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Multimorbidity matters in low and middle-income countries

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Abstract

Multimorbidity is a complex challenge affecting individuals, families, caregivers, and health systems worldwide. The burden of multimorbidity is remarkable in low- and middle-income countries (LMICs) given the many existing challenges in these settings. Investigating multimorbidity in LMICs poses many challenges including the different conditions studied, and the restriction of data sources to relatively few countries, limiting comparability and representativeness. This has led to a paucity of evidence on multimorbidity prevalence and trends, disease clusters, and health outcomes, particularly longitudinal outcomes. In this paper, based on our experience of investigating multimorbidity in LMICs contexts, we discuss how the structure of the health system does not favor addressing multimorbidity, and how this is amplified by social and economic disparities and, more recently, by the COVID-19 pandemic. We argue that generating epidemiologic data around multimorbidity with similar methods and definition is essential to improve comparability, guide clinical decision-making and inform policies, research priorities, and local responses. We call for action on policy to refinance and prioritize primary care and integrated care as the center of multimorbidity.

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Introduction

Multimorbidity is defined as the co-existence of two or more chronic diseases.[1] The topic has been gaining momentum for population health as populations age and the prevalence of physical and mental conditions increases. Most clinical practices and public health responses emphasize a single-disease approach, ignoring that many diseases share common risk factors and manifest jointly. Multimorbidity increases the clinical complexity of cases and the need for polypharmacy, hindering treatment and increasing the likelihood of poor health outcomes.

The multimorbidity challenge for low- and middle-income countries (LMICs) is high. The burden of chronic non-communicable diseases (NCDs)[2,3] in LMICs is already large, due to the rapid urban, nutrition, and epidemiological transitions,[4–9] which are superimposed on fragile health and social protection systems.[10–13] These are further exacerbated by external factors such as the very limited international aid available for combating NCDs,[14–16] the commercial determinants of health,[17,18] and climate change.[19,20] Public health and health systems in LMICs need to swiftly and effectively adapt to accommodate this challenge.[21,22]

Measuring multimorbidity is not simple. A scoping review in LMICs showed multimorbidity prevalence among adults 18 or older ranged from 3.2% to 67.8%.[23] The authors discussed marked differences between studies in defining and measuring multimorbidity and that most evidence in LMICs comes from a few countries: Brazil, China, South Africa, India, Mexico, and Iran.[23] Meta-analytic evidence showed a multimorbidity prevalence of 30% for LMICs and 43% for Latin America and the Caribbean.[24,25] Table 1 provides a summary of selected publications addressing multimorbidity in LMICs highlighting the heterogeneity of prevalence estimates and different methodologies employed. The studies were selected to place emphasis on methodological differences such as age groups, representativeness, number of conditions included, and how diseases were measured.[26–30]

Building upon previous works and first-hand experience with LMIC contexts across all world regions, in this paper, we aim to discuss five characteristics of the uniqueness of the challenge of multimorbidity in LMICs, the methodological limitations of measuring multimorbidity in LMIC, and advance the debate by signaling future directions.

Why does multimorbidity matter for low- and middle-income countries?

Double burden of diseases

Low- and middle-income countries are experiencing a rapid increase in the prevalence of obesity and NCDs, while infectious diseases and undernutrition remain important burdens.[8,31] In 2019, the three leading causes of death in LMICs were non-communicable diseases, that is, cardiovascular disease, neoplasms, and chronic respiratory, followed by communicable diseases: respiratory and enteric infections.[32] This double burden of infectious and non-infectious diseases represents a challenge for population health and health systems in LMICs.[31,33]

The rapid increase in chronic diseases

Comparing to high-income countries, the burden of NCDs in LMICs is not only increasing at a higher pace but also occurring at younger ages.[34] Behavioral risks in LMICs, such as consuming high volumes of ultra-processed foods are increasing across all ages, but more so in adolescents and young adults, increasing the burden of NCDs in these age groups.[35] Early appearance of chronic conditions, paired with poor treatment and care, results in the development of new conditions and complications, thus heavily impacting the mortality risk of LMICs populations. As NCDs are occurring on average at younger ages, multimorbidity also appears sooner, reducing quality of life, life expectancy, and productivity.[36,37]

Health systems are not designed to deal with multimorbidity

Many health systems in LMICs remain fragmented, have limited resources and infrastructure, and remain unable to cope with multimorbidity. Primary care is poorly financed and the health system often fails to timely diagnose and manage chronic disease progression. Systems designed primarily for reactive acute care persist,[38] resulting in a lack of continuity of care for most chronic conditions, perhaps except for some chronic infectious diseases such as HIV.[39] As in high-income countries, health systems are designed to treat individual conditions, resulting in an inefficient model of care that promotes multiple visits to multiple health care providers.[1] These deficiencies discourage patients to seek care and many diseases progress towards disease-related

Table 1. Summary of selected publications addressing multimorbidity in low- and middle-income countries.

	Prevalence, %	Age group	Year	Representativeness	Number and type of diseases considered	How diseases were measured
El Salvador	15.5	18+	2013/14	National	8 diseases: arthritis, asthma, cancer (any type), depression, diabetes, heart disease, hypertension, and high cholesterol)	Self-reported[26]
Panamá	18.3					
Jamaica	25.1					
Brazil	16.8					
Mexico	14.4					
Colombia	12.4					
Argentina	33.1	18+	2014/15	Within-country regional	>9 diseases: diabetes, AMI, stroke, hypertension, asthma, high cholesterol, hypothyroidism, celiac disease and cancer) and other chronic diseases (do not mention which)	Biomarkers, self-reported data (diagnostic or taking medications)[27]
Peru	19.1	35+	2013/14	Within-country regional	12 diseases: alcohol disorder, asthma, chronic bronchitis, COPD, depression, gastroesophageal reflux, heart disease, hypertension, lung cancer, peripheral artery disease, stroke, and diabetes	Biomarkers, self-reported data (diagnostic or taking medications)[28]
China	45.1	50+	2008/10	National	12 diseases: angina, arthritis, asthma, cataract, COPD, depression, diabetes, edentulism, hypertension, cognitive impairment, obesity, and stroke	Self-reported data (diagnosis) or symptom-based algorithms or measurements[29]
Ghana	48.3		2007/08			
India	57.9		2007/08			
Mexico	63.9		2010			
South Africa	63.4		2007/08			
Russia	71.9		2007/10			
Bogotá	40.0	60+	2012	Within-country regional	11 diseases: hypertension, diabetes, cancer, COPD, heart attack, heart failure, stroke, arthritis, osteoporosis, gastroesophageal reflux disease, gastritis, and ulcer	Self-reported[30]

AMI: acute myocardial infarction; COPD: Chronic obstructive pulmonary disease.
All studies use the multimorbidity definition as two or more diseases.

complications. These factors all contribute to premature morbidity and mortality.[40,41]

Evidence shows that health system demands are higher in people with multimorbidity. In Brazil, having more than one disease increased the health services utilization by 46% in men and by 39% in women, and hospitalizations by 55% in men and by 45% in women in comparison with zero or one disease.[42] The higher utilization of health services will require countries to adapt towards ensuring access to high-quality health services and integrated people-centered care for people with multimorbidity. Health services need to be tailored to people's needs and provided in cooperation with them, their families, and communities. Health services need to engage, respect, and support people with multimorbidity, particularly considering the chronicity of many of these conditions and the need for long-term follow-up. The WHO Framework on integrated people-centered health services (IPCHS) was approved in 2016 and calls for a fundamental shift in the way health services are funded, managed, and delivered.[43,44]

Existing clinical practice guidelines (CPG) do little to address the care of individuals with multimorbidity. Clinical practice guidelines are usually developed with a single disease approach, but patients with multimorbidity have different clinical profiles, different clusters of diseases and complex needs, hindering the design of standardized approaches of care. In high-income countries, CPGs have been developed to guide the management of multimorbidity, such as the one proposed by the National Institute for Clinical and Care Excellence,[45] but they are generic documents about the principles of care. Indeed, multiple studies question the ability of current CPGs to guide the care of individuals with complex multimorbidity in HIC, while no evidence from LMICs exists.[46–50] Current CPGs may be inappropriate for LMICs settings and may lead to poor quality of care, failing to address the complexity of therapeutic schemes to manage multimorbidity.

Social disparities in multimorbidity

The contextual effects of multimorbidity are especially evident in LMIC where they reinforce the mechanisms that cause poverty and perpetuate the poverty cycle.[51,52] Individuals in low socio-economic groups frequently have greater exposure to NCD risk factors such as air pollution and poor nutrition, and limited opportunities to engage in preventive efforts including physical activity.[17–20] This is compounded by weak social protection systems, which means individuals are less able to withstand significant health care expenditure, paired with a limited agency to forego income-generating activities and an inability to negotiate time to attend to health care needs.[53,54] For individuals in the lowest socioeconomic strata, the highest burden of multimorbidity is observed at the household level, with financial and non-financial costs transferred to families in the form of out-of-pocket expenditure to cover health services, as well as the invisible non-remunerated and emotional costs of caregiving largely provided by family members.[54–56]

COVID and multimorbidity

The COVID-19 pandemic, in combination with health inequalities and limited access to healthcare systems, is increasing the burden of multimorbidity and decreasing the quality of life of people with multimorbidity in LMICs. On one hand, multimorbidity increases the risk of developing COVID-related complications; on the other hand, the epidemic itself has magnified the problems for preventing and managing multimorbidity.[57–59] The COVID-19 pandemic has been disrupting the existing fragmented health system, adding another layer of burden to the routine management of the multimorbidity. We are observing an increase in underdiagnoses and undertreatment of NCDs, a reduction in the availability of medicines, prescriptions, and routine check-ups in a timely manner,[60] and an increasing burden of mental health problems.[61,62]

Both multimorbidity and COVID-19 are linked to socioeconomic characteristics,[62–64] augmenting the challenges faced in dealing with multimorbidity alone. For example, women with multimorbidity adhered more to social isolation than men,[65] and reducing mobility was estimated to reduce incidences of COVID-19 in Latin America.[66] Taking this observation one step further, in Chile, people living in low-income municipalities adhered less to social isolation and reduced less their mobility than people living in high-income municipalities. As a result, mortality was higher among people in low socioeconomic status.[64] If we were to consider the burden of the treatment framework applied to persons living with multimorbidity,[67,68] additional insights are needed into the multiple failures in protecting the population health.[65,69]

Patients with multimorbidity have a higher risk of COVID-19 complications and death than those without diseases.[57] A study in Mexico showed a higher risk of mortality from COVID-19 in multimorbidity patients, especially among younger adults.[58] Compared to disease-free individuals of the same age group, adults aged 20–39 years with multimorbidity had 8.2 times higher risk of death, and adults aged 40–59 years had 2.8 times higher risk of death. Another study showed that multimorbidity contributed to 28% of hospitalizations and 36% of deaths from COVID-19 in Mexico,[59] suggesting that multimorbidity significantly increases the population susceptibility to the pandemic.

How is multimorbidity measured and why is it imperfect?

Multimorbidity estimations are difficult to compare due to different definitions, different conditions included and different contexts. Multimorbidity is generally defined as the presence of two or more chronic diseases, but controversies around the definition remain.[1] Other definitions include the coexistence of physical and mental health conditions, or three or more diseases affecting different body systems, referred to as "complex multimorbidity."[70–73] The lack of a harmonized definition has created difficulties to compare multimorbidity data across studies and explore its impact.[73] The number and types of conditions included also reduces comparability between studies. For example, studies including intermediate cardiovascular risk factors such as obesity, dyslipidemia, or age-related diseases such as cataracts show a high prevalence of multimorbidity. Finally, the context of multimorbidity studies make comparisons difficult. Prevalence estimates can be lower in population-based studies than in hospital settings, as observed in the study in rural and urban Peruvian sites.[28]

Misclassification of diseases included in multimorbidity remains problematic. Disease determination may differ from study to study and is usually assessed using self-report, medication usage, or biological measurements. Using objective approaches to ascertain multimorbidity in LMICs has the intrinsic trade-off that conditions are objectively assessed. Using self-reported data to ascertain multimorbidity will underestimate its prevalence as a high proportion of chronic diseases are undiagnosed in LMICs. In Mexico, for example, 30% of individuals with diabetes and 40% of those with hypertension are unaware of their diagnosis,[74,75] and rates of unawareness for major chronic conditions in LMICs are generally high.[76,77] The use of prescribed medications is limited due to reporting bias: patients may be unaware of what medications they are taking and they may also be used for more than one indication.[78] Biomarker measurements, while robust, may be expensive and difficult to access in some settings. On a related topic, whilst the study of multimorbidity in high-income countries leverages the availability of electronic medical records,[62] these are not necessarily the norm in LMICs.

Multimorbidity estimations do not account for different combinations of conditions or severity of diseases, being inappropriate to determine the level of care required, a crucial question in LMIC. Some indices, such as the Charlson Index,[79] predict survival in patients with multiple comorbidities, by assigning weighted scores to different conditions that account for disease severity or survival. Multimorbidity indices are relevant to tailor clinical care responses, but having the level of disaggregation of multiple diseases at the population level is challenging. Also, little is known about the performance of these indices in LMIC settings.

Call to action

We have outlined the challenges of multimorbidity on LMICs and the deficiencies in its assessment and reporting. Improvement in multimorbidity-associated outcomes can only be achieved through concerted efforts by researchers, funders, and decision-makers.

Multimorbidity research agenda in low- and middle-income countries

We call for a harmonization of the multimorbidity definition. Multimorbidity evidence will be valuable if it can be harmonized under a common core of conditions that can be adopted by multimorbidity researchers and used by policymakers to inform resource allocation. The research agenda to address multimorbidity in LMICs should be sensitive to existing capacities. Countries with no available data should prioritize resources to generate a country-representative multimorbidity prevalence estimates. In the same way in which LMICs differ from HICs, they also differ from each other, and context-specific data are essential. Countries with available data should progress towards additional multimorbidity-related initiatives, such as estimating the most frequent co-occurring conditions.

Evidence about co-occurring conditions and which combinations most affect health should be generated and aligned with context-specific disease burdens and the the health system capacity to respond. Investigating common disease clusters may assist in understanding underlying pathophysiology and may provide a useful framework to characterize the health and socioeconomic impacts of multimorbidity. Network analysis can be used to evaluate disease combinations and clusters,[80] providing insight into the complex interactions among diseases. Previous studies have documented the prevalence of multimorbidity from cross-sectional studies,[23] but the evidence from longitudinal studies in LMICs is absent.[81] Longitudinal characterization is essential to understand the aggregation of conditions or clusters, and the progression and consequences of multimorbidity.

Multimorbidity evidence employing innovative methods is needed targeting vulnerable groups in LMIC. We call for a focus on contextually relevant analyses, considering the heterogeneity of risk factors and health capacities available to specific subpopulations, such as differences observed in urban and rural environments or specific needs and conditions of indigenous populations. Developing a comprehensive understanding of multimorbidity patterns,

correlates, and outcomes across subpopulations and geographies will require the use of multiple complex data sources including research data from epidemiological studies, national surveys, disease registries, hospital records, administrative data, and also the potential to include data from social media platforms.[82,83] Although the absence of a unique national identifier in many LMICs may limit individual-level data linkages across multiple sources, it may still be possible to link data at an area level and study associations using multilevel methods.[84] Machine learning techniques can also contribute to algorithms that can predict which individuals are more likely to have poorer outcomes.

Political actions

The urgent multimorbidity research agenda in LMICs cannot be pursued in the absence of political will. Multimorbidity is challenging everywhere, and policymakers have a vested interest in tackling multimorbidity given its significant health and economic impacts, affecting patients, families, the health system, and society in general. Potential solutions are only being trialed in HICs with little evidence of its effectiveness. Still, the challenge of multimorbidity in LMICs is exacerbated by the multiple factors highlighted in this article. The burden for LMICs, as countries experience demographic aging overlapped with other societal transitions, results in severe consequences for the population health and health services.

The need to adapt health systems to address multimorbidity in LMICs could be an opportunity to act on remediating historical socioeconomic inequities and the lack of high quality of care.[85–87] On one hand, we need prompt political actions to address the underlying risk factors of multimorbidity, such as food environment and physical activity, targeting children, adolescents, and young adults. On the other hand, we need secondary prevention programs to address the high prevalence of multimorbidity, inadequate control of diseases, along with the consequences and sequelae of COVID-19.[88,89]

Low- and middle-income country-led innovations in prevention and healthcare delivery have the opportunity to advance the frontiers in multimorbidity. The World Economic Forum has emphasized the need and opportunity for "leapfrogging" health systems in LMICs, taking advantage of distinct structural environments and disruptive technologies to move towards sustainable health systems without replicating the path of developed economies.[85,90,91] The current COVID-19 pandemic has, to some extent, accelerated this demand by, for example, calling for building stronger health systems.[88,92]

Despite multimorbidity being increasingly recognized as a public health priority, little progress has been made to develop integrated care models for patients with multimorbidity. From a LMIC perspective, rather than focusing on a one-size-fits-all remedy, one solution may be to focus on particular patterns of multimorbidity, that is, specific combinations of co-occurring conditions,[93] which are different even within countries as shown in the case of Peru's high altitude and sea-level communities.[28]

Focusing on continuous, coordinated, and comprehensive approaches to the care of people with multimorbidity through the health system is increasingly needed. The primary level of care should be refinanced by having family doctors with a comprehensive understanding of each disease and how they interact between them. It is at the primary level that care for people with multiple diseases should be coordinated, and health care systems should prepare themselves.[94] The COVID-19 pandemic has signaled the challenges and limitations of depending on hospital-based healthcare delivery. LMIC-led innovations to address simultaneously multiple chronic physical and mental conditions utilizing existing scarce resources show promising routes to address the integration of care leveraging the use of digital technologies.[95,96] Digital approaches for multimorbidity are, however, still in their early stages.[97]

The WHO Framework IPCHS presents a vision of all people having access to health services, according to their needs and preferences, being safe, effective, timely, affordable, and with acceptable quality. The Framework can be adapted to all countries including LMIC, with mature or fragile health systems.[43,44] In so doing, we contribute to redesigning health systems in LMICs around the people's needs instead of diseases, so that everyone receives the right care, at the right time, and in the right place.[43,44] To implement it, we need to change how health services are organized, managed, and delivered, and multimorbidity offers a unique opportunity to do so in an integrated manner.[43,44]

Closing remarks

In this paper, we have reviewed many challenges in LMICs in dealing with multimorbidity, from inequities to the pressure on health systems in terms of healthcare utilization. We have signaled the unseen challenges in terms of personal and family burdens, alongside the limited capacity of existing health systems to provide high-quality care for all. The current adversities that many LMICs have faced in dealing with COVID-19 are an opportunity to rethink how health systems should be organized to address the challenges of multimorbidity that require integrated care, particularly at the primary care level. This paper calls for action to refinance primary care at the core of a health service model to appropriately tailor integrated care approaches for multimorbidity. In doing so, health systems in LMICs will be better equipped to foster high-quality health systems, with impacts on the physical, emotional, and financial

pressure of dealing with multimorbidity at the household level.

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