of ICT infrastructure does not necessarily translate into enhanced integration of HMIS in primary care as the majority of the platforms are funded by international non-governmental organizations and lack ownership by the local governments (39, 40). The lack of government ownership results in duplication and fragmentation of HMIS services for chronic illnesses as most platforms under implementation are not aligned with the national health information system hence resulting in interoperability challenges.

Similar to previous studies (41, 42), the system integration facilitators for the management of hypertension and type 2 diabetes in our study included multi-sectoral partnerships, interdependency, and decentralization of services. However, the barriers included policy implementation gaps, devolution challenges, and inadequate monitoring and evaluation frameworks. As noted, by previous studies (43, 44), the development and implementation of care integration policies are distinct, with the former considerably more challenging.

The findings of this study highlight important implications to health systems strengthening for the integrated management of hypertension and type 2 diabetes in Kenya. A patient-centered approach at the primary care level using interventions such as patient support groups or health education and promotion on shared risk factors for cardiovascular diseases could be useful in promoting integrated care. Furthermore, the health system needs to promote collaborative and coordinated care between and within care teams, health facilities, and including community resources. Decentralization of services and multisectoral partnerships will be important policy-level enablers of promoting integrated health care. Reinforcing leadership and strengthening the implementation of integrated management of hypertension and type 2 diabetes through capacity building and budgetary allocations should be a key priority of the Kenyan government. To realize this, an actionable framework should be developed and

integrated into the NCD and UHC action plans to enable the implementation and scaling of integrated care for common chronic diseases including hypertension and diabetes.

Strengths and limitations

This study triangulated perspectives from multiple stakeholders including healthcare providers, patients and policymakers to understand the barriers and facilitators to the integrated management of hypertension and type 2 diabetes. This study has high credibility due to several reasons. Firstly, the interview topic guides were developed with reference to the established WHO framework of health systems building blocks, which ensured that questions on the integrated care for hypertension and type 2 diabetes were adequately addressed to obtain accurate and relevant data. In addition, the involvement of trained experienced qualitative researchers, the use of rigorous methods of data collection and analysis and interpretation enhanced the credibility of the findings. The selection of a diverse range of participants from different counties sampled through a multi-stage approach provides rich information from diverse contexts that promotes an in-depth understanding of perceived facilitators and barriers to the integrated management of hypertension and type 2 diabetes in Kenya.

The findings of this study should be read against the backdrop of two major limitations. First, due to the purposeful selection of the study participants, our results cannot be generalized to all patients with hypertension and type 2 diabetes but may generate hypotheses for further research on integrated care in Kenya. Second, the results are based on self-reports and may therefore differ from actual health service delivery. These notwithstanding, we believe that the broad patterns of facilitators and barriers to care integration are likely to remain. Several practical lessons can be drawn from the findings of this study to inform policies that seek to improve the management of hypertension and type 2 diabetes in Kenya.

Conclusions

Our results provide useful insight into the broader health system factors that enhance or impede the integrated management of hypertension and type 2 diabetes in Kenya. The study identified the barriers and facilitators that may be harnessed to improve the integrated management of hypertension and type 2 diabetes. The facilitators should be strengthened, and barriers to care integration redressed. A multipronged approach that includes health systems thinking and integrated care are imperative for bridging the gap for unmet need for hypertension and type 2 diabetes prevention and treatment.

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Competing interests: None declared.

Data sharing statement: The datasets used in this study are available upon a reasonable request to the African Population and Health Research Center (APHRC) through its Microdata portal (https:// microdataportal.aphrc.org/index.php/catalog/124). No additional data are available.

Ethics approval: The original health service provision assessment in Kenya was approved by the Amref Health Africa Ethics and Scientific Review Committee based in Nairobi, Kenya (ref: DOR/2019/017). All participants were fully informed during the consent process that their participation was voluntary with the freedom to decline any question or withdraw from the study at any point in time and that no harm would occur to them or anyone in their family regardless of their participation decisions. Sensitive data collected during this study were de-identified. Efforts were made to guarantee anonymity by removing identifiable information. All data were confidentially stored and with password protection and access restricted only to invited necessary personnel for research-oriented needs.

Patient consent for publication: Not required

Author contributions: PO conceptualized the study, reviewed literature, and analysed the data. CA, EOAW, CW, EI, RO, JO, and GA made substantive contributions to the conceptualization of the study, and data analysis and reviewed the manuscript. All authors read and approved the final manuscript. PO takes full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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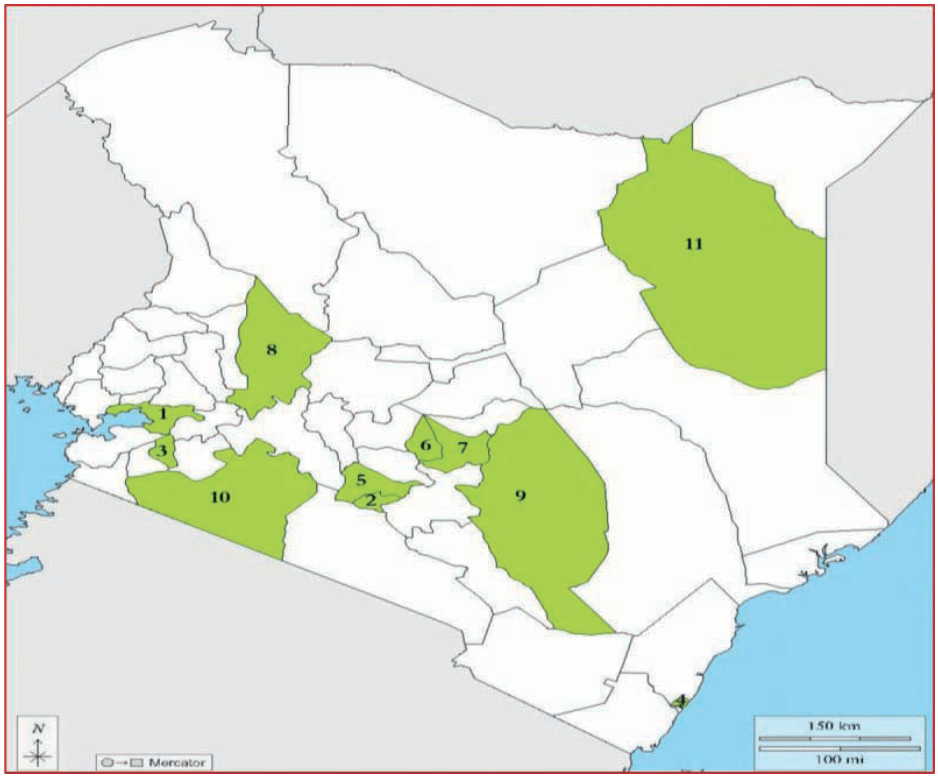
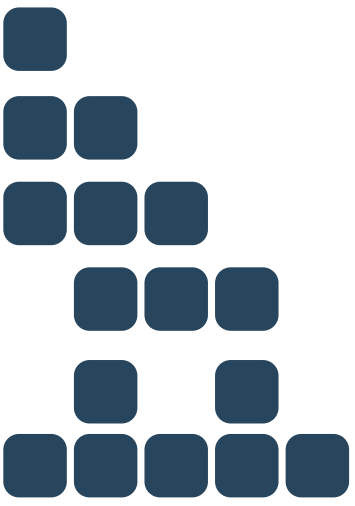
Supplementary files

Supplementary file 1: Map of Kenya counties included in the sample of health facilities assessed.

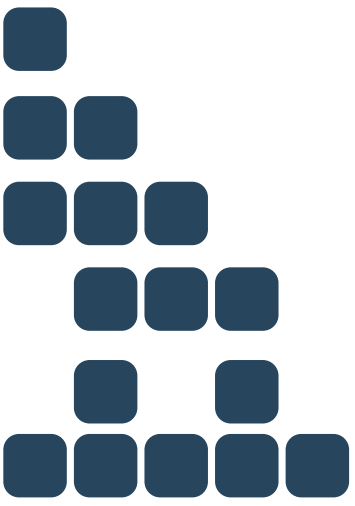


1 = Kisumu, 2 = Nairobi, 3 = Nyamira, 4 = Mombasa, 5 = Kiambu, 6 = Kirinyaga, 7 = Embu, 8 = Baringo, 9 = Kitui, 10 = Narok, 11 = Wajir. Blank map retrieved and adapted from: https://d-maps.com/ [Accessed: 16 May 2022].



PART 4

The effect of multimorbidity on self-care interventions in sub-Saharan Africa



8

Effect of Patient Support Groups for Hypertension on Blood Pressure among Patients with and without Multimorbidity: Findings from a Cohort Study of Patients on a Home-Based Self-Management Program in Kenya

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Abstract

Introduction: Patient support group interventions have been widely used to manage chronic diseases in Kenya. However, the potential benefits of these groups on patient health outcomes, and how this is influenced by multimorbidity, have not been rigorously evaluated.

Objective: We assessed the effect of a patient support group intervention on blood pressure (BP) management and the potential moderating effect of multimorbidity among low- and middle-income patients with hypertension in Kenya.

Methods: We analysed data from a non-randomized, quasi-experimental study of 410 patients with hypertension on a home-based self-management program conducted from September 2019 to September 2020. The program included the formation and participation in patient support groups. Using a modified STEPS questionnaire, data were collected on BP, anthropometry and other measurements at enrolment and after 12 months of follow-up. Multimorbidity was defined as the simultaneous presence of hypertension and at least one or more related conditions with similar pathophysiology (concordant multimorbidity) or unrelated chronic conditions (discordant multimorbidity). Propensity score (PS) weighting was used to adjust for baseline differences among 243 patients who participated in the support groups and 167 who did not. We estimated the effects of patient support groups and moderating effects of multimorbidity on BP management using multivariable ordinary linear regression weighted by PS.

Findings: Participation in support groups significantly reduced systolic BP by 5.4 mmHg compared to non-participation in the groups [β=-5.4; 95% CI -1.9 to -8.8]. However, among participants in the support group intervention, the mean systolic BP at follow-up assessment for those with concordant multimorbidity was 8.8 mmHg higher than those with no multimorbidity [β=8.8; 95% CI 0.8 to 16.8].

Conclusion: Although patient support groups are potentially important adjuncts to home-based self-care, multimorbidity attenuates their effectiveness. There is a need to tailor patient support group interventions to match the needs of the people living with multimorbidity in low- and middle-income settings in Kenya.

Keywords: patient support groups, home-based self-care, hypertension, multimorbidity, blood pressure

Background

Hypertension is the leading global risk factor for cardiovascular disease (CVD) (1, 2). Low- and middle-income countries (LMICs) are disproportionately affected with over 80% of global CVD deaths (3). In Kenya, one-in-four adults live with hypertension [2]. However, less than half of people on treatment for hypertension have controlled blood pressure (BP) (4, 5). Management of hypertension is a complex process requiring collaborative efforts of the patients, the health sector, and wider society (6-11). The World Health Organization (WHO) proposes peer support groups as an intervention to promote patients' coping behaviour, psychosocial functioning, medication adherence, and retention in care (12). A patient support group comprise a group of patients sharing common experiences and concerns and who provide moral and emotional support to each other by fulfilling functions such as health education and behaviour change communication, public awareness, health advocacy, and fundraising (13).

Patient-led support groups represent an ideological shift away from patients as 'passive' recipients of treatment to empowered individuals who are partners in the effective management of their health (14). In Kenya, patient support group interventions have been widely used (15-18). However, their impacts have not been systematically evaluated. A study by Pastakia et al. conducted in 2017 demonstrated the success of a patient support group intervention in helping to improve care for hypertension in rural settings in Kenya (18). However, this study did not incorporate the impact of multimorbidity on the self-care intervention. People living with hypertension often have multiple rather than a single condition, also known as multimorbidity (19). One in every two people with hypertension has a multimorbidity (20). Despite the potential implications of multimorbidity on the effectiveness of patient support groups (21)**,** existing interventions have not adequately incorporated its impact on health outcomes (21). Hence, it is not possible to determine whether the interventions are particularly effective for people living with multimorbidity. Given the rising prevalence of multimorbidity in Kenya (22, 23), it is important to understand the effects of multimorbidity on patient support group interventions to inform on the appropriate models to deploy.

In this study, we registered patients from low- and middle-income settings in Kenya and provided access to self-management tools such as blood pressure devices to help them with self-measurements at home. They were also provided with mobile phone applications to relay their measurements to primary clinics via their mobile phones. The patient support groups were introduced during the follow-up period to improve the uptake of self-measurements. Secondary data analysis was used to evaluate the moderating effects of multimorbidity on the effectiveness of patient support groups. We hypothesized that multimorbidity would moderate the effectiveness of patient support group intervention among low and middle-income patients in Kenya.

Methods

Study design

We analysed data from a nonrandomized, quasi-experimental pilot study of hypertension patients undergoing a home-based self-care program from September 2019 to September 2020. Therefore, we utilized inverse probability of treatment weighting using propensity scores (IPTW-PS) to create a comparison (non-exposed) group which was similar to the exposed group on all measured covariates except for the exposure. The propensity score (PS) is defined as the probability of being in the intervention group conditional on the observed participant's baseline characteristics (24). IPTW-PS is a statistical approach that weights the exposed and nonexposed groups using PS. Thus minimizing the selection bias and confounding.

Study setting

The study population included patients seeking healthcare services from facilities serving low- and middle-income populations from three Kenyan Counties: Nairobi, Kiambu, and Vihiga. These facilities were selected because they were involved in a chronic disease care program called *Ngao Ya Afya-Tiba Yako*. The program was supported by the African Population and Health Research Center (APHRC) and the PharmAccess Foundation. Nairobi, the capital city of Kenya is the most populous county and represents an urban metropolitan setting (25). Kiambu County is the second most populous county after Nairobi and represents a semi-urban setting while Vihiga represents a rural setting (25, 26) . The three counties included in this study are in different geo-political areas. The inclusion of these three counties accounted for the variations in the burden of hypertension and lifestyle risk factors in different geographical and social contexts.

Participant recruitment

Participants were recruited from June 2019 to September 2019 and followed up for one year (September 2019 to September 2020). Known and new patients with essential hypertension who were receiving care at one of the study clinics were invited to participate in the study. To recruit new patients, screening was performed at clinics during triage for regular visits. The inclusion criteria comprised, (i) patients with a new diagnosis of essential hypertension (diagnosis made by treating clinician), (ii) patients known to have essential hypertension (diagnosis made by treating physician) who were already receiving medication, (iii) patients with intervention receiving intervention provided by the recruiting site, (iv) adult (>18 years old), and (vi) ownership of a mobile phone.

The exclusion of the study participants was based on seven criteria: (i) patients with suspected secondary hypertension from the assessment of the treating physician acting in accordance with the clinical guidelines, (ii) patients requiring intervention (secondary, tertiary hypertension care) not provided by the recruiting site, (iii) arm circumference

greater than or less than the 22–42 cm for which the used cuffs are validated, (iv) failure to obtain valid BP-values (e.g. cardiac arrhythmias), (v) pregnancy, (vi) unsuitability for receipt of mobile hypertension care as judged by the treating physicians (for instance, patients with life-threatening diseases or dementia), and (vii) an acute cardiovascular event in the past three months preceding the survey.

Sample size

Given that the uptake of patient support group intervention from the original study was 60%, a sample size of 465 participants, 278 in the intervention group and 187 in the control group was required to reject the null hypothesis that BP control was equal in the intervention and control groups (27). This provides 80% power to detect a 15% increase in BP control in the support group intervention compared to the control group assuming a 5% level of significance (two-sided test) and a non-response rate of 20%. However, baseline and follow-up data were available for 410/465 participants. Thus the response rate was 243/278 (87.4%) in the intervention arm and 167/187 (89.3%) in the control arm.

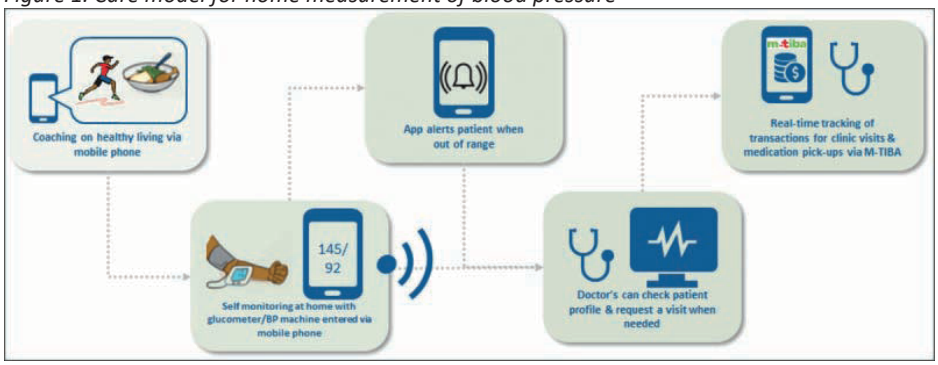
Description of the intervention

The intervention included a home-based self-care program and patient support groups. All the 410 recruited participants were enrolled in the home-based self-management program. The control group received the home-based care program only while the intervention group received home-based care program and the patient support group intervention.

Home-based self-management

Self-management devices (BP machines) were distributed to all the participants to measure BP at home. Figure 1 shows the care model for home-based measurement of BP. All participants were trained to take their measurements at home and enter their readings on a mobile phone application (*Afya Pap*), to relay their measurements to their healthcare provider. Further details about the *Afya Pap* application are available elsewhere (28). In addition, health education messages were sent to all the enrolled patients through the *Afya Pap* application. Finally, all the participants were also enrolled in a mobile health wallet (*M-TIBA*) that gives access to discounts on consultations, medical tests for hypertension and medicines at the study clinics (29).

Figure 1: Care model for home measurement of blood pressure



Retrieved and adapted from: https://www.pharmaccess.org/update/a-a-scalable-low-cost-quality-service-for-patients-with-diabetes-and-hypertension-partnership-with-sanofi/ [Accessed: 16 July 2022].

Patient support groups

The support group intervention involved formation of patient support groups and comprised four components: peer-led training, peer support for home-based self-care and lifestyle modification, BP measurement demonstrations, and group measurements. For the peer-led training, leader volunteer members of patient support groups participated in the training of peers through face-to-face health coaching and information support for self-management of hypertension, emotional support using motivation-counselling techniques and appraisal support using self-management skills. A clinical officer at the health facility attached to the peer group conducted BP measurement demonstrations. The clinical officer ensured that the group members were well equipped with the necessary knowledge of hypertension management and peer leadership skills. In the support groups, the patients participated in group measurement of BP and exchanged knowledge and experiences on hypertension self-management and healthy lifestyles.

Participants were invited to join these facility-based patient support groups which met monthly. In total 243/410 individuals joined and participated in groups. Each group had an average of 32 members. For purposes of understanding whether the patient support groups augmented the home-based self-management intervention, participants were grouped into two categories: those who joined the patient support groups (n=243) and those who did not (n=167).

Data collection

We used a modified WHO STEPwise approach to non-communicable disease risk factor surveillance (STEPS) questionnaire to collect data at enrolment and after 12 months of follow-up. The details of the measurements of variables used in this study are shown in the online supplementary file 1. The interview questions consisted of socio-demographic

characteristics (age, sex, and employment), CVD risk factors (physical activity, use of alcohol, smoking status, and healthy diet), medication adherence, and frequency of self-measurement of BP. The variables were measured using the WHO criteria (30). Briefly, the history of smoking tobacco products was self-reported and defined as a current smoker. Physical activity was measured as the average days of planned physical activity in a week. Diet was measured as the self-reported daily number of servings of fruits and vegetables. Medication adherence was measured as the average number of days the patients took hypertension medicine in the week preceding the survey.

The diagnosis of hypertension was made following an objective assessment by the attending clinician. Multimorbidity was assessed by screening and self-reports. Patients were screened for type 2 diabetes during regular clinic visits and the diagnosis made by the attending clinician. Self-reports were used to document the presence of other chronic diseases such as CVD, hypercholesterolemia, chronic kidney disease, asthma, arthritis, chronic neuromuscular disease, HIV/AIDS, tuberculosis, cancer, ulcers, depression, chronic liver disease, and depression. Weight (in kg) and height (in metres) were also measured. Since the patients enrolled in this study had BP measuring devices previously issued at enrolment, they were requested to take their BP measurements at the time of the follow-up interview and relay the information to the interviewer via short message texts. All the data were electronically captured on tablets using the Survey CTO platform (Dobility, Inc. Cambridge, USA), synchronized with the master database and exported to Stata version 17.0 (StataCorp LP, USA) for analysis.

Definition and measurement of variables

The primary outcome was endline mean systolic and diastolic BP. The explanatory variables were participation in the patient support group (intervention), multimorbidity status, and interaction of multimorbidity with the intervention arms. Multimorbidity was defined as the simultaneous presence of hypertension and one other condition with related pathophysiology i.e., type 2 diabetes, CVD, obesity, hypercholesterolemia, chronic kidney disease (concordant multimorbidity), and unrelated conditions such as asthma, arthritis, chronic neuromuscular disease, HIV/AIDS, tuberculosis, cancer, ulcers, depression, chronic liver disease, and depression (discordant multimorbidity). Participants were classified into the following four mutually exclusive multimorbidity categories: no multimorbidity, concordant multimorbidity, discordant multimorbidity, and both concordant and discordant multimorbidity. Other covariates were age, sex, occupation, smoking, alcohol, diet, medication adherence, and baseline BP.

Data analysis

Propensity score weighting

We used PS weighting (31) to adjust for baseline differences in participation in the peer support groups. The PS scores were generated using a multivariable logistic regression model, with participation in peer support group as the outcome variable

and the following baseline characteristics as predictors: age, sex, employment, diet, physical activity, medication adherence, and BP control. We used the estimated PS to weight the groups, with the exposed group weighted using the inverse of PS (1/PS) and the comparison group weighted using the inverse of one minus the PS (1/(1 – PS)). This created a pseudo-population with balanced covariates. Baseline categorical data were summarized using frequencies, percentages, and numerical data using means with standard deviation. Group comparisons comprising paired sample t-test for continuous variables, McNemar's Chi-squared test, and marginal homogeneity test for categorical variables were used to test the differences in the baseline characteristics by study arms.

Regression analysis

We estimated the moderating effects of multimorbidity on BP using multivariable ordinary linear regression with robust error variances, weighted by PS. The primary outcome was regressed against dummy variables, indicating whether the participant participated in the patient support groups, multimorbidity status and interaction of patient support with multimorbidity status. The interaction can be interpreted as a test of whether the difference between intervention and control patients was the same by multimorbidity status. Other covariates included in the model comprised baseline characteristics such as age, sex, employment, diet, smoking, alcohol, physical activity medication adherence, and baseline BP. Variable selection for the multivariable models was based on known risk factors for hypertension (32). The intervention effect was assessed using adjusted β coefficients (mean differences) and 95% confidence intervals (CIs). The margins and *margins plot* command in Stata was used to graph the output from the predictive margins of significant interactions.

Results

Baseline characteristics of the participants

In total, 410 participants were included in the analysis. Table 1 shows no significant differences in the study arms by baseline characteristics. The weighted sample comprised the intervention arm with 243 patients who participated in the peer support group and a control arm with 167 patients who did not participate in the peer support groups.

Table 1: Baseline characteristics of the participants

Baseline characteristics	Patient support group		
	Intervention	Control	Std. Diff
	n=243	n=167	
Age, Mean ± SD	57.3 ±11.4	58.1 ±11.7	0.1
Sex			
Male	30.5	31.1	0.0
Female	69.6	68.9	
Employment			
Employed	58.0	52.7	0.1
Unemployed	42.0	47.3	
Smoking	1.2	4.2	0.2
Alcohol use	3.3	4.2	0.1
Adequate diet	63.8	59.9	0.1
Medication adherence	86.0	88.0	0.1
Average days of physical activity in a week ± SD	2.2 ±2.2	2.3 ±21.2	0.0
Multimorbidity			
Type 2 diabetes	39.5	42.0	0.0
Obesity	43.7	39.9	0.1
CVD	16.7	9.1	0.2
Arthritis	6.6	7.0	0.0
Asthma	3.6	4.1	0.0
Chronic Kidney Disease	3.6	2.1	0.1
Tuberculosis	3.0	1.7	0.1
Cancer	3.6	1.7	0.1
Chronic neuromuscular disease	2.4	1.2	0.1
HIV/AIDS	0.6	1.2	0.1
Ulcers	1.2	1.2	0.0
Depression	0.0	0.8	-
Chronic liver disease	0.6	0.4	0.0
Cataract	0.0	0.4	-
Hypercholesterolemia	4.6	0.0	-
Multimorbidity type			0.1
No multimorbidity	26.8	25.2	
Both concordant & discordant multimorbidity	10.3	14.4	
†Concordant multimorbidity	57.6	55.7	
‡Discordant multimorbidity	5.4	4.8	

Table 1: Continued

Baseline characteristics	Patient support group		
	Intervention	Control	Std. Diff
Systolic BP ± SD	136.5 ±19.2	139.0 ±20.7	0.1
Diastolic BP ± SD	87.8 ±12.7	89.5 ±12.3	0.1
BP Control	46.9	45.5	0.0

Notes: Data presented as column %, unless otherwise specified.
BP: blood pressure; SD: standard deviation; Std Diff: standardized difference
Std Diff = Difference in means or proportions divided by standard error; imbalance defined as an absolute value greater than 0.2
† Concordant multimorbidity refers to conditions with shared pathophysiology such as type 2 diabetes, CVD, obesity, hypercholesterolemia, and chronic kidney disease.
‡ Discordant multimorbidity refers to conditions with unrelated pathophysiology such as asthma, arthritis, chronic neuromuscular disease, HIV/AIDS, tuberculosis, cancer, ulcers, depression, chronic liver disease and depression.

Changes in lifestyle risk factors and BP by intervention arms

Table 2 shows the changes in lifestyle risk factors and BP by intervention arms. Physical activity, frequency of self-measurement of BP, and consumption of adequate diet increased substantially during follow-up in the intervention and control arms. Medication adherence declined slightly in both study arms from 88.0% to 83.5% in control and 86.0% from 83.5% in the intervention arm. There was a slight increase in alcohol consumption in both study arms. However, substantial smoking decline was observed in the control arm but not in the intervention arm. The proportion of controlled BP among patients in the intervention arm significantly increased from 44.9% to 57.6% compared to a slight increase from 45.5% to 46.1% in the control arm. The mean BP reduced marginally among patients in the intervention arm (from 136.5/87.9 mmHg at baseline to 133.0/85.8 mmHg at end line). There was no significant change in the systolic BP in the control arm. However, the mean diastolic BP reduced marginally (from 90 mmHg at baseline to 87 mmHg at endline).

Table 2: Changes in lifestyle risk factors and BP by intervention arms

	Peer support groups					
	Intervention (N=243)			Control (N=167)		
	Baseline	Follow-up	P value*	Baseline	Follow-up	P value*
Adequate diet						
Yes	36.2	55.1	<0.001	40.1	56.9	<0.001
Smoking						
Yes	1.2	0.8	0.65	4.2	0.0	0.01

Table 2: Continued

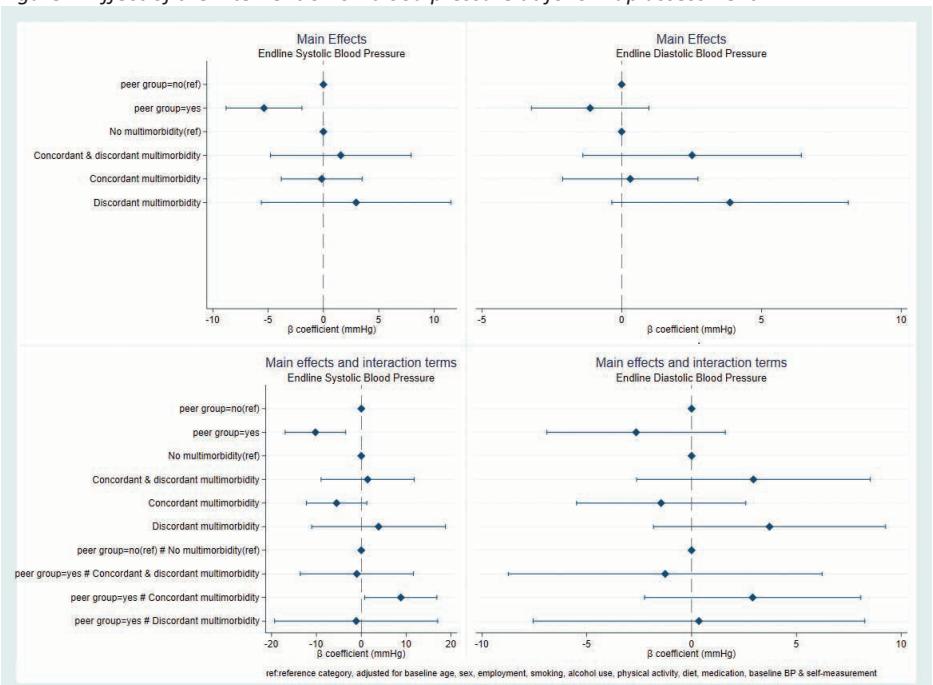
	Peer support groups					
	Intervention (N=243)			Control (N=167)		
	Baseline	Follow-up	P value*	Baseline	Follow-up	P value*
Alcohol use						
Yes	3.3	6.2	0.05	4.2	7.8	0.08
Days of planned physical activity in a week, Mean ± SD						
	2.2±2.2	3.1±2.5	0.00	2.3±2.2	2.7±2.4	0.07
Medication adherence						
Yes	86.0	83.5	0.24	88.0	83.8	0.09
Frequency of self-measurement of BP						
Never	47.7	0.8	<0.001	53.3	3.0	<0.001
Daily	5.4	32.9		4.2	28.1	
Weekly	11.5	63.0		12.6	67.1	
Monthly	35.4	3.3		29.9	1.8	
Systolic BP, Mean ± SD						
	136.5±19.2	133.0±15.2	0.01	139.0±20.7	138.8±19.5	0.91
Diastolic BP, Mean ± SD						
	87.9±11.7	85.8±10.5	0.01	89.5±12.3	87.0±11.2	0.01
BP control						
Yes	46.9	57.6	0.01	45.5	46.1	0.89

Notes: Data presented as column %, unless otherwise specified.
BP: blood pressure; SD: standard deviation.
*P-values for paired sample t-test for continuous variables, McNemar's Chi-squared test, and marginal homogeneity test for categorical variables.

Effect of the intervention on blood pressure at follow-up assessment

Figure 2 shows the effect of the intervention on BP at the follow-up assessment, moderated by multimorbidity. Participation in support groups significantly reduced systolic BP by 5.4 mmHg compared to non-participation in the groups [β=-5.4; 95% CI -1.9 to -8.8]. A significant interaction was observed between participation in a patient support group and concordant multimorbidity in their effects on BP management. Among participants in th8e support group intervention, the mean systolic BP at follow-up assessment for those with concordant multimorbidity was 8.8 mmHg higher than those with no multimorbidity [β=8.8; 95% CI 0.8 to 16.8]. The main effect of patient support groups on diastolic BP was not significant [β=-1.1; 95% CI -3.2 to 1.0]. Similarly, the interaction effect of patient support groups with multimorbidity was also not significant for diastolic BP [β=-2.6; 95% CI -6.9 to 1.6].

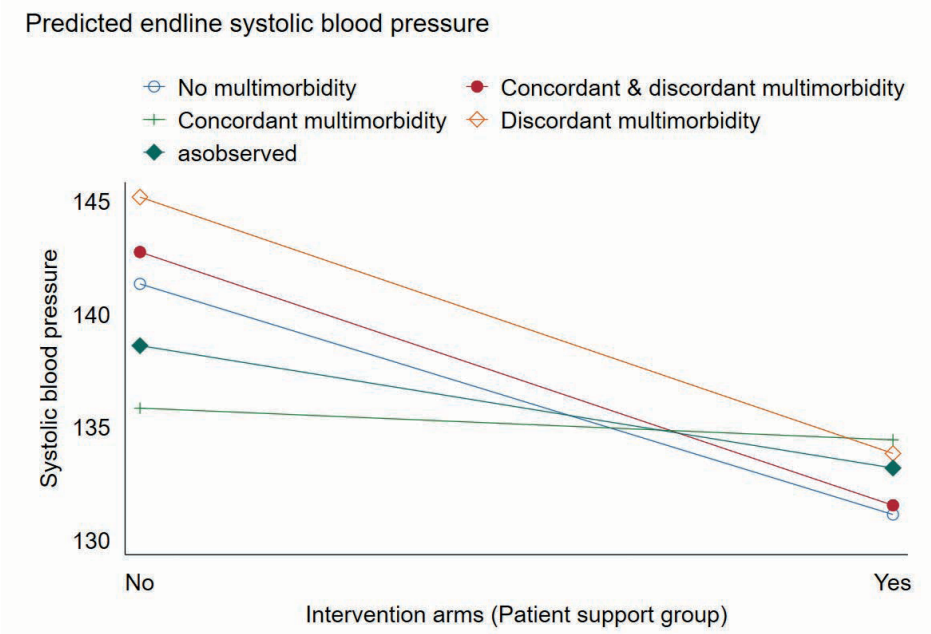
Figure 2: Effect of the intervention on blood pressure at follow-up assessment



Predicted marginal effects of the intervention on BP at the follow-up assessment, moderated by multimorbidity

Figure 3 shows the predicted marginal effects of the intervention on BP at the follow-up assessment, moderated by multimorbidity. The examination of the interaction plot for the predicted marginal effects shows that participation in the patient support groups conferred significantly lower predicted mean systolic BP among participants without multimorbidity than those with multimorbidity.

Figure 3: Predicted endline systolic blood pressure



Discussion

In this study, we assessed whether the benefits of a patient support group intervention for hypertension in low and middle-income settings in Kenya varied by the presence of multimorbidity. Our results showed that participation in support groups significantly reduced systolic BP compared to non-participation in the groups. However, participation in support groups had a better effect on patients with no multimorbidity as shown by a significant reduction in systolic BP among patients with no multimorbidity compared to those with concordant multimorbidity. These findings confirmed our hypothesis that multimorbidity attenuates the effectiveness of patient support group intervention.

A possible explanation for patient support groups as an important adjunct to home-based self-care could be due to in part the improvement in compliance, as patients become more involved in their care (33-36). Our study shows that the patient support group intervention was less effective in patients with concordant multimorbidity. The mechanisms by which multimorbidity affects patient support group interventions among hypertensive patients are unclear. We found two studies with contrasting suggesting that multimorbidity is either a threat or an opportunity for self-care (37, 38).

The study by Kerr et al. shows that patients with multimorbidity are more likely to report poor health outcomes from self-care behaviours (37). People living with

multimorbidity face a number of self-care challenges such as limited resources, attention and complex decision-making on self-management priorities. This may impede the self-care behaviours necessary for hypertension management. For example, patients with multimorbidity often have complex intervention regimens with little or no coordination between healthcare services for different conditions. Secondly, therapeutic interventions for multimorbidity are a major challenge due to polypharmacy, drug-disease interactions, and drug-drug interactions (39). In addition, management of dominant multimorbidity that poses an immediate threat to life such as chronic kidney disease often shifts away the focus from other pre-existing chronic conditions (37). Worthy of mention also is that failure to find significant interactions between discordant multimorbidity and BP management may a due to the fact that tests for interaction often have limited power (40).

The study by Voorham et al. contrasts our findings and demonstrates that patients with concordant multimorbidity are more likely to report favourable health outcomes from self-care behaviours (38). Concordant multimorbidities such as type 2 diabetes and CVD share overall pathophysiologic profile and care management plans with hypertension. For example, BP and BG self-monitoring are overlapping CVD risk reduction goals for hypertension and type 2 diabetes and are likely to lead to better health outcomes for both conditions (38). However, this study was conducted among type 2 diabetes patients in the Netherlands and can be an underestimation of all actual problems or events that may compete with chronic disease management in hypertension patients living with multimorbidity in low- and middle-income settings. Thus, more rigorous studies with large samples are needed to assess the variations in the benefits of self-care interventions by multimorbidity types in Sub-Saharan Africa.

Overall, our findings imply that concordant multimorbidity attenuates the effectiveness of patient support group intervention among low- and middle-income patients in Kenya. The results of this study may contribute to the design of future patient support group interventions, to address the needs of hypertension patients with multimorbidity. The finding of a stronger program effect among hypertensive patients without multimorbidity may help to explain why previous support group interventions sometimes have worked and sometimes have not. Support group interventions for hypertension are more effective when delivered to populations with a low prevalence of concordant multimorbidity. However, more studies are needed to identify the mechanism that underlie poor health outcomes from support group interventions among hypertensive patients with concordant multimorbidity in low and middle-income settings.

Strengths and limitations

Our study has several strengths. First, we used a quasi-experimental, longitudinal study design to examine whether the benefits of a patient support group intervention for

hypertension in low- and middle-income settings in Kenya varied by the presence of multimorbidity. This has enhanced the external validity of the original intervention and the degree to which the findings can be applied to the underserved populations exhibiting high levels of multimorbidity in Kenya. Second, the screening and diagnosis of hypertension and type 2 diabetes multimorbidity were based on an assessment by the treating clinician. This provided for a more objective assessment rather than the self-reporting used in over three-quarters of previous studies (41). Third, the use of PSM (31) accounted for the conditional probability of participation in the patient support groups, thus allowing for a reduction of bias when examining the effect of support groups on BP management.

These findings need to be interpreted in the context of some inherent limitations. First, the results are based on a post hoc analysis and are clearly in need of replication in future trials. Second, recruitment clinics were not considered as cluster units and thus recruited any number of patients leading to a wide variation in the distribution of patients in the clinics and clinician practices. Third, the screening questions for multimorbidity were partially based on self-reports. This may have resulted in the underestimation of the true prevalence of multimorbidity. Lastly, the multimorbidity classification used in the analysis considered whether the patients had concordant or discordant multimorbidity. Hence, the moderation effect of specific multimorbidity combinations was not explored due to the small sample size. Despite these limitations, our findings provide crucial evidence on the effects of patient support groups and moderating effects of multimorbidity on BP management among low and middle-income patients in Kenya.

Conclusions

We found evidence that patient support groups can help with reduction in systolic BP among patients with hypertension in low- and middle-income settings in Kenya. However, the findings demonstrate less effectiveness in patients with concordant multimorbidity compared to those without multimorbidity. Thus, tailoring patient support group intervention to match the needs of the people living with concordant multimorbidity may optimize their efficacy. More rigorous cluster randomized trials and operational lessons are needed to maximize the benefits of support groups as an integral component of home-based self-care for hypertension.

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Competing interests: None declared.

Data sharing statement: The datasets used in this study are available upon a reasonable request to the African Population and Health Research Center (APHRC) through its Microdata portal (https:// microdataportal.aphrc.org/index.php/catalog/124).

Ethics approval: The original home-based self-management program for hypertension in Kenya was approved by the Amref Health Africa Ethics and Scientific Review Committee based in Nairobi, Kenya (ref: AMREF-ESRCP 530/2018). During the consent process, all participants were fully informed that their participation was voluntary with the freedom to decline any question or withdraw from the study at any point in time and that no harm would occur to them or anyone in their family regardless of their participation decisions.

Author contributions: PO conceptualized the study, reviewed literature, and analysed the data. CA, CW, RS, SI, WW, JA, BK, JT, AS, and GA made substantive contributions to the conceptualization of the study, data analysis, and reviewed the manuscript. All authors read and approved the final manuscript

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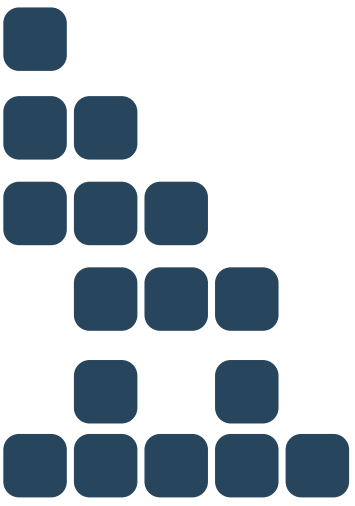

9

General Discussion

General Discussion

The discussion chapter has four main parts. First, a summary of the key findings of the preceding chapters is presented. A discussion of the overarching methodological strengths and limitations is presented in the second part. The third part presents a detailed reflection on the key findings of this thesis. The potential implications for policy and recommendations for future research on multimorbidity in SSA are presented in the last section

Summary of Key Findings

PART 1: Burden of cardiometabolic multimorbidity in SSA

1. Cardiometabolic diseases in SSA occur in distinct clusters of concordant and discordant multimorbidity. The concordant multimorbidity comprised type 2 diabetes, hypercholesterolemia, hypertension, and CVD; discordant multimorbidity included hypertension, abdominal obesity, type 2 diabetes, cataracts, and arthritis; and cardiopulmonary multimorbidity included angina, chronic lung disease, asthma, and depression. These clusters are significant predictors of healthcare utilization, functional disability and quality of life.
2. Multimorbidity cluster including depression and cardiopulmonary diseases was associated with the highest risk of functional disability, hospitalization, and poor quality of life.
3. The occurrence of cardiometabolic multimorbidity is disproportionately highest among persons in the highest socioeconomic positions, women, middle and old-aged men and women, the obese and those with sedentary lifestyles.

PART 2: Chronic care models for cardiometabolic multimorbidity in SSA

1. Integrated care featuring at least two elements of Wagner's chronic care model versus standard care conferred improvement in systolic BP among persons with cardiometabolic multimorbidity in SSA. Wagner's chronic care model elements included self-management support, delivery system design, decision support and clinical information systems, community resources and policies, and healthcare organization
2. There is substantial variability in the combinations of the elements of integrated chronic care models implemented by studies from SSA. Self-management support and delivery system design were the most predominant components of the integrated chronic care models in SSA while healthcare organization and community resource elements were less common.

PART 3: Health system readiness to manage cardiometabolic multimorbidity in Kenya

1. Only one in every four healthcare facilities in Kenya was ready to provide integrated care for CVD and type 2 diabetes.
2. The major clinical integration barriers comprised vertical and unresponsive healthcare services characterized by service unavailability, unresponsiveness, and unaffordability.
3. The care integration implementation gaps are rooted in factors such as inadequate enforcement, health insurance coverage gaps, inadequate budget allocation, and shortage of essential resources such as a trained healthcare workforce, treatment guidelines, treatment and follow-up services, and essential medicine.

PART 4: Effect of multimorbidity on self-care interventions for cardiometabolic diseases in Kenya

1. Participation in patient peer support groups for hypertension significantly reduced systolic BP compared to non-participation in the groups.
2. Multimorbidity attenuated the effectiveness of the patient support groups for hypertension.

Methodological Considerations

A multimethod approach was used to analyse the burden of cardiometabolic multimorbidity and health systems response in SSA. Part one presents the burden of cardiometabolic multimorbidity in SSA using secondary data analysis of the WHO STEPS surveys (2014-2017) and the WHO SAGE surveys (2015). Part two presents a systematic review and meta-analysis of chronic care models for cardiometabolic multimorbidity in SSA. Part three describes the readiness of healthcare facilities to provide integrated management of hypertension and type 2 diabetes in Kenya using a mixed-method approach. Finally, using a quasi-experimental study, the effect of multimorbidity on self-care interventions in Kenya is presented in part four.

By using a multimethod approach, this thesis maximizes strengths and minimizes the limitations of quantitative and qualitative methods in addressing the different facets of cardiometabolic multimorbidity in SSA. The multimethod approach improved the complementarity and triangulation of evidence, resulting in an enriched understanding of the multimorbidity of cardiometabolic diseases and integrated healthcare system response in SSA. In this concluding chapter, the overarching methodological considerations are discussed in detail.

WHO STEPWise Surveys (2014-2017) and SAGE Survey Wave 2 (2015)

Using data from the WHO STEPWise (STEPS) and SAGE surveys conducted in eleven countries in SSA, part one of this thesis examined the clusters of cardiometabolic multimorbidity and the implications of multimorbidity patterns on functional disability,

healthcare utilization, and quality of life. The STEPS and SAGE surveys are standardized national household surveys coordinated by the WHO in LMICs (1, 2). The STEP survey aims to monitor the patterns of cardiometabolic diseases in persons aged 15 years and above while the SAGE survey monitors the health and well-being of persons aged 50 years and above (1, 2).

The STEPS and SAGE survey data used in this thesis have several important strengths. First, a standardised protocol was used in all the study countries (1, 2). This facilitated comparison within and across the study countries. Secondly, the data are based on nationally representative population-based surveys. Thus, inferences may be made to the general populations of the study countries. Although the SAGE survey targets older persons aged 50 years and above at risk of chronic diseases, the STEPS survey complements this by including a broad range of age categories targeting the young, middle-aged, and older persons. Finally, the screening for chronic diseases was based on an objective assessment including symptomatology algorithms, and physical measurement of BP and anthropometrics. Key biomarkers such as blood sugar and cholesterol levels were also measured in addition to the self-reported history of clinical diagnosis of chronic diseases.

The data from STEPS and SAGE surveys have some limitations. First, the number of chronic conditions included in the surveys are limited thus limiting the number of chronic conditions included in this analysis. This may have introduced a bias in the estimation of the true prevalence of cardiometabolic multimorbidity from undiagnosed chronic conditions. Second, the surveys were conducted in eleven countries in SSA (nine countries with STEPS surveys and two countries with SAGE surveys). Given that the countries in SSA are heterogenous in genetic and cultural diversity, the findings of this thesis may not be generalizable to other countries in SSA. Finally, temporal patterns of cardiometabolic multimorbidity and causal associations could not be assessed due to the cross-sectional design of the SAGE and STEPS surveys.

A systematic review and meta-analysis of integrated chronic care models in SSA

A systematic review and meta-analysis of chronic care models for cardiometabolic multimorbidity among adults aged 18 years and older in SSA is presented in part two. All the included studies were RCTs. Hence, the results are more robust than previous reviews on integrated care from observational studies in LMICs (3-8). Secondly, the review comprehensively evaluated the applicability of the constructs of Wagner's chronic care model to manage cardiometabolic multimorbidity in SSA. Thus, the findings provide crucial insights for the future development of chronic care models for multimorbidity in SSA. Thirdly, the inclusion of chronic infectious diseases and NCDs in the review provides evidence on the elements of integrated care models for chronic infectious diseases and NCDs in SSA.

The results of the review on chronic care models for cardiometabolic multimorbidity should be read against the backdrop of some limitations. First, the elements of integrated care models were not classified in most of the included studies. Hence, the changes in health outcomes could not be attributed to the specific components of integrated care models. Second, the variations in chronic care models resulted in the heterogeneity of the integrated care interventions. Thirdly, the included studies did not have a uniform standard of care. This resulted in heterogeneity in the usual standard of care among the control groups. Lastly, the included studies exhibited substantial heterogeneity in the outcome assessments and follow-up periods. Thus, the final meta-analysis comprised only six of the ten included studies.

National facility assessment survey in Kenya (2019 – 2020)

Part three presents a readiness assessment survey of healthcare facilities' capacity to provide integrated management of CVDs and type 2 diabetes and the health system facilitators and barriers to integrated care in Kenya. The facility assessment survey has several important strengths. First, a nationally representative sample of public and private facilities were surveyed. Hence, the findings are generalizable to other healthcare facilities in Kenya. Secondly, the WHO standardized facility assessment questionnaires and observation checklists were used. This facilitated the comparison of the study findings with other SARA surveys conducted in LMICs. Thirdly, the qualitative study, embedded in the facility assessment survey, provides deeper insights into the perceived health system facilitators and barriers to integrated care. Lastly, using qualitative interviews with multiple stakeholders, the findings of the facility assessment survey highlight the facilitators and barriers to the integrated care for CVDs and type 2 diabetes that are intrinsic to the health system domains including the micro, meso and macro environment.

The facility assessment survey in Kenya has a few limitations. First, some of the domain tracer items used in the assessment of care integration readiness could not be verified by visual observation. Secondly, this being a cross-sectional study means that temporal associations between facility characteristics and care integration readiness cannot be inferred. Thirdly, the care integration readiness indicator was computed based on the supply-side factors such availability of trained staff, diagnostic equipment and treatment services rather than the patient-perceived quality of healthcare services for CVDs and type 2 diabetes. While patient perceptions is important in understanding the quality of healthcare services (9), previous studies have shown a higher social-desirability bias from self-reports than objective assessments (10-12).

Ngao ya Afya study (2019 – 2020)

The effect of patient peer support groups for hypertension on BP among patients with and without multimorbidity in Kenya is presented in part four. Data are from a quasi-experimental pilot study of a home-based self-management program for hypertension

conducted in Kenya between 2019 and 2020 (*Ngao ya Afya study*). The *Ngao ya Afya* study has important strengths. First, a quasi-experimental, longitudinal study design was used to examine the moderating effects of multimorbidity on peer support group intervention for the management of hypertension among low and middle-income patients in Kenya. This improved the application of the findings to poor resource settings in Kenya with a high prevalence of multimorbidity. Second, the diagnosis of hypertension and type 2 diabetes was based on an objective assessment by the treating clinician in the study facility rather than the self-reporting used in the majority of previous studies (13). Lastly, the use of propensity score matching (14) to account for the conditional probability of participation in the patient support groups minimized the treatment allocation bias.

The data from the *Ngao ya Afya* study has some limitations. First, the moderating effects of multimorbidity on peer support group intervention for hypertension is based on a post hoc analysis that needs to be replicated in future studies. Secondly, study clinics were not considered as cluster units leading to a wide variation in the number of patients enrolled in each clinic. Third, the screening for multimorbidities was based on self-reports by the patients. This may have resulted in a recall bias in the estimation of the true prevalence of multimorbidity. Lastly, multimorbidity was classified into concordant or discordant groups. Given the small sample size, the moderating effect of specific disease combinations on the efficacy of the patient peer support group was not explored.

Measurement of multimorbidity

There is no universal consensus on the definition and measurement of multimorbidity. A recent systematic review (15) identified simple disease counts as the most commonly used measure of multimorbidity in primary care and community care settings. However, the operationalization of multimorbidity based on disease counts may not provide informative information on the clusters of chronic diseases. In this thesis, multimorbidity was measured beyond simple counting of chronic diseases.

Two independent clustering algorithms were implemented. First, LCA was used to describe the patterns of cardiometabolic multimorbidity. The LCA uses structural equation modelling and a maximum likelihood approach to classify a set of homogenous outcomes into coherent latent classes (16). This involves assigning a probability distribution of class membership. The selection of class solution was based on model fit indices and theoretical interpretability. The BIC index was used to assess the relative fit and adequacy of the LCA models (17). The lowest values of BIC suggest better-fitting LCA models (18). The BIC has been shown in a Monte Carlo simulation to be more reliable in the assessment of class solutions compared to other information criteria such as the AIC (19).

To investigate the stability of the latent classes of multimorbidity identified from LCA, hierarchical agglomerative cluster analysis was separately applied. The hierarchical agglomerative cluster analysis uses a bottom-up approach iterative process with algorithms that separate distinct clusters of chronic diseases (20). The average linkage method and Jaccard dissimilarity index were used to accommodate the spread of clusters (21). A dendrogram plot was used to assess the number of multimorbidity clusters (21). Given the probability of uncertainties associated with class membership from the LCA analysis, the replication of the cluster solutions from the LCA results using the agglomerative hierarchal cluster analysis improved the quality of the findings of this thesis.

Reflections on the Key Finding of this Thesis

The burden of cardiometabolic multimorbidity in sub-Saharan Africa

Although LMICs bear 80% of the global burden of NCDs (22), evidence from a systematic review (23) found that only 5% of research studies on multimorbidity are conducted in LMICs. In part one of this thesis, secondary data from the STEPS surveys conducted in SSA were used to analyse the clustering of cardiometabolic diseases including type 2 diabetes, hypercholesterolemia, hypertension, and CVDs such as heart attack, angina, and stroke. Next, data from the SAGE surveys conducted in Ghana and South Africa were used to analyse the clustering of cardiometabolic diseases with unrelated chronic conditions such as asthma, chronic lung disease, arthritis, cataracts, and depression. The clusters identified included concordant multimorbidity comprising participants with type 2 diabetes, hypercholesterolemia, hypertension, and CVD; discordant multimorbidity including hypertension, abdominal obesity, type 2 diabetes, cataracts, and arthritis; and a cardiopulmonary class comprising angina, chronic lung disease, asthma, and depression.

The findings of this thesis show that cardiometabolic diseases in SSA occur in distinct clusters of concordant and discordant multimorbidity. Although previous reviews from LMICs and HIC show a rising prevalence of multimorbidity (23-28), the methodological differences in the assessment of multimorbidity and the variations in the number of chronic diseases included in the measurement of multimorbidity limit the comparison of findings. A systematic review by Asogwa et al. (25) identified cardiometabolic and cardiorespiratory conditions as the most common chronic disease combinations across different regions in LMICs. While this finding is consistent with the multimorbidity patterns identified in this thesis, most of the studies included in the review by Asogwa et al. (25) were based on disease counts without details on the most common clusters of chronic diseases.

The occurrence of concordant and discordant multimorbidity in this thesis may be due to in part, the shared lifestyle risk factors, insulin resistance and abnormalities of vascular

reactivity (29-32). In this thesis, cardiometabolic multimorbidity was highest among participants with sedentary lifestyles and obesity. Previous studies have shown that physical activity improves blood pressure control (33), cholesterol levels (34), C-reactive protein, and other inflammatory markers (35, 36). Thus, lifestyle modifications targeting physical inactivity and obesity are important in delaying the onset of cardiometabolic multimorbidity (37). The clustering of cardiopulmonary conditions and depression in this thesis is congruent with prior studies from LMICs (23, 28, 38, 39) and highlights the importance of including physical and mental health conditions in the assessment of multimorbidity.

Using the WHO STEPS survey data from nine countries in SSA, this thesis shows that the occurrence of cardiometabolic multimorbidity is disproportionately highest among persons of high socioeconomic status, women, and the middle and old-aged. Previous systematic reviews on the global burden of multimorbidity in LMICs and HIC have shown a disproportionately higher prevalence of multimorbidity in women than in men (24, 25, 40, 41). The sex differences in the cardiometabolic multimorbidity observed in this thesis could be due to in part the inequalities in domestic and occupational activities, health-care-seeking behaviour and the gender differences in lifestyle risk factors such as physical activity and diet (42, 43). Women in SSA seek healthcare services more frequently than men (44, 45). This may partly influence the detection of multimorbidity (25). Future studies on multimorbidity need to incorporate a gender lens to strengthen the evidence base for women's unique multimorbidity risks.

This thesis found that cardiometabolic multimorbidity in SSA was most common among middle-aged and older persons. This finding is consistent with several studies in support of the high prevalence of multimorbidity among middle-aged persons in LMICs (46-49). In HICs, the onset of chronic diseases at earlier ages is unequally distributed across the socioeconomic segments of society (50). In particular, persons living in socioeconomically deprived settings tend to experience multimorbidity 10-15 years earlier than persons living in least deprived settings (51). Previous studies show that chronic diseases tend to occur much earlier in life among people from LMIC than in HIC due to in part poverty and inadequate access to healthcare services (52-54).

Contextually, people with high socioeconomic status in SSA are generally physically inactive and consume unhealthy diets rich in fats, salts and processed foods (55). This could partly explain the high prevalence of cardiometabolic among people with high socio-economic status in this thesis. In addition, people of higher socioeconomic status have greater access to healthcare services than those with lower socioeconomic status (25). This may have influenced the detection of multimorbidity. In contrast, other studies conducted in SSA have a reported lower prevalence of multimorbidity among those in a higher socio-economic status than in those with lower socio-economic status (40, 56, 57). A higher education achievement may be also associated with a low likelihood

of unhealthy lifestyles, possibly because a high level of education may increase the awareness of healthy lifestyles and capacity for behaviour change (58, 59).

Understanding the association between different combinations of chronic diseases and functional status is an important step toward sustaining independent living among older persons. The findings of this thesis show that the risk of functional disability among older persons in Ghana and South Africa was highest in participants with cardiopulmonary multimorbidity and depression followed by those with co-occurring cardiometabolic diseases, cataracts, and arthritis. Previous studies have attributed functional impairment to the presence of multimorbidity (60-63). Clusters of chronic disease may interact and curtail compensatory mechanisms (64). Thus, accelerating functional decline. Similarly, functional disability may increase the treatment burden and limit response capacity, thereby increasing the risk of multimorbidity (65). This results in a vicious circle of multimorbidity and functional impairment.

Although the association of multimorbidity with a high frequency of healthcare utilization and poor quality of life is well recognized (57, 60, 66), the specific disease combinations associated with outpatient visits, hospitalization and poor quality of life are less well described. The findings of this thesis suggest that cardiometabolic multimorbidity among older persons in Ghana clusters in distinct patterns with varying implications on healthcare utilization and quality of life. Consistent with previous studies (67-72), the frequency of outpatient visits among older persons in Ghana was highest among those with co-occurring cardiometabolic diseases, cataracts, and arthritis followed by cardiopulmonary diseases and depression. However, the odds of hospitalization were highest in participants with cardiopulmonary diseases and depression. In contrast, no significant association existed between hospitalization and the clustering of cardiometabolic diseases, cataracts, and arthritis. These findings, along with other published studies (67-72), showed that certain combinations of cardiometabolic multimorbidity substantially differ in healthcare utilization patterns. This evidence may be useful for healthcare planning to optimize resources required for treatment and care for multimorbidity in SSA.

Similar to previous studies (62, 72), the findings of this thesis show that the multimorbidity cluster including depression and cardiopulmonary diseases was associated with greater functional disability, hospitalization, and poor quality of life than the cluster with co-occurring cardiometabolic diseases, cataracts, and arthritis. These findings may suggest that older persons with co-occurring multimorbidity and depression have unmet healthcare needs for depression (73, 74). The unmet healthcare needs for depression could be due to in part poor healthcare-seeking behaviours and delays in seeking care and treatment (73) Thus, persons with depression may need more hospitalization later when the condition worsens.

Chronic care models for cardiometabolic multimorbidity in SSA

Part two of this thesis presents a systematic review and meta-analysis of the effectiveness of integrated care models for cardiometabolic multimorbidity in SSA. The review focused on the applicability of the elements of Wagner's chronic care model including community resources and policies, health care organizations, self-management support, delivery system design, decision support, and clinical information systems. The results show that integrated care featuring at least two elements of Wagner's chronic care model significantly reduced SBP among patients living with cardiometabolic multimorbidity compared to standard care. However, the findings show mixed results with regard to HbA1c, depression, medication adherence and quality of life, with some studies showing a significant effect and some no effect.

The results of this thesis mirror the findings of reviews of studies from HIC and LMICs in support of the emerging evidence on the effectiveness of integrated chronic care models for the management of hypertension (3-8). However, most prior reviews are based on observational studies with very low certainty of evidence on the effectiveness of integrated care models. The findings of the current review contrast the results of a systematic review conducted by Rohwer et al (75). According to Rohwer et al, the integrated care model for hypertension and diabetes versus standard care conferred no significant effect on blood pressure and sugar control among patients from LMICs. Nevertheless, the evidence presented in the review by Rohwer et al had very low certainty and did not explicitly focus on integrated care models for the management of multimorbidity.

The meta-analysis included in this thesis found that integrated care reduced 5 mmHg of SBP in individuals with cardiometabolic multimorbidity compared to standard care. This finding is clinically significant considering that each reduction of 5 mmHg in SBP confers a 13% reduction in the risk of stroke (76). Previous studies show that increasing the number of chronic care model elements may elicit more health benefits over single elements (6, 77-79). A systematic review conducted by Goh et al (80) found greater improvement in blood sugar control for care models with more elements over few elements. Nevertheless, most of the studies included in this thesis had only two to three elements of the chronic care model. This could partly explain the mixed findings on the effect of integrated care on blood sugar control, depression, medication adherence and quality of life, with some studies included in this current review showing a significant effect and some suggesting no effect.

One of the key findings of the systematic review included in this thesis was the considerable variability in the combinations of the elements of integrated chronic care models implemented by studies from SSA. The results of this thesis show that self-management support and delivery system design were the most predominant components of the integrated chronic care models in SSA while healthcare organization

and community resource elements were less common. In this thesis, self-management support included structured interventions that emphasized the patient's role in managing their health. Examples included self-monitoring, patient peer support groups, patient-centered care and home-based self-care. Delivery system design included the organizational design, structure of the health workforce and delivery of care services. Examples included collaborative care, task shifting, patient care planning and regular follow-up. Several prior reviews have identified self-management support and delivery system as the most dominant components of chronic care models (3, 7, 81-85). However, most of these studies were conducted in HIC with sophisticated health services and therefore lack contextual relevance to people living with multimorbidity in SSA.

Given the variability in the combination of chronic care model elements in this thesis, it was not possible to identify the optimal combination of the six elements of Wagner's chronic care model that could lead to improvements in the intermediate health outcomes. The findings show no significant differences in intermediate health outcomes by the elements of integrated care since a majority of studies includes in the review had two to three elements. However, this is based on small number of studies with limited power to detect the difference in the health outcomes by type of chronic care model element. Previous studies that compared the effects of different combinations of the elements of Wagner's chronic care model did not find any significant variation in the intermediate health outcomes (86-91). This suggests that factors other than the combination of chronic care model elements may influence the health outcomes for people living with chronic diseases (92). Prior studies have shown that the intensity of the intervention rather than the number of intervention components may have a causal effect on the targeted health outcomes (5, 6). However, the review included in this thesis did not explore the effects of the intervention intensity due to the lack of an explicit description of intervention intensity from the original studies.

Health system readiness to manage cardiometabolic multimorbidity in Kenya

The WHO envisages integrated care as a "one-stop center" with essential resources for integrated care (93). These include a trained workforce, essential drug supplies, treatment and diagnostic resources and structural improvements to support integrated care (93, 94). Part three of this thesis presents the care integration readiness and the perceived facilitators and barriers to the integrated management of hypertension and type 2 diabetes in Kenya. The findings show that only one in every four healthcare facilities in Kenya was ready to provide integrated care for CVDs and type 2 diabetes with significant variations by facility type, ownership, and location. The major clinical integration barriers identified by the patients interviewed comprised vertical and unresponsive healthcare services characterized by service unavailability, unresponsiveness, and unaffordability. These findings align with the SARAM surveys conducted in Kenya and other LMICs (95-104), however, the SARAM surveys focused on the service availability and readiness assessment of single NCDs rather than integrated

care for multiple conditions. Historically, healthcare systems in SSA are primarily built around single diseases (105, 106). Against the backdrop of the WHO's global target to reduce 25% of premature NCD mortality by 2025 (107), healthcare systems in developing countries face significant challenges in providing integrated management of NCDs (108). The results of this thesis reinforce the need for effective implementation of integrated management of hypertension and type 2 diabetes in Kenya.

Basic screening and diagnostic equipment for hypertension and type 2 diabetes were generally available in most of the healthcare facilities surveyed in Kenya. These results indicate progress in the supply of equipment such as BP machines and glucometers compared to the 2008-2012 strategic report by the Ministry of Health in Kenya (109). Despite this progress, the diagnostics gaps for hypertension and type 2 diabetes in Kenya remain wide (110, 111). A major challenge in Kenya is the low levels of awareness of hypertension and type 2 diabetes among those with elevated blood pressure and sugar (110, 111). This has resulted in a large proportion of undiagnosed, untreated, or inadequately treated patients with hypertension or type 2 diabetes at risk of morbidity and mortality from potentially preventable complications such as stroke and heart disease (110, 111). A systematic review and meta-analysis on the burden of undiagnosed hypertension in SSA revealed that only 27% were aware of their hypertensive status, 18% of individuals with hypertension were receiving treatment, and only 7% had controlled blood pressure (112).

The gaps in the capacity of healthcare facilities particularly primary healthcare facilities in Kenya to provide integrated care services for CVD and type 2 diabetes may partly explain the high prevalence of unmet need for hypertension and type 2 diabetes care as described by previous studies (110, 111). The findings of this thesis show that trained staff, clinical guidelines and essential medicines for type 2 diabetes and CVD were generally unavailable in most health facilities, especially primary care facilities. For example, less than a third of the health facilities surveyed had the minimum threshold for trained staff and clinical guidelines. Such clinical guidelines are crucial in primary care facilities in Kenya where most healthcare services are primarily offed by non-medical-doctor clinicians and nurses (113-115). Consistent with previous studies from SSA (116-118), the health workforce in Kenya was perceived by both health stakeholders and patients as insufficient to meet the need for integrated healthcare services. However, task shifting from doctors to nurses and clinicians bridged the professional integration gaps. Kenya has long viewed staffing its public health facilities as an important challenge to overcome (119) and the findings of this thesis reinforce the continued need to address the equitable distribution of human resources for health especially in rural settings.

The national health insurance coverage in Kenya was identified from the qualitative interviews with patients and health stakeholders as a major facilitator for the functional integration of hypertension and type 2 diabetes care. However, extant data shows that

only 20% of Kenyans possessed health insurance in 2018 (120) and about 1.5 million Kenyans are pushed into poverty each year as a result of catastrophic expenditures for healthcare (121). Additional financial pressures ensue from the association of NCDs such as hypertension and type 2 diabetes with a reduction in household income by approximately 23% (122). Private health service providers have attempted to bridge the gap in demand for health care services, but lack service quality guarantee (123). The findings of this thesis show that private health facilities had a better capacity to provide integrated care services for CVDs and type 2 diabetes, than public health facilities. Similar findings have been reported in other LMICs (124-126).

Studies from LMICs have reported rural-urban disparities in the readiness of health facilities to provide care and services for NCDs (127-129). Similar findings were observed in evidence presented in this thesis where facilities located in Central Kenya, and the Rift Valley region were less likely to be ready compared to the capital Nairobi. The regional disparity in the care integration readiness for CVD and type 2 diabetes in Kenya may be in part due to the high concentration of the health workforce in the capital Nairobi. Furthermore, the rapid urbanization in Kenya as a result of rural-urban migration may have resulted in the high influx of people into cities including Nairobi, thus creating the need to expand and improve integrated health services for NCDs such as improved supply chain logistics, medicines and equipment (130). However, primary healthcare services for CVDs and type diabetes in Kenya's Rift Valley and Central region remain under-resourced.

Similar to previous studies (131-134), the findings from the facility-level interviews identified patient-centred care models such as peer support groups as major facilitators for the integrated management of hypertension and type 2 diabetes in Kenya. This finding is consistent with a recent systematic review that found a reduction in systolic blood pressure and sugar among patients from LMICs enrolled in self-financing peer groups, although the evidence was very uncertain (135). The patients interviewed in this thesis perceived peer support groups as important adjuncts to clinical care for reinforcing positive behaviours. Consistent with earlier studies (136-138), the availability of the national HMIS was cited by the health stakeholders as key to expanding and supporting the integrated management of hypertension and type 2 diabetes in Kenya. Even though the HMIS provided an opportunity for the integration of e-health in the management of hypertension and type 2 diabetes, the lack of interoperable platforms emerged as a major obstacle to integrated care. These findings corroborate the results of previous studies on the integration of HMIS in LMICs (27, 137, 139). The fragmentation of the national HMIS platform in Kenya is in part due to inadequate national regulatory framework and standards to guide the implementation of HMIS in Kenya (140-142).

In general, driven by economic constraints and weak technical capacities, LMICs grapple with challenges in the preparedness of their healthcare systems to respond to the

growing burden of multimorbidity (143). Expectedly, the primary healthcare systems in SSA are still struggling to re-orient services to simultaneously respond to infectious diseases and NCDs (144). In Kenya, the integrated management of CVDs and type 2 diabetes is gaining recognition from policymakers. However, the policy response for adapting primary healthcare services for the prevention and control of CVD and type 2 diabetes is not in tandem with the growing burden of multimorbidity (145). Primary healthcare revitalization is considered an equitable and cost-effective way to attain population health (146) and is thus pivotal in improving the integrated management of hypertension and type 2 diabetes.

Effect of multimorbidity on self-care interventions for cardiometabolic diseases in Kenya

Management of multimorbidity is a complex process that requires coordinating healthcare appointments, taking multiple medicines and making lifestyle changes (147-152). As such, the centrality of self-management support to patient-centered care cannot be overemphasized (153). Peer-led interventions to improve self-management of chronic diseases have been widely used in Kenya (154-157). However, there is limited evidence of their potential health benefits. Furthermore, there is a paucity of evidence to guide the rollout of patient support group interventions among patients with multimorbidity. Part four of this thesis presents the effect of a patient support group intervention on BP management and the potential moderating effect of multimorbidity among low and middle-income patients with hypertension in Kenya. The findings show that a patient-led peer support group intervention was effective in reducing systolic BP among people with hypertension compared to non-participation in the groups. However, multimorbidity attenuated the effectiveness of the support groups.

Consistent with our findings, previous studies from other LMICs found improvement in blood pressure management among patients attending peer support groups for hypertension (131-134). However, generalizing the evidence to the Kenyan context may not be feasible due to the differences in the organization of primary care systems across countries. The mechanisms by which patient support groups improve blood pressure management remain unclear. It is plausible that the social support received from the peer groups may enhance compliance and active involvement of the patients in their care, with positive consequences for BP management (158-161). Evidence from a study conducted in India showed that a community-based self-help group for hypertension significantly reduced systolic BP among women with hypertension (133). The support groups in our intervention focused on home-based self-monitoring, lifestyle modification, group measurement of BP, sharing of personal-emotional experiences, motivation-counselling and appraisal. Thus, it is conceivable that patient activation in the groups may have resulted in the observed improvements in systolic BP in this thesis.

Evidence presented in this thesis shows that concordant multimorbidity attenuates the effectiveness of patient support groups for blood pressure management. However, earlier studies show that multimorbidity is both a threat and an opportunity to self-care (162, 163). The study by Kerr et al (162) is consistent with the findings of this thesis and shows that multimorbidity may limit self-care abilities. First, coexisting conditions may serve as competing demands, thus reducing time and resources for hypertension care. Second, multimorbidity may result in poor medication adherence due to complex drug regimens, polypharmacy, drug-disease interactions and drug-drug interactions (164-166). Lastly, the co-existence of a dominant chronic condition that poses an immediate threat to life such as chronic kidney disease may obscure hypertension care and self-monitoring (162). The study by Voorham et al. (163) contrasts the findings of this thesis and demonstrates that concordant multimorbidity such as hypertension and type 2 diabetes presents an opportunity for a shared treatment plan and CVD risk reduction goals that may improve overall health outcomes for hypertension and type 2 diabetes. However, this study was conducted in the Netherlands and cannot be generalised to the Kenyan context due to the variations in the actual problems that compete with hypertension care in LMICs.

Implications for policy and public health practice

This thesis provides a compendium of information on the burden of cardiometabolic multimorbidity in SSA and has several practical implications for integrated health system response. The importance of examining the clustering multimorbidity in lieu of focusing on single chronic conditions cannot be overemphasized. In part one of this thesis, three distinct clusters of multimorbidity were identified to include concordant multimorbidity comprising participants with type 2 diabetes, hypercholesterolemia, hypertension, and CVD; discordant multimorbidity including hypertension, abdominal obesity, type 2 diabetes, cataracts, and arthritis; and a cardiopulmonary class comprising angina, chronic lung disease, asthma, and depression. The clustering of concordant and discordant multimorbidity among persons with cardiometabolic diseases underscores the need for targeted screening for coexisting chronic conditions in patients presenting with cardiometabolic diseases in primary care settings in SSA. The coexistence of cardiopulmonary diseases and depression highlights the need for inclusion of screening and treatment of depressive symptoms occurring in older patients presenting for the treatment of cardiopulmonary conditions.

Although previous studies show that multimorbidity is a “normal state of affairs” for older persons aged 60 years and above (23, 27, 167), this thesis has highlighted that multimorbidity is also common among middle-aged persons in SSA. A life course approach focusing on the prevention of NCDs earlier in life is needed. Practical examples include targeted policy interventions during childhood such as health-promoting schools and restriction of marketing of unhealthy foods to children. This may structure children’s environment in ways that promote physical activity and minimize the consumption of unhealthy diets. The transition from childhood to adulthood presents unique

opportunities for targeted interventions for comorbidity at workplaces. A healthy workplace environment is an important setting during adulthood. This includes policies that promote healthy lifestyles such as physical activity and restricted alcohol and tobacco use. Targeted interventions for older persons may include developing and operationalising of policies for improving functional capacity and involvement in wider social and physical activities.

Policies are required that target the social risk factors for multimorbidity in SSA. Gender is a well-known social risk factor for chronic diseases (23). The findings in chapter one show that being female was associated with a higher risk of cardiometabolic multimorbidity than males. This finding implies that a gender lens for integrated management of multimorbidity is needed. In particular, integrating maternal and child health services and chronic disease management programs in primary care settings represents an opportunity for an equitable health systems response to the burden of multimorbidity in line with the sustainable development agenda of leaving no one behind. Unlike previous studies which have shown that multimorbidity is a common problem among socio-economically deprived persons (40, 56, 57), chapter two of this thesis shows that cardiometabolic multimorbidity is highest among persons of high socio-economic status in SSA. This highlights the need for a systems thinking approach to address the socio-economic risk factors for multimorbidity. Unless a holistic system thinking approach is used to address the interactions between multimorbidity and the social and economic drivers of lifestyle risk factors, the integrated care interventions may fail to address the burden of multimorbidity at multiple levels.

Chapters three and four in this thesis provide crucial evidence to health services providers in SSA on the cardiometabolic multimorbidity combinations that are more disabling among older adults and those that require more or fewer outpatient visits and hospitalization. This information is important in planning the health systems' response capacity and resources for long-term care. The findings of the systematic review on chronic care models for multimorbidity in SSA show that integrated care may improve hypertension management in patients with multimorbidity. Although Kenya adopted a national guideline for the integrated management of type 2 diabetes in 2010 and CVDs in 2018 (168, 169), this thesis found substantial gaps in their implementation. The implementation gaps are partly due to the shortage of essential resources such as a trained healthcare workforce, treatment guidelines, treatment and follow-up services, and essential medicine. The implementation gaps are also rooted in factors such as inadequate enforcement, health insurance coverage gaps, and inadequate budget allocation. In 2021, only 6.8% of the Kenyan national budget was allocated to the health sector against the 15% recommended by the Abuja Declaration that was ratified by the Kenyan government in 2001 (170). Thus, to maximize universal health coverage, the Kenyan government needs to increase resource allocation to the health sector to enhance access to integrated care and fulfil the national commitments to universal health coverage.

The design and implementation of integrated healthcare need to employ macro, meso and micro-lenses. At the micro level, the barriers to clinical integration such as vertical and unresponsive healthcare services need to be redressed. There is a need to strengthen the clinical integration facilitators identified in this thesis including patient-centered care models such as peer support groups and health promotion on shared risk factors. At the meso level, policies that promote organizational and professional integration such as task shifting and strengthening national referral systems are vitally important in improving the coordination of healthcare services across facilities. Although the national referral system for public health facilities in Kenya is well established, this can be extended to the private facilities that serve 42% of the population in Kenya (120). Finally, at the macro level, the system integration policies that target healthcare services linkages need to be strengthened.

Implications for future research on multimorbidity

This thesis provides valuable evidence on the burden of cardiometabolic multimorbidity and integrated health system response in SSA. This is especially important because studies on multimorbidity in SSA are very limited. A systematic review conducted in 2018 showed that 95% of studies on multimorbidity are from HIC countries (171). Thus, this thesis provides baseline estimates on cardiometabolic multimorbidity clusters in SSA for future researchers to design longitudinal studies on the pathogenesis and causal risk factors.

The absence of a global consensus on the definition of multimorbidity signals substantial heterogeneity in multimorbidity studies. The identification of clusters of cardiometabolic diseases and other chronic diseases in this thesis fosters a greater understanding of the burden of the most common disease combinations. Nevertheless, adopting a global standard definition of multimorbidity is important for laying a firm foundation for future studies on multimorbidity in SSA. Chapters two and three of this thesis show distinct clusters of multimorbidity associated with functional disability, healthcare utilization and quality of life. However, further evidence on the magnitude of these associations from longitudinal studies is needed to elucidate these results. In addition, future studies on multimorbidity in SSA should also focus on chronic disease syndemics and the rate of transition between different clusters of multimorbidity.

The number of chronic conditions included in this thesis was limited to those included in the STEPS and SAGE surveys conducted in SSA. Therefore, to increase external validity, future studies on multimorbidity in SSA need to include more chronic conditions. A systematic review of chronic care models for cardiometabolic multimorbidity in SSA in Chapter 6 signals a substantial evidence gap in integrated care models in SSA since the included trials were only from a few countries. Therefore, more rigorous cluster RCTs on integrated management of multimorbidity in SSA are needed. In addition, the relative impact, cost-effectiveness and implementation effectiveness of different elements of integrated chronic care models need to be explored in future research.

The section of the thesis assessing the burden of cardiometabolic multimorbidity in SSA is based on studies conducted in Ghana and South Africa, while the assessment of care integration readiness, and patient support groups is based on studies conducted in Kenya. To enhance the generalizability of the findings to SSA, there is a need to replicate these studies in other SSA countries. This is because the countries in SSA exhibit substantial variation in genetic, and cultural diversity and the organization of primary care services. The findings of this thesis suggest that patient support groups for hypertension may be an important adjunct to clinical care. A quasi-experimental pilot study conducted in Kenya on the effectiveness of patient support groups for hypertension presented in Chapter 7 showed that participation in the groups significantly improved systolic BP compared to non-participation. However, the support groups did not benefit patients with multimorbidity. Further studies on the sustainability of the support groups and operational lessons are needed to inform scale-up. Furthermore, more cluster randomized control trials are needed to elucidate these results. Finally, more prospective and longitudinal studies are needed to understand the risk factors for uncontrolled hypertension among patients with multimorbidity.

Conclusions

This thesis challenges the single-disease framework by which health service delivery in SSA is configured. In SSA, cardiometabolic diseases occur in distinct clusters of concordant and discordant multimorbidity. These clusters are significant predictors of healthcare utilization, functional disability and quality of life. The occurrence of cardiometabolic multimorbidity is disproportionately highest among persons in high socioeconomic status, women, the middle and old-aged, and those with sedentary lifestyles and obesity. These results provide useful evidence for multimorbidity risk stratification by identifying groups of high-risk persons with unique lifestyles and sociodemographic characteristics, around which targeted integrated chronic disease management frameworks can be designed. Integrated chronic care conferred improvement in systolic BP among persons with cardiometabolic multimorbidity in SSA. In addition, patient peer support groups for hypertension improved systolic BP among patients on home-based self-care programs. These findings have important public health significance given that a reduction of systolic BP could significantly reduce the risk of major cardiovascular events. Multimorbidity attenuated the effectiveness of patient support groups for hypertension. Therefore, there is a need to tailor patient-centered care interventions in SSA to match the needs of people with multimorbidity. Despite the observed benefits of the integrated management of cardiometabolic multimorbidity, this thesis found substantial gaps in its implementation. For example, in Kenya, only one in every four healthcare facilities (at all levels) was ready to provide integrated management of CVD and type 2 diabetes. These findings provide crucial insights for strengthening the responsiveness of the healthcare system to the management of cardiometabolic multimorbidity in SSA.

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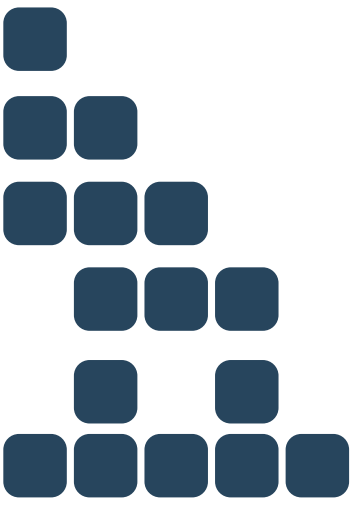


Summary

Summary

Chronic conditions that include type 2 diabetes, dyslipidemia, hypertension, heart attack, coronary heart disease and stroke, commonly known as cardiometabolic diseases are the leading causes of global morbidity and mortality. People living with cardiometabolic diseases often have multiple rather than one condition. Cardiometabolic diseases also co-occur with other discordant chronic diseases such as mental disorders, chronic respiratory disease, and musculoskeletal disorders. In 2019, one in every three adults globally lived with multimorbidity. The risk of multimorbidity in SSA is compounded by the rise in globalization and rapid epidemiological transitions. The rapid urbanization in SSA and demographic transitions have led to an unprecedented increase in life expectancy and prolonged exposure to unhealthy lifestyles including unhealthy diets, harmful alcohol consumption, tobacco use, and physical inactivity coupled with the existence of chronic infectious diseases such as HIV.

The care pathways for people with cardiometabolic multimorbidity is complex and demanding for the health system in SSA. However, evidence supporting the management of multimorbidity has been largely inferred from studies focusing on single chronic diseases. The overarching aim of this thesis is to strengthen the responsiveness of the healthcare system to the management of cardiometabolic multimorbidity in SSA. By using a multimethod approach, this thesis investigates four main issues on cardiometabolic multimorbidity in SSA: the burden of cardiometabolic multimorbidity; the effectiveness of integrated chronic care models; the readiness of healthcare facilities to provide integrated chronic disease management; and the effect of multimorbidity on self-care interventions.

Using data from the WHO STEPS and SAGE surveys conducted in SSA, part one of this thesis examined the clusters of cardiometabolic multimorbidity and the implications of multimorbidity patterns on functional disability, healthcare utilization, and quality of life. The findings show that cardiometabolic diseases in SSA occur in distinct clusters of concordant and discordant multimorbidity. These clusters are significant predictors of healthcare utilization, functional disability and quality of life. The occurrence of cardiometabolic multimorbidity is disproportionately highest among persons of high socioeconomic status, women, the middle and old-aged, and those with sedentary lifestyles and obesity.

Part two reports on a systematic review and meta-analysis of the effectiveness of integrated chronic care models for cardiometabolic multimorbidity in SSA. The review focused on the applicability of the elements of Wagner's chronic care model including community resources and policies, health care organizations, self-management support, delivery system design, decision support, and clinical information systems. The results show that integrated care featuring at least two elements of Wagner's chronic care

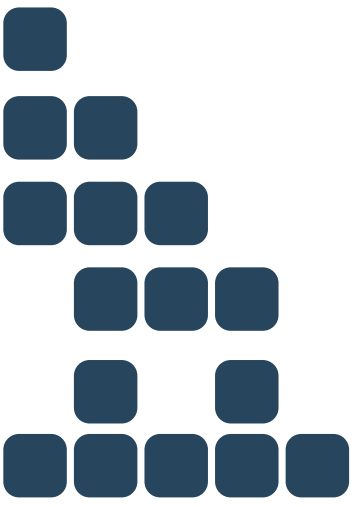
model conferred improvement in systolic BP among persons with cardiometabolic multimorbidity in SSA.

Part three presents a readiness assessment of healthcare facilities' capacity to provide integrated management of CVDs and type 2 diabetes in Kenya and a qualitative study of the health system facilitators and barriers to integrated care. The findings show that only one in every four healthcare facilities in Kenya was ready to provide integrated care for CVDs and Type 2 diabetes. The major clinical integration barriers included vertical healthcare services characterized by service unavailability, unresponsiveness, and unaffordability. The gaps in the implementation of integrated care were also rooted in factors such as inadequate enforcement, gaps in health insurance coverage, and inadequate budget allocation.

The effect of patient peer support groups for hypertension on blood pressure among patients with and without multimorbidity in Kenya is presented in part four. The findings show that patient-led peer support group intervention was effective in reducing systolic BP among people with hypertension compared to non-participation in the groups. However, multimorbidity attenuated the effectiveness of the support groups.

This thesis provides crucial insights for strengthening the responsiveness of the healthcare system to the management of cardiometabolic multimorbidity in SSA. The findings on the burden of cardiometabolic multimorbidity clusters in part one may help in identifying groups of high-risk persons with unique lifestyles and sociodemographic characteristics, around which targeted integrated chronic disease management frameworks in SSA can be designed. The effectiveness of integrated chronic care models in the management of BP among people with cardiometabolic multimorbidity in part two of this thesis has important public health significance given that BP control could significantly reduce the risk of major cardiovascular events. The substantial gaps in the implementation of integrated care models in part three highlight the need to strengthen the resource capacity of the healthcare system in SSA to respond to the emerging needs of people with cardiometabolic multimorbidity. The moderating effect of multimorbidity on the effectiveness of patient peer support groups for hypertension as presented in part seven of the thesis signals the need to tailor patient-centered care interventions in SSA to match the needs of people with multimorbidity.

The number of chronic conditions in this thesis was limited to those in the STEPS and SAGE surveys conducted in SSA. Therefore, future studies on multimorbidity in SSA need to consider more chronic conditions to increase external validity. Furthermore, the assessment of the burden of cardiometabolic multimorbidity in SSA and care integration readiness in parts three and four of this thesis was based on cross-sectional studies from a few countries. Thus, to enhance the generalizability of the findings to the SSA region, there is a need to replicate these studies in other countries in SSA using longitudinal studies.



Samenvatting

Samenvatting

Chronische ziekten zoals type 2-diabetes, dyslipidemie, hypertensie, myocard en herseninfarcten, en coronaire hartziekte en hartinfarct, ook wel bekend als cardiometabole ziektes, zijn hoofdoorzaken van morbiditeit en mortaliteit wereldwijd. Mensen die leven met dit soort ziektes hebben vaak meer dan één chronische aandoening. Cardiometabole ziektes gaan ook vaak samen met andere chronische ziektes zoals psychische aandoeningen, chronische obstructieve pulmonale ziekte (COPD) en musculoskeletale afwijkingen. In 2019 leed een op de drie volwassenen wereldwijd aan multimorbiditeit. Het risico op multimorbiditeit in sub-Sahara Afrika (SSA) wordt versterkt door een toename in globalisering en snelle epidemiologische transities. De toenemende urbanisatie in Sub-Sahara Afrika en demografische veranderingen hebben geleid tot een enorme toename in levensverwachting, en daardoor ook tot een toename in blootstelling aan ongezonde leefstijl zoals een vet of suikerrijk dieet, schadelijke alcoholconsumptie, roken, en fysieke inactiviteit, in combinatie met het voortbestaan van chronische infectieziektes zoals HIV.

De zorgmodellen voor mensen met cardiometabole multimorbiditeit zijn complex en vragen veel van het zorgsysteem in SSA. Echter, het wetenschappelijk bewijs voor de behandeling van multimorbiditeit is met name afkomstig van studies die zich focusten op enkelvoudige chronische ziektes. Het overkoepelende doel van dit proefschrift is om de responsiviteit van het zorgsysteem in SSA te vergroten op de benodigde behandeling van cardiometabole multimorbiditeit. Dit proefschrift onderzoekt vier belangrijke factoren die invloed hebben op cardiometabole multimorbiditeit in SSA met een multi-methode benadering: de impact van cardiometabole multimorbiditeit; de effectiviteit van geïntegreerde chronische zorg modellen; de mate van geschiktheid van zorginstellingen om geïntegreerde chronische zorg te leveren; en het effect van multimorbiditeit op zelf-zorg interventies.

Met behulp van data van de WHO STEPS en SAGE surveys die uitgevoerd zijn in SSA, zijn er in deel een van dit proefschrift clusters van cardiometabole multimorbiditeit en de implicaties van multimorbiditeits patronen op functionele beperkingen, gebruik van gezondheidszorg en kwaliteit van leven onderzocht. Deze bevindingen laten zien dat cardiometabole ziektes in SSA voorkomen in typische clusters. Deze clusters zijn significante voorspellers van zorg gebruik, functionele beperkingen en kwaliteit van leven. Het voorkomen van cardiometabole multimorbiditeit is disproportioneel hoog onder mensen met een hoge sociaal-economische status, vrouwen, mensen van middelbare en oudere leeftijd, en mensen met een zittende levensstijl en obesitas.

Deel twee beschrijft een systematische review en meta-analyse van de effectiviteit van geïntegreerde zorg modellen voor cardiometabole multimorbiditeit in SSA. Deze review richtte zich op de toepasbaarheid van de elementen van Wagners' chronische

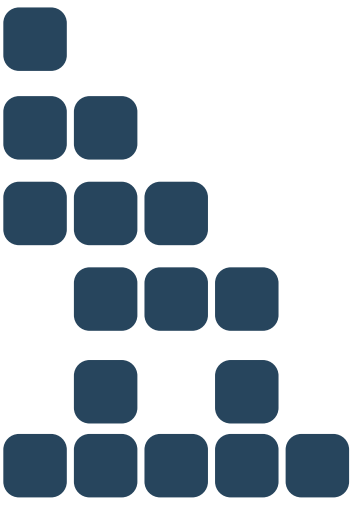
zorg model, waaronder de beschikbare middelen en beleid vanuit de gemeenschap, gezondheidszorg organisaties, ondersteuning van zelf-management, de manier waarop zorg geleverd wordt, beslisondersteuning en klinische informatie systemen. De resultaten laten zien dat geïntegreerde zorg met in elk geval twee elementen uit het chronische zorg model van Wagner, de systolische bloeddruk verlaagt onder personen met cardiometabole multimorbiditeit in SSA.

Deel drie onderzoekt de mate waarin zorginstellingen klaar zijn om geïntegreerde behandeling van cardiovasculaire ziektes en type 2 diabetes in Kenia te verlenen, en beschrijft een kwalitatieve studie van de factoren die invloed hebben op geïntegreerde zorg. Deze bevindingen laten zien dat maar een op de vier zorginstellingen in Kenia, klaar was om geïntegreerde zorg te leveren voor cardiovasculaire ziektes en type 2 diabetes. De grootste hindernissen voor klinische integratie waren zorgverlening alleen gericht op specifieke aandoeningen, met een tekort aan middelen en personeel, weinig flexibiliteit en dure zorg. Andere barrières voor de implementatie van geïntegreerde zorg behelsden suboptimale uitvoering, weinig sociale bescherming en inadequate toewijzing van budgetten.

Het effect van patiënt peer support groepen op de bloeddruk van patiënten met en zonder multimorbiditeit in Kenia wordt besproken in deel vier. De resultaten laten zien dat een interventie door middel van een patiëntgeleide peer-support groep effectief was om de systolische bloeddruk te verlagen van mensen met hypertensie. Het effect van de support groepen was minder groot voor mensen met multimorbiditeit.

Dit proefschrift biedt cruciale inzichten voor het versterken van de responsiviteit van het gezondheidszorgsysteem op het beheren en behandelen van cardiometabole multimorbiditeit in SSA. De bevindingen met betrekking tot de invloed van verschillende cardiometabole clusters in deel één, kunnen bijdragen aan het indentificeren van hoog-risico personen met een typerende leefstijl en sociodemografische karakteristieken, voor wie gerichte geïntegreerde chronische zorg frameworks in SSA ontwikkeld kunnen worden. De effectiviteit van geïntegreerde chronische zorg modellen bij de behandeling van hoge bloeddruk bij mensen met cardiometabole multimorbiditeit in deel twee van dit proefschrift, is van groot belang voor de volksgezondheid aangezien een beter gecontroleerde bloeddruk het risico op grote cardiovasculaire gebeurtenissen kan verminderen. De grote barrières die komen kijken bij het implementeren van geïntegreerde zog modellen in deel drie, benadrukken de urgentie om de middelen en capaciteit van gezondheidszorgsystemen in SSA te vergroten om te voorzien in de toenemende behoeftes van mensen met cardiometabole multimorbiditeit. Het feit dat de effectiviteit van lotgenoten contact middels groepsbijeenkomsten minder groot was in de groep met multimorbiditeit zoals beschreven in deel zeven van dit proefschrift, suggereert dat het nodig is om patiënt-gerichte zorg interventies in SSA te ontwikkelen die passen bij de behoeftes van de mensen met multimorbiditeit.

Het aantal bestudeerde chronische aandoeningen in dit proefschrift was beperkt tot de aandoeningen die afkomstig zijn uit de STEPS en SAGE surveys uitgevoerd in SSA. Toekomstige studies naar multimorbiditeit zouden zich daarom moeten richten op meer chronische aandoeningen om de externe validiteit te vergroten. Daarnaast was de evaluatie van het voorkomen van cardiometabole multimorbiditeit in SSA en geschiktheid voor het integreren van zorg in deel drie en vier van dit proefschrift op cross-sectionele studies uit een beperkt aantal landen. Om de resultaten te kunnen generaliseren voor de hele SSA regio zouden toekomstige longitudinale studies zich ook moeten richten op andere landen in SSA.



Acknowledgements

Roles of Co-Authors

Article 1

Multimorbidity of cardiometabolic diseases: a cross-sectional study of patterns, clusters and associated risk factors in sub-Saharan Africa

- Prof. dr. Charles Agyemang-Promoter
- Dr. Gershim Asiki-Co-promotor
- Dr. Frederick Wekesah, Dr. Calistus Wilunda, Dr. Richard Sanya and Dr. Welcome Wami are members of the Chronic Disease Management Unit at APHRC. They contributed intellectually to the preparation of the manuscript.

Article 2

Cardiometabolic Multimorbidity Associated with Moderate and Severe Disabilities: Results from the Study on Global AGEing and Adult Health (SAGE) Wave 2 in Ghana and South Africa

- Prof. dr. Charles Agyemang -Promoter
- Dr. Gershim Asiki-Co-promotor
- Dr. Justice Moses K. Aheto is a Senior Lecturer of Biostatistics at the School of Public Health, University of Ghana, Legon, Accra. He helped with the statistical analyses and preparation of the manuscript.
- Dr. Calistus Wilunda, Dr. Richard Sanya and Dr. Welcome Wami are members of the Chronic Disease Management Unit at APHRC. They helped to shape the research questions and preparation of the manuscript.

Article 3

Cardiometabolic multimorbidity and associated patterns of healthcare utilization and quality of life: results from the Study on Global AGEing and Adult Health (SAGE) Wave 2 in Ghana.

- Prof. dr. Charles Agyemang -Promoter
- Dr. Gershim Asiki-Co-promotor
- Dr. Calistus Wilunda and Dr. Welcome Wami are members of the Chronic Disease Management Unit at APHRC. They made substantive contributions to the conceptualization of the study, and data analysis and reviewed the manuscript

Article 4

Effectiveness of integrated chronic care models for cardiometabolic multimorbidity in sub-Saharan Africa: a systematic review and meta-analysis.

- Prof. dr. Charles Agyemang -Promoter
- Dr. Gershim Asiki:Co-promotor
- Dr. Hesborn Wao is the training coordinator for Research Capacity Strengthening Division at APHRC. He provided overall methodological guidance for the systematic review.
- Elvis Wambiya and James Oguta are PhD fellows at The University of Sheffield, Sheffield, United Kingdom. They contributed to the screening of titles and abstracts and the meta-analyses. Maurine N'gonda, Daniel Mwanga and Peter Kibe are researchers at APHRC. They screened titles and abstracts and participated in the full-text screening of the selected articles.

Article 5

Assessing the Readiness to Provide Integrated Management of Cardiovascular Diseases and Type 2 Diabetes in Kenya: Results from a National Survey.

- Prof. dr. Charles Agyemang -Promoter
- Dr. Gershim Asiki:Co-promotor
- Dr. Welcome Wami is a Research Fellow at The Amsterdam Institute of Global Health and Development (AIGHD) and a member of Joep Lange Research project on the healthcare system response to chronic disease management in SSA. He helped with the statistical analyses and preparation of the manuscript.
- Dr. Calistus Wilunda and Dr. Richard Sanya, are members of the Chronic Disease Management Unit at APHRC. They helped to shape the research questions and preparation of the manuscript.

Article 6

Perceived health system facilitators and barriers to integrated management of hypertension and type 2 diabetes in Kenya.

- Prof. dr. Charles Agyemang -Promoter
- Dr. Gershim Asiki:Co-promotor
- Dr. Emmy Igonya, Dr. Ramatou Ouedraogo, Jane Osindo, and Caroline Wainana are qualitative researchers at APHRC. They contributed to the conceptualization of the study and data analysis.
- Elvis Wambiya is a PhD fellow at The University of Sheffield, Sheffield, United Kingdom. He contributed intellectually to the preparation of the manuscript

Article 7

Effect of Patient Support Groups for Hypertension on Blood Pressure among Patients with and Without Multimorbidity: Findings from a Cohort Study of Patients on a Home-Based Self-Management Program in Kenya.

- Prof. dr. Charles Agyemang -Promoter
- Dr. Gershim Asiki:Co-promotor
- Dr. Calistus Wilunda, Dr. Richard Sanya, Dr. Samuel Iddi, and Dr. Welcome Wami are members of the Chronic Disease Management Unit at APHRC. They helped to shape the research questions and preparation of the manuscript.
- Dr. Judith Van Andel, Babette van der Kloet, Julia Teerling, and Angela Siteyi led the implementation of a chronic disease care program called *Ngao Ya Afya-Tiba Yako* at PharmAccess Foundation in Nairobi, Kenya. They contributed intellectually to the preparation of the manuscript.

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"Progress is not achieved in isolation; it is a testament to the giants whose contributions have propelled us forward. We build upon their foundations as we sculpt our future."

Anonymous

My doctoral journey is a culmination of inspiration from special people from different walks of life who have shaped my thoughts and actions. I will remain forever grateful for their kindness and support. First and foremost, I would like to express my deepest sense of gratitude to the Almighty God whose grace guided me from the very inception to the completion of this doctoral journey. I have returned to give thanks to God for His mercies endures forever.

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I would like to express my gratitude to my PhD thesis committee members: Prof. dr. Jacqueline Broerse (Vrije Universiteit), Prof. dr. Tobias Rinke de Wit (AMC-UvA), Prof. dr. Anton Kunst (AMC-UvA), dr. Kerstin Klipstein-Grobusch (Utrecht University), Prof.dr. Pieter Willem Kamphuisen (AMC-UvA), and Prof.dr. Bert-Jan van den Born (AMC-UvA). Thank you very much for the valuable feedback and thought-provoking insights that have greatly enriched the quality of my work.

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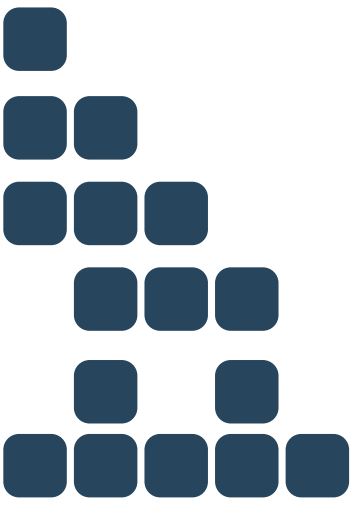


About the author

About the Author

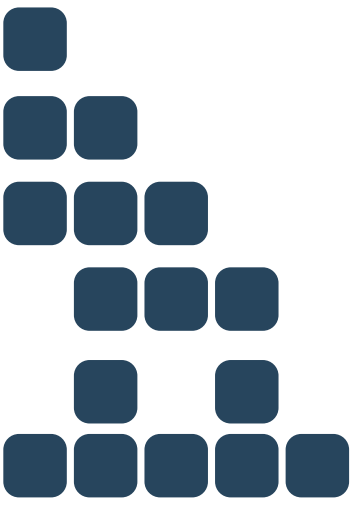
Peter Otieno is a researcher at the African Population and Health Research Center (APHRC) based in Nairobi, Kenya implementing studies on health system strengthening through the development of evidence-based decision models to inform public health policy. He is currently a co-investigator in projects implementing studies on health systems that span observational and intervention research to policy analysis. Peter works very closely with African governments in providing scientific support in implementing national health policies. He has identified multimorbidity as a further area for his research

Education and Awards

Peter is a PhD fellow in Epidemiology and Public Health at Amsterdam University Medical Center in the Netherlands. He holds a Masters degree in Geroscience (Ageing and Health) from the Commonwealth Fellowship at the University of Southampton, United Kingdom (2016). Peter is a recipient of three international research fellowships; Impact Evaluation Fellowship for the Transfer Project in Africa by UNICEF Office of Research – Innocenti & Carolina Population Center, University of North Carolina at Chapel Hill, USA. (2021): Emerging Voices for Global Health Fellowship (2021) by Health Systems Global (HSG) and Institute of Health Policy (IHP): and Impact Evaluation Fellowship at the Center for Effective Global Action (CEGA) and the University of California, Berkeley, USA (2023).

Recent research projects

- Co-Investigator: Timeliness of administering Birth-dose Vaccines in Nairobi urban slums. Global Challenges Exploration (Bill and Melinda Gates Foundation): Awarded in 2018.
- Co-investigator; Evaluating a service model for the management of hypertension and diabetes among low and middle-income patients in Kenya. SANOFI. Awarded in 2018.
- Co-Investigator: Chronic disease management: an entry point for bridging the gap between population and health care needs for non-communicable diseases in low and middle-income countries Sub- Saharan Africa. Joep Lange Institute. Awarded 2018.
- Co-Investigator: Epilepsy Pathway Innovation in Africa (EPInA). National Institute of Health Research (NIHR). Awarded in 2020



List of Publications

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Articles included in this thesis

1. **Otieno P**, Asiki G, Wekesah F, Wilunda C, Sanya RE, Wami W, Agyemang C. Multimorbidity of cardiometabolic diseases: a cross-sectional study of patterns, clusters and associated risk factors in sub-Saharan Africa. BMJ Open. 2023 Feb 9;13(2):e064275. doi: 10.1136/bmjopen-2022-064275. PMID: 36759029

2. **Otieno P**, Asiki G, Aheto JMK, Wilunda C, Sanya RE, Wami W, Mwanga D, Agyemang C. Cardiometabolic Multimorbidity Associated with Moderate and Severe Disabilities: Results from the Study on Global AGEing and Adult Health (SAGE) Wave 2 in Ghana and South Africa. Global Heart. 2023. DOI: https://doi.org/10.5334/ gh.1188

3. **Otieno P**, Asiki G, Wilunda C, Wami W, Agyemang C (2023) Cardiometabolic multimorbidity and associated patterns of healthcare utilization and quality of life: Results from the Study on Global AGEing and Adult Health (SAGE) Wave 2 in Ghana. PLOS Global Public Health 3(8): e0002215. https://doi.org/10.1371/journal.pgph.0002215

4. **Otieno, P.**, Agyemang, C., Wao, H., Wambiya, E., Ng'oda, M., Mwanga, D., . . . Asiki, G. (2023). Effectiveness of integrated chronic care models for cardiometabolic multimorbidity in sub-Saharan Africa: a systematic review and meta-analysis. BMJ open, 13(6), e073652. doi:10.1136/bmjopen-2023-073652

5. **Otieno, P.**, Agyemang, C., Wami, W., Wilunda, C., Sanya, R. E., & Asiki, G. (2023). Assessing the Readiness to Provide Integrated Management of Cardiovascular Diseases and Type 2 Diabetes in Kenya: Results from a National Survey. Global Heart, 18(1). Doi: 10.5334/gh.1213

6. **Otieno P**, Agyemang C, Wainaina C, Igonya EK, Ouedraogo R, Wambiya EOA, et al. Perceived health system facilitators and barriers to integrated management of hypertension and type 2 diabetes in Kenya: a qualitative study. BMJ Open. 2023;13(8):e074274.

7. **Otieno P**, Agyemang C, Wilunda C, Sanya RE, Iddi S, Wami W, Van Andel J, van der Kloet B, Teerling J, Siteyi A, Asiki G. Effect of Patient Support Groups for Hypertension on Blood Pressure among Patients with and Without Multimorbidity: Findings from a Cohort Study of Patients on a Home-Based Self-Management Program in Kenya. Global Heart. 2023;18(1). Doi: 10.5334/gh.1208

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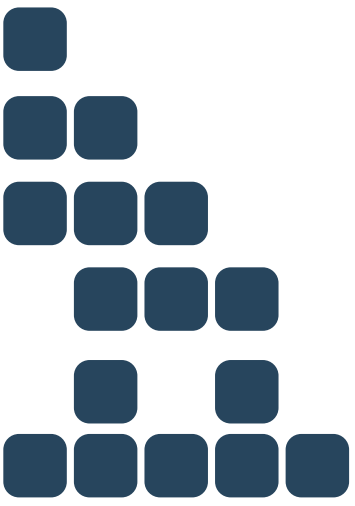
1. Xiong S, Palileo-Villanueva L, Shrestha A, **Otieno P**, Lu H and Yan L. Use of e-health programmes to deliver urban primary health-care services for noncommunicable diseases in middle-income countries. New Delhi: World Health Organization Regional Office for South-East Asia; 2021
2. Ammoun R, Wami WM, **Otieno P**, Schultsz C, Kyobutungi C, Asiki G. Readiness of health facilities to deliver non-communicable diseases services in Kenya: a national cross-sectional survey. BMC Health Services Research. 2022 Dec;22(1):1-1.
3. **Otieno P**, Angeles G, Quiñones S, van Halsema V, Novignon J, Palermo T. Health services availability and readiness moderate cash transfer impacts on health insurance enrolment: evidence from the LEAP 1000 cash transfer program in Ghana. BMC Health Services Research. 2022 May 4;22(1):599.
4. Donfouet, H. P. P., Mohamed, S. F., **Otieno, P.**, Wambiya, E., Mutua, M. K., & Danaei, G. (2020). Economic valuation of setting up a social health enterprise in urban poor-resource setting in Kenya. *Social Science & Medicine*, 113294.
5. **Otieno PO**, Kiroro F, Runyenje C, et al. Unmet need for primary healthcare and associated individual and household-level factors in Kenya: results from a national survey BMJ Open 2021;11:e041032. doi: 10.1136/bmjopen-2020-041032
6. **Otieno, P.O**., Wambiya, E.O.A., Mohamed, S.M. *et al.* Access to primary healthcare services and associated factors in urban slums in Nairobi-Kenya. *BMC Public Health* **20,** 981 (2020). https://doi.org/10.1186/s12889-020-09106-5
7. **Otieno, P. O**., Wambiya, E. O. A., Mohamed, S. F., Donfouet, H. P. P., & Mutua, M. K. (2019). Prevalence and factors associated with health insurance coverage in resource-poor urban settings in Nairobi, Kenya: a cross-sectional study. *BMJ open*, *9*(12).
8. Wambiya, E.O.A., **Otieno, P.O**., Mutua, M.K. *et al.* Patterns and predictors of private and public health care utilization among residents of an informal settlement in Nairobi, Kenya: a cross-sectional study. *BMC Public Health* **21,** 850 (2021). https://doi.org/10.1186/s12889-021-10836-3
9. Kisiangani I, Elmi M, Bakibinga P, Mohamed SF, Kisia L, Kibe PM, **Otieno P**, Afeich N, Nyaga AA, Njoroge N, Noor R. Persistent barriers to the use of maternal, newborn and child health services in Garissa sub-county, Kenya: a qualitative study. BMC Pregnancy and Childbirth. 2020 Dec;20:1-2
10. Wambiya, E., Ochieng', V., **Otieno, P.**, & Ibisomi, L. (2020). Implementation of an exploratory sequential study on acceptability of isoniazid preventive therapy among health care providers in selected HIV clinics in nairobi county, Kenya. *SAGE Research Methods Cases.* doi:10.4135/9781529744095



PhD Portfolio

PhD portfolio

Name PhD student: Peter Otieno
PhD period: June 2020- December 2023
Name PhD supervisors: Prof. Dr C.O. Agyemang and Dr. G. Asiki

Course attended	Year	ECT	Institution/Location
General courses		**3.9**	
Scientific writing in English	2021	1.5	AMC-UvA
Practical Biostatistics	2021	1.1	AMC-UvA
Systematic Reviews	2021	0.7	AMC-UvA
Good Clinical Practice	2021	0.6	Global Health Network
Specific courses		**25.1**	
Randomized Controlled Trials	2021	0.6	AMC-UvA
Clinical Epidemiology: Evaluation of Medical Tests	2021	0.9	AMC-UvA
Observational Epidemiology	2021	0.6	AMC-UvA
Global Chronic Conditions: epidemiology, health systems and policy	2022	1.5	London School of Hygiene and Tropical Medicine
Summer School: Challenges in Global Health: Non-communicable diseases	2023	1.5	University Medical Center Utrecht
2021 Global Alliance for Chronic Diseases (GACD): Implementation Science	2021	1.5	University of Melbourne, Australia
Quantitative Methods and Impact Evaluation	2023	5.0	University of California, Berkeley
Epidemiologic Methods	2023	3.0	University of California, Berkeley
Epidemiological Analysis	2023	3.0	University of California, Berkeley
Statistics for Program Evaluation	2023	3.0	University of California, Berkeley
Data Visualization for Public Health	2023	3.0	University of California, Berkeley
Longitudinal Data Analysis	2023	3.0	University of California, Berkeley
Fellowships		**35.0**	
1 year UNICEF Transfer Project Impact Evaluation Fellowship	2021	15.0	University of North Carolina
3 months Emerging Voices for Global Health Fellowship	2022	8.0	University of Antioquia, Colombia
4 months Center for Effective Global Action (CEGA) Impact evaluation Fellowship	2023	12.0	University of California, Berkeley

PhD portfolio Continued

Course attended	Year	ECT	Institution/Location
International conferences		**0.3**	
Seventh Global Symposium on Health Systems Research (Oral presentation)	2022	0.1	Bogota, Colombia
Africa Evidence Summit	2023	0.1	Nairobi, Kenya
UNICEF Transfer Workshop (Oral presentation)	2023	0.1	Nairobi, Kenya
Mentoring and supervising		**6.0**	
Sofie Eerligh, APHRC MPH intern.	2020	1.5	Amsterdam-UMC
Koeter Maartje, APHRC MPH intern	2020	1.5	Amsterdam-UMC
Quincy Mongare, APHRC MMed intern	2022	1.5	University of Nairobi, Kenya
Abigael Machuka, APHRC MMed intern	2022	1.5	University of Nairobi, Kenya
Peer Review		**0.3**	
Lancet Global Health	2021	0.1	
International Journal of Health Equity	2021	0.1	
Wellcome Open	2023	0.1	
Parameters of Esteem			
Impact evaluation seed grant: USD 10,000	2023		CEGA
Impact evaluation peers training grant: USD 5000	2023		CEGA
Impact evaluation grant; secondary data analysis: USD 5000	2021		UNICEF Transfer Program
Total		**70.6**	

ECTS: European Credit Transfer and Accumulation System: 1 ECTS = 28 hours workload, AMC: Academic Medical Center, APHRC: African Population & Health Research Center, UvA: University of Amsterdam, CEGA: Center for Effective Global Action, UNICEF: The United Nations Children's Fund, MPH: Master of Public Health, Msc: Master of Science. MMed: Masters of Medicine.