# Global Multimorbidity Patterns: A Cross-Sectional, Population-Based, Multi-Country Study 

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#### Abstract

Background. Population ageing challenges health care systems due to the high prevalence and impact of multimorbidity in older adults. However, little is known about how chronic conditions present in certain multimorbidity patterns, which could have great impact on public health at several levels. The aim of our study was to identify and describe multimorbidity patterns in low-, middle-, and high-income countries. Methods. We analyzed data from the Collaborative Research on Ageing in Europe project (Finland, Poland, and Spain) and the World Health Organization's Study on Global Ageing and Adult Health (China, Ghana, India, Mexico, Russia, and South Africa). These cross-sectional studies obtained data from 41,909 noninstitutionalized adults older than 50 years. Exploratory factor analysis was performed to detect multimorbidity patterns. Additional adjusted binary logistic regressions were performed to identify associations between sociodemographic factors and multimorbidity. Results. Overall multimorbidity prevalence was high across countries. Hypertension, cataract, and arthritis were the most prevalent comorbid conditions. Two or three multimorbidity patterns were found per country. Several patterns were identified across several countries: "cardiorespiratory" (angina, asthma, and chronic obstructive pulmonary disease), "metabolic" (diabetes, obesity, and hypertension), and "mentalarticular" (arthritis and depression). Conclusions. A high prevalence of multimorbidity occurs in older adults across countries, with low- and middle-income countries gradually approaching the figures of richer countries. Certain multimorbidity patterns are present in several countries, which suggest that common underlying etiopathogenic factors may play a role. Deeper understanding of these patterns may lead to the development of preventive actions to diminish their prevalence and also give rise to new, comprehensive approaches for the management of these co-occurring conditions.


Key Words: Multimorbidities—Public health—Health disparities—Epidemiology—Morbidity—Socioeconomic issues

Worldwide, the proportion of those aged 60 years or older is projected to almost triple by 2050 (1). This rapid ageing is accompanied by a significant increase in chronic conditions, especially in low- and middle- income countries (LMICs). The World Health Organization declared the rise in chronic conditions a worldwide epidemic, accounting for $63 \%$ of the 57 million global deaths in a report from 2008 (2,3). Multimorbidity, defined as the co-occurrence of at least two chronic conditions, is observed in two thirds of older adults (4), and has been related to poor clinical and financial outcomes (3,5-8). Indeed, multimorbidity is responsible for $65 \%$ of total health care expenditure in high-income countries due to the extensive use of health services (8). The increasing trends in multimorbidity may have considerable financial implications over the next few decades, especially in LMICs $(8,9)$, which face an unfinished agenda of communicable diseases and must now simultaneously address chronic conditions with scarce resources and limited health care systems.

The epidemiology of multiple chronic conditions is poorly understood since the majority of studies have assessed single diseases or comorbid pairs in association with a single index disease $(10,11)$. Thus, efforts to describe the full patterns of co-occurring diseases in the population have recently emerged to provide a complete picture of the distribution of chronic conditions (12). However, variations in methodology and the scarcity of studies, especially in LMICs, show that further research is needed $(12,13)$. Distinct patterns may be observed in LMICs with respect to high-income countries due to differences in population age structures, socioeconomic status, disease burden, and health care systems (9).

To address multimorbidity from a public health perspective, previous studies have underlined the importance of integrating multimorbidity into clinical guidelines, providing self-care management strategies, prioritizing the prevention of chronic conditions and avoiding fragmented care $(10,14,15)$. However, if genuine progress is to be achieved, more evidence on multimorbidity patterns is required. Thus, the current study aims to elucidate the epidemiology of multiple chronic conditions, including correlation patterns in the older population, using nationally representative data from the World Health Organization's (WHO) Study on Global AGEing and Adult Health (SAGE) survey (China, Ghana, India, Mexico, Russia, and South Africa), and the Collaborative Research on Ageing in Europe (COURAGE) survey (Finland, Poland, and Spain).

## Methods

## Study Design and Data Extraction

We analyzed data from the COURAGE and SAGE studies. Nationally representative samples were generated by multistage clustered sampling (Table 1). At the time of the survey, countries included in the COURAGE and SAGE surveys corresponded to high-, and low/middle-income countries respectively, according to the World Bank Classification (16). The sample included noninstitutionalized adults aged 18 years or older, with oversampling of adults 50 years or older as they were the principal target of the study. Briefly, the two projects followed the same protocol and used equivalent standardized questionnaires to gather information on health and well-being. The survey protocol was translated from English into participating countries’ languages following WHO guidelines for translation and adaptation of instruments
(17). Face-to-face structured interviews were conducted by trained interviewers at respondents' homes. In cases where the interviewer judged that the respondent was not capable of answering the questions due to severe cognitive problems, a short version of the survey was administered to proxy respondents. Blood pressure, weight, and height measurements were collected by the interviewer using standard protocols. Sampling weights were generated to adjust for the population structure reported by the United Nations Statistical Division for the SAGE study and the National Institutes of Statistics for the COURAGE study. Ethical approval was obtained from local research review boards and the WHO Ethical Review Committee. Informed consent was obtained from all participants.

## Variables

We selected 12 chronic conditions with high prevalence in most settings that affect significantly on health (angina, arthritis, asthma, cataract, chronic obstructive pulmonary disease [COPD], depression, diabetes, edentulism, hypertension, cognitive impairment, obesity, and stroke). To assess conditions, a combined method was used consisting of self-reported physician's diagnosis and/or symp-tom-based algorithms or measurements (Supplementary Appendix). Questions on specific symptoms were used to detect undiagnosed cases. Multimorbidity was defined as having at least 2 of the 12 chronic conditions (4). Sociodemographic data on age, gender, marital status, education level, urbanicity, and household income (wealth quintiles were generated based on country-specific income) were also collected.

## Statistical Analyses

Unweighted frequencies, weighted proportions, means, standard deviations, cross tabulations, and graphical displays were used for descriptive analysis. Multimorbidity patterns were analyzed through exploratory factor analysis. This statistical technique reveals the factors that summarize the correlation between a series of variables, providing information on the underlying structure of the data. A tetrachoric correlation matrix was used due to the binary nature of the variables, assuming that diseases have a progressive course until they reach a certain threshold (diagnosis). A combined approach (parallel analysis and scree test) was used to extract the number of factors as recommended (Supplementary Appendix). The Kaiser-Meyer-Olkin method was used to estimate the adequacy of the sample, while cumulative variance was calculated to demonstrate the variance explained by each selected factor. Oblique rotation was performed to provide easier interpretation of the factor analysis. Multivariable logistic regressions were used to examine the relationship between sociodemographic variables and multimorbidity, while adjusting for age, gender, education, marital status, urbanicity, and wealth. Results are reported as adjusted odds ratios with $95 \% \mathrm{CI}$. The regression analyses took into account the sampling weights and the complex sampling design. Rates of missing values were low overall. More than $10 \%$ of data were missing for only three variables: obesity (Mexico $11.9 \%$; Russia $11.2 \%$ ), education (South Africa $15.7 \%$ ), and wealth (Spain 20.7\%). We analyzed data with Stata version 12.1 (Stata Corp LP, College Station, TX). Those who participated in the survey through a proxy respondent were excluded as most data pertaining to the current analysis were not collected. The level of statistical significance was set at $p<.05$.
Table 1. Details of the SAGE and COURAGE Surveys

| Country | Survey | Sampling Characteristics* | Field Dates | Age ${ }^{\dagger}$ (years) | Response Rate ${ }^{\ddagger}$ (\%) | Sample <br> Size | Sample 50+ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| China | SAGE | Stratified, multistage cluster sampling design, stratified by eight provinces. NR. | 2008-2010 | $18+$ | 93 | 14,794 | 13,157 |
| Finland | COURAGE | Stratified, multistage cluster sampling design. Strata were based on the largest towns and university hospital regions and smaller health center districts. NR. | 2011-2012 | 18+ | 53 | 1,934 | 1,452 |
| Ghana | SAGE | Stratified multistage cluster sampling design, stratified by administrative region and locality (urban/rural). NR. | 2007-2008 | 18+ | 80 | 5,108 | 4,305 |
| India | SAGE | Stratified multistage cluster sampling design, from 19 of the 28 states and 7 union territories. NR. | 2007-2008 | 18+ | 68 | 11,230 | 6,560 |
| Mexico | SAGE | Stratified, multistage cluster sampling design. Strata were defined by locality (metropolitan, urban, rural). NR. | 2010 | 18+ | 51 | 2,733 | 2,301 |
| Poland | COURAGE | Stratified, multistage cluster sampling design, stratified by 16 administrative regions and by 4 categories of size of habitat. NR. | 2011-2012 | 18+ | 67 | 3,940 | 2,910 |
| Russia | SAGE | Stratified, multistage cluster sampling design, stratified by seven federal districts. NR. | 2007-2010 | 18+ | 83 | 4,152 | 3,763 |
| South Africa | SAGE | Stratified, multistage cluster sampling design, stratified by provinces, locality (urban/rural) and race. NR. | 2007-2008 | 18+ | 77 | 4,221 | 3,836 |
| Spain | COURAGE | Stratified, multistage cluster sampling design, stratified by 17 communities and by 4 categories of size of habitat. NR. | 2011-2012 | 18+ | 70 | 4,583 | 3,625 |
| Total |  |  |  |  |  | 52,695 | 41,909 |

Notes: COURAGE = Collaborative Research on Ageing in Europe; NR = nationally representative; SAGE = Study on Global AGEing and Adult Health. *Studies followed a stratified, multistage cluster sampling design methodology with distinct strata used according to country characteristics
${ }^{\dagger}$ The populations aged above 50 and 80 years were oversampled as they were the principle target of the study.
 lack of fluency in the language used for the interview, individuals who were not accessible (eg, institutionalized, imprisoned, hospitalized, or those with severe mental disorder).

## Role of the Funding Source

There was no external funding source for this study. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

## Results

We analyzed data from 41,909 individuals aged 50 years or older (Table 1). The mean age ranged from 61.5 (India) to 66.3 years (Spain) (Table 2). India, Russia, and South Africa had extremely high prevalence of cataract ( $47.4 \%$ ), angina ( $37.3 \%$ ), and obesity $(46.9 \%)$ respectively. Russia had the highest prevalence of multimorbidity $(71.9 \%)$, whereas China ( $45.1 \%$ ) and Ghana ( $48.3 \%$ ) had the lowest (Table 2). Overall, multimorbidity increased with age although the rate of increase in the oldest age groups was modest at best in most countries with declines observed in some countries. South Africa showed a unique pattern with a gradual decrease in multimorbidity among those aged 60 years or older (Figure 1; figures for males and females are provided in the Supplementary Appendix).

The multivariable analysis showed significantly higher odds for multimorbidity for the following factors: higher age (except South Africa); female (except Finland, Poland, and Spain), lower education (except China, Ghana, and Mexico); separated/divorced/widowed in Ghana, India, South Africa, and Spain; and rural inhabitance in China, Ghana, and South Africa (Table 3). Mixed results were observed for wealth with opposing trends observed between some countries.

The prevalence of comorbidity in people with each chronic condition, based on the pooled sample, is illustrated in Figure 2. The patterns observed in individual countries were similar to that of the overall sample and are shown in the Supplementary Appendix. The most prevalent comorbid condition was hypertension, especially among those with obesity, stroke, diabetes, and angina. Arthritis and cataract were also common comorbid conditions.

The exploratory factor analysis revealed two or three relevant multimorbidity patterns per country (Supplementary Appendix). Several multimorbidity patterns were identified across countries (Table 4). First, a "cardio-respiratory" pattern, including angina, asthma, and COPD, was present in most countries except Finland and Russia, explaining the largest proportion of the variance in all countries. Other conditions in this pattern for some countries were stroke, depression, arthritis, and cataract. Secondly, a "metabolic" pattern was present in all countries except Mexico. This pattern included diabetes, obesity, and hypertension, in addition to other specific conditions depending on the country. A "mental-articular" pattern was observed in China, Ghana, and India and a "respiratory" pattern in Finland and Russia. Finally, single separate patterns in Finland and Mexico, including cardiovascular disorders, were also detected but could not be categorized into any of the previous groups.

## Discussion

To the best of our knowledge, this is the first cross-national, multicontinent study on multimorbidity patterns. We found a high prevalence of multimorbidity across all participating countries. Several multimorbidity patterns of chronic diseases emerged and were similar across countries. The main strengths of our study are the large
sample size and the use of nationally representative datasets from diverse settings. Also, our diagnostic definition incorporating symptoms or blood pressure measurement is likely to have reduced underdiagnosis especially in resource-limited settings.

Russia, Spain, Poland, and Finland accounted for the highest multimorbidity burden for similar age groups. The high prevalence of multimorbidity observed in high-income countries has been associated with increased level of development. Lower cardiovascular mortality and/or case fatality rates due to better medical management may, for example, allow people with multimorbidity to live longer (3). The already high prevalence of multimorbidity in LMICs may eventually become similar to that in developed countries due to the rapid increase in risk factors such as unplanned urbanization, ageing trends, unhealthy dietary patterns, sedentary lifestyles, globalization of product marketing (tobacco, alcohol, unhealthy food, etc.), and availability of better health care (3). In Russia, the country with the highest prevalence of stroke and angina in our study, cardiovascular mortality remains strikingly high and is the cause of $57 \%$ of all deaths, whereas this rate has decreased over time in other European countries (18). Certain risk factors, such as the high rate of alcohol consumption, and rapid societal changes may have resulted in an markedly increased risk of morbidity and mortality from circulatory diseases in Russia $(18,19)$. In the systematic review by Marengoni and coworkers, which included data from 41 articles, the prevalence of multimorbidity in older adults ranged from $55 \%$ to $98 \%$ (4). This prevalence is similar to the figures obtained in our study ( $45.1 \%-71.9 \%$ ).

Multimorbidity prevalence generally increased with age with the exception of South Africa where a gradual decrease after 60 years was observed. The unique age-related trend in South Africa is concordant with previous data (20) and may be associated with the prevalence of HIV, which is a risk factor for noncommunicable diseases, across age groups (9). In rural areas of South Africa in 2008, the prevalence of HIV was reported to be $17.3 \%$ (women) and $29.5 \%$ (men) in those aged $50-55$ years, falling to $1.4 \%$ in those aged 75 years or older (21). Furthermore, women had a higher risk of multimorbidity except in Finland, Poland, and Spain, which suggests that social, biological, or physical gender differences may underlie the higher prevalence of multimorbidity in LMICs. Lower educational level was associated with higher odds for multimorbidity in all countries except China, Ghana, and Mexico. As highlighted in previous studies (22), education may have an important role in the development of preventive measures for multimorbidity. China was the only country where a higher level of wealth but not education was associated with lower odds for multimorbidity. In this setting, it may be that wealth has a more direct impact on multimorbidity than education because of the lack of universal health coverage, where the wealthiest are more likely to have better access to health care (23). In Ghana and South Africa, the directionality was the opposite in terms of income, where higher income was associated with higher rates of multimorbidity. Averett and colleagues highlighted the association between rising income and increasing high-calorie foods intake in Africa, leading to higher rates of obesity and metabolic conditions (24). In addition, Barnett and colleagues found a strong association between socioeconomic deprivation and multimorbidity in Scotland (13). This may be the case for Spain, where we found a similar gradient with lower rates of multimorbidity in the wealthiest group. We hypothesize that this result may also be applicable to other European countries since the results in Finland and Poland were of a similar pattern with borderline statistical significance. Furthermore, marital
Table 2. Main Characteristics of the Sample

| Characteristic | Category | China | Finland | Ghana | India | Mexico | Poland | Russia | South Africa | Spain |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Age (years) | Mean (SD) | 62.57 (16.67) | 64.98 (12.26) | 64.37 (19.86) | 61.48 (13.66) | 63.04 (18.94) | 64.18 (13.07) | 63.91 (15.44) | 61.61 (18.42) | 66.26 (14.78) |
| Sex | Female | 6,990 (50.25) | 834 (53.97) | 2,056 (47.55) | 3,256 (49.01) | 1,393 (53.19) | 1,765 (56.50) | 2,432 (61.12) | 2,201 (55.95) | 1,982 (53.65) |
| Education | $\geq$ Tertiary | 595 (4.50) | 407 (25.88) | 151 (3.61) | 325 (5.14) | 181 (8.10) | 420 (15.72) | 727 (18.25) | 162 (5.72) | 393 (10.81) |
|  | Secondary | 4,282 (32.47) | 787 (56.91) | 878 (21.11) | 1,195 (18.77) | 193 (12.30) | 1,579 (59.27) | 2,620 (74.21) | 657 (22.84) | 949 (25.61) |
|  | $\leq$ Primary | 8,280 (63.03) | 255 (17.21) | 3,250 (75.28) | 5,040 (76.09) | 1,825 (79.60) | 911 (25.01) | 413 (7.54) | 2,416 (71.43) | 2,282 (63.59) |
| Marital status | Married/cohabiting | 10,898 (85.04) | 921 (59.32) | 2,434 (64.70) | 4,862 (76.93) | 1,341 (73.00) | 1,650 (68.12) | 2,106 (58.34) | 2,004 (55.90) | 2,258 (62.43) |
|  | Never married | 131 (1.13) | 118 (1.27) | 50 (8.50) | 64 (0.73) | 185 (7.01) | 266 (7.87) | 106 (2.69) | 512 (14.30) | 310 (8.47) |
|  | Divorced* | 2,118 (13.83) | 412 (39.41) | 1,798 (26.80) | 1,634 (22.34) | 673 (19.98) | 994 (24.00) | 1,541 (38.97) | 1,249 (29.80) | 1,057 (29.10) |
| Location | Urban | 6,419 (47.34) | 1,112 (75.77) | 1,761 (41.09) | 1,676 (28.91) | 1,676 (78.79) | 1,663 (68.98) | 2,851 (72.74) | 2,559 (64.86) | 3,138 (83.85) |
| Chronic conditions | Angina | 1,323 (9.37) | 179 (11.82) | 554 (12.75) | 1,060 (16.98) | 145 (6.72) | 598 (19.17) | 1,417 (37.29) | 333 (8.91) | 287 (7.88) |
|  | Arthritis | 3,432 (26.73) | 721 (48.79) | 1,122 (26.16) | 1,799 (27.89) | 421 (14.48) | 1,047 (35.51) | 1,580 (38.24) | 1,079 (30.60) | 1,203 (32.74) |
|  | Asthma | 655 (4.27) | 182 (12.62) | 222 (4.97) | 807 (12.52) | 140 (4.94) | 325 (9.79) | 287 (6.54) | 252 (7.71) | 375 (10.32) |
|  | Cataract | 2,124 (14.21) | 295 (18.99) | 778 (18.07) | 3,055 (47.35) | 579 (25.76) | 568 (17.53) | 930 (20.27) | 253 (6.38) | 872 (24.10) |
|  | COPD | 1,152 (8.23) | 62 (4.49) | 56 (1.21) | 477 (8.03) | 158 (4.45) | 291 (8.99) | 690 (15.11) | 134 (4.26) | 319 (8.83) |
|  | Cognitive impairment | 1,539 (11.75) | 133 (10.76) | 511(12.58) | 795 (12.52) | 302 (9.51) | 366 (11.48) | 496 (17.52) | 465 (11.29) | 483 (12.45) |
|  | Depression | 171 (1.28) | 219 (15.42) | 342 (7.98) | 969 (15.95) | 361 (16.89) | 417 (13.50) | 280 (5.63) | 185 (4.79) | 956 (26.43) |
|  | Diabetes | 843 (6.60) | 185 (12.89) | 167 (3.80) | 478 (6.91) | 446 (17.62) | 441 (13.56) | 319 (7.01) | 359 (9.20) | 598 (16.29) |
|  | Edentulism | 1,410 (9.10) | 257 (17.07) | 120 (2.96) | 932 (15.14) | 547 (21.66) | 879 (26.10) | 694 (18.07) | 368 (8.45) | 677 (18.55) |
|  | Hypertension | 7,760 (60.63) | 958 (66.35) | 2,518 (59.64) | 2,601 (37.51) | 1,519 (61.87) | 1,962 (67.59) | 2,674 (72.06) | 2,917 (78.29) | 2,223 (63.00) |
|  | Obesity | 684 (5.84) | 367 (27.01) | 393 (9.98) | 189 (2.51) | 654 (28.67) | 940 (35.36) | 1,133 (34.46) | 1,505 (46.90) | 1,115 (31.96) |
|  | Stroke | 526 (3.64) | 71 (4.99) | 165 (3.75) | 258 (3.71) | 149 (5.59) | 178 (5.78) | 267 (6.44) | 177 (4.94) | 158 (5.31) |
| Multimorbidity | $\geq 2$ conditions | 6,115 (45.07) | 1,005 (68.25) | 2,050 (48.30) | 3,799 (57.92) | 1,581 (63.89) | 2,041 (69.39) | 2,779 (71.93) | 2,376 (63.44) | 2,478 (68.73) |

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Figure 1. Multimorbidity prevalence across age groups. Prevalence calculation was based on weighted sample. Multimorbidity defined as having at least two of the following conditions: angina, arthritis, asthma, cataract, COPD, depression, diabetes, edentulism, hypertension, cognitive impairment, obesity, and stroke.
status and urbanicity showed mixed results across countries. Further studies are needed to understand these between-country differences. Our results suggest that country-specific strategies may be necessary to address multimorbidity.

The conditions that most frequently coexisted with others were hypertension, arthritis, and cataract. For example, hypertension was present in $79 \%$ and $71 \%$ of stroke and angina patients respectively in the overall sample. Similar trends were observed in the countrywise analyses. It is noticeable that in Russia, these comorbidities reached $95 \%$ and $88 \%$ respectively, which highlights the burden of cardiovascular diseases in this country. Apart from hypertension, conditions such as arthritis and cataract also often coexisted with other conditions. In particular, the coexistence of depression and cataract deserves special attention as $52 \%$ of the depressed had co-occurring cataract, reaching $67 \%$ in India, the country with the highest prevalence of cataract. This highlights the potential relevance of studies on mood disorders in the context of visual impairment, especially in India.

We classified and named the patterns according to their characteristics. In line with the recent systematic review by PradosTorres and colleagues, most of the patterns included were not identical but clear trends allowed for the identification of several distinct patterns (12). First of all, the "cardio-respiratory" pattern underlined the association among angina, asthma, and COPD. An association between respiratory diseases and coronary heart disease was previously described in clinical settings (25). This association may involve inflammation, hypoxia, oxidative stress, or ageing. The pro-inflammatory systemic state presents in patients with COPD and asthma may exacerbate the inflammatory pathway leading to atherosclerosis. This correlation led to further studies being performed to assess the effect of inhaled corticoids on cardiovascular outcomes among COPD patients but contradictory results have been found (26-28). Because this pattern is widespread across countries, regardless of the region or the income level, it may be suggested that this is part of the natural biological and pathologic course of these illnesses and is related to general risk factors such as smoking or pollution. Other studies on multimorbidity have also found multimorbidity patterns with car-dio-respiratory variables, in line with our findings. For example,

Sinnige and colleagues, Prados-Torres and colleagues, PobladorPlou and colleagues, and Newcomer and colleagues found patterns that included a wide range of cardio-respiratory conditions in Spain, the Netherlands, and the United States, although they did not characterize those patterns as "cardio-respiratory" (29-32). Secondly, the "metabolic" pattern consisted of diabetes, obesity, and hypertension and was found in eight of the nine countries. The association between metabolic syndrome and negative cardiovascular outcomes or mortality has been documented extensively (33). The presence of related conditions such as angina, stroke, cataract, and edentulism in some countries confirms the robustness of this pattern. It should be highlighted that in the systematic review by Prados-Torres and colleagues, metabolic diseases had a dominant role in multiple multimorbidity patterns, in accordance with our results (12). Moreover, as in our case, some of the studies in the review also included additional diseases in those patterns ( $31,32,34$ ). Finally, the "mental-articular" pattern including arthritis and depression was found only in China, Ghana, and India. This result is in line with previous studies such as that from the World Mental Health surveys, which found that mood disorders and other mental disorders were associated with arthritis in 17 countries (35). Furthermore, several studies on multimorbidity patterns have also found patterns with mental-articular conditions ( $30-32,36-38$ ). A study from Spain which included anxiety disorders in the analysis also showed a clear "mental-articular" pattern (39). It is possible that this pattern could have emerged in more countries if anxiety and other mental disorder diagnoses had been available. The underlying cause of this association remains unclear but previous studies have suggested that the psychological burden of arthritis may lead to the onset of psychiatric disorders (35). Alternatively, other mechanisms such as the inflammatory pathway may also be involved.

Health care models need to adapt to increasing multimorbidity rates. This is especially relevant in LMICs, where all levels of care must be carefully planned in the context of economic restraints. The Innovative Care for Chronic Conditions framework developed by the World Health Organization provides a roadmap to cope with chronic conditions in developing countries but there still is need to fully incorporate multimorbidity according to recent recommended modifications (9). From a biological perspective, the need to study the interaction of diseases has been highlighted as a first step to a better understanding of health care population needs. From the patients' perspective, burden (managing self-care, behavior changes, treatment modalities, and clinic visits) and capacity to cope with this burden are fundamental issues when addressing multimorbidity (9). Minimally disruptive health care should be provided with integrated generalist care that prevents fragmentation, aiming to improve capacity, care, and reduce the workload of medical personnel. From the community perspective, activities such as adherence clubs and monitoring systems have also been recommended. The goal would be a care continuum with prevention of chronic conditions as one of the pillars of that care.

Our study has several limitations. Multimorbidity studies would benefit from standardized conceptualization and inclusion of conditions $(4,39)$. For example, a higher number of included conditions would logically result in a higher prevalence of multimorbidity. Thus, studies using different approaches regarding the inclusion of diseases are limited in terms of comparability. The SAGE and COURAGE studies selected a limited number of conditions based on their high prevalence and impact on health outcomes with a methodology that allowed cross-national
Table 3. Correlates of Multimorbidity Estimated by Multivariable Logistic Regression

| Characteristic | Category | China | Finland | Ghana | India | Mexico | Poland | Russia | South Africa | Spain |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Age (years) | 50-59 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
|  | 60-69 | 2.06 (1.86-2.28) | 1.76 (1.31-2.36) | 1.4 (1.16-1.68) | 1.49 (1.27-1.75) | 2.47 (1.57-3.89) | 2.15 (1.65-2.80) | 1.78 (1.08-2.94) | 1.46 (1.11-1.93) | 1.82 (1.43-2.31) |
|  | 70-79 | 3.34 (2.94-3.79) | 2.71 (1.91-3.86) | 1.67 (1.37-2.03) | 2.45 (1.78-3.38) | 3.06 (1.89-4.98) | 5.82 (3.85-8.78) | 5.25 (3.44-8.00) | 1.21 (0.84-1.76) | 3.47 (2.56-4.70) |
|  | $\geq 80$ | 3.38 (2.76-4.14) | 5.61 (3.22-9.77) | 1.88 (1.44-2.46) | 2.32 (1.54-3.51) | 3.57 (1.89-6.72) | 2.99 (1.85-4.83) | 8.73 (4.42-17.23) | 0.75 (0.45-1.25) | 4.88 (3.09-7.72) |
| Gender | Male | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 |
|  | Female | 1.46 (1.35-1.56) | 1.16 (0.90-1.50) | 1.48 (1.25-1.76) | 1.42 (1.23-1.64) | 4.5 (2.43-8.34) | 0.89 (0.68-1.17) | 1.57 (1.01-2.44) | 1.59 (1.24-2.03) | 1.15 (0.91-1.45 |
| Education | $\geq$ Tertiary | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
|  | Secondary | 1.08 (0.88-1.34) | 1.22 (0.99-1.50) | 1.21 (0.79-1.85) | 1.73 (1.14-2.63) | 0.96 (0.31-2.93) | 1.46 (1.06-2.02) | 2.06 (1.39-3.06) | 1.82 (1.01-3.25) | 1.72 (1.12-2.62) |
|  | $\geq$ Primary | 1.20 (0.95-1.53) | 1.68 (1.09-2.60) | 0.99 (0.64-1.51) | 1.97 (1.33-2.91) | 1.41 (0.55-3.61) | 2.96 (1.97-4.44) | 2.89 (1.52-5.49) | 1.66 (0.89-3.11) | 2.32 (1.69-3.19) |
| Wealth quintile | 1 (poorest) | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 |
|  | 2 | 0.99 (0.86-1.15) | 1.21 (0.79-1.85) | 1.31 (1.02-1.69) | 1.07 (0.83-1.39) | 0.66 (0.32-1.37) | 1.12 (0.77-1.62) | 1.38 (0.90-2.13) | 1.12 (0.74-1.69) | 1.37 (1.01-1.85) |
|  | 3 | 0.94 (0.81-1.09) | 0.99 (0.66-1.49) | 1.39 (1.07-1.80) | 0.98 (0.78-1.23) | 1.12 (0.51-2.47) | 0.65 (0.44-0.96) | 1.13 (0.68-1.90) | 1.32 (0.87-2.02) | 0.94 (0.68-1.31) |
|  | 4 | 0.89 (0.75-1.05) | 0.74 (0.49-1.12) | 1.47 (1.12-1.93) | 1.01 (0.79-1.29) | 0.79 (0.41-1.50) | 0.65 (0.44-0.94) | 1.70 (0.87-3.31) | 1.66 (1.06-2.60) | 0.83 (0.63-1.10) |
|  | 5 (wealthiest) | 0.75 (0.64-0.89) | 0.71 (0.44-1.13) | 1.83 (1.36-2.47) | 1.06 (0.84-1.35) | 0.79 (0.35-1.75) | 0.67 (0.44-1.03) | 1.20 (0.62-2.35) | 1.89 (1.14-3.13) | 0.63 (0.45-0.89) |
| Marital status | Married/cohabiting | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 | 1,00 |
|  | Never married | 1.12 (0.61-2.03) | 1.32 (0.81-2.15) | 0.63 (0.32-1.23) | 1.33 (0.66-2.66) | 0.26 (0.09-0.73) | 1.19 (0.80-1.76) | 0.74 (0.35-1.56) | 1.22 (0.84-1.76) | 0.88 (0.58-1.35) |
|  | Divorced* | 1.01 (0.88-1.16) | 1.15 (0.74-1.81) | 1.35 (1.14-1.61) | 1.26 (1.00-1.59) | 0.67 (0.39-1.15) | 1.13 (0.81-1.58) | 1.03 (0.69-1.55) | 1.43 (1.08-1.91) | 1.38 (1.11-1.71) |
| Location | Rural | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
|  | Urban | 1.17 (1.00-1.36) | 0.93 (0.69-1.24) | 1.29 (1.05-1.58) | 1.01 (0.79-1.29) | 1.16 (0.68-1.98) | 1.18 (0.93-1.49) | 0.9 (0.57-1.41) | 1.46 (1.10-1.93) | 1.02 (0.75-1.40) |

[^1]

Figure 2. Comorbidity prevalence using overall pooled data. For country-wise information see Supplementary Appendix. To interpret the graph, choose one condition in the left column and then from the total patients with this condition check the percentage of those who have one of the co-occurring conditions from the list below.

Table 4. Multimorbidity Patterns in the SAGE and COURAGE Countries

| Pattern | Number of Countries | Countries | Conditions |
| :---: | :---: | :---: | :---: |
| Cardiorespiratory | 7 | China, Ghana, India, Mexico, Poland, South Africa, Spain | Angina, asthma, COPD, stroke ${ }^{\mathrm{G}, \mathrm{M}, \mathrm{P}, \mathrm{SA}}$, depression ${ }^{\mathrm{C}, \mathrm{I}, \mathrm{M}, \mathrm{P}, \mathrm{SA}, \mathrm{S}}$, arthritis ${ }^{\mathrm{C}, \mathrm{M}, \mathrm{P}, \mathrm{SA}, \mathrm{S}}$, cataract ${ }^{\mathrm{C}, \mathrm{M}, \mathrm{P}}$ |
| Metabolic | 8 | China, Finland, Ghana, India, Poland, Russia, South Africa, Spain | Diabetes, obesity, hypertension, angina ${ }^{\text {C,F,P,R,SA,S }}$, stroke ${ }^{\mathrm{C}, \mathrm{G}, \mathrm{R}, \mathrm{SA}, \mathrm{S}}$, cataract ${ }^{\mathrm{C}, \mathrm{R}, \mathrm{SA}, \mathrm{S}}$, arthritis ${ }^{\mathrm{P}, \mathrm{R}, \mathrm{SA}, \mathrm{S}}$, edentulism ${ }^{\mathrm{R}, \mathrm{SA}, \mathrm{S}}$, depression ${ }^{\mathrm{R}}$ |
| Mentalarticular | 3 | China, Ghana, India | Arthritis, depression, stroke ${ }^{\mathrm{C}}$, cataract ${ }^{\mathrm{C}, \mathrm{I}}$, angina ${ }^{1}$ |
| Respiratory | 2 | Finland, Russia | Asthma, COPD, cataract ${ }^{R}$ |
| Other | 1 | Finland | Angina, cataract, diabetes, edentulism, hypertension, stroke |
| Other | 1 | Mexico | Cataract, diabetes, stroke |

Notes: Each pattern includes those conditions characteristics, in bold, present in all countries with the pattern. For conditions that were only present in a specific pattern for some countries, superscript was used. Superscript: C = China; $\mathrm{F}=$ Finland; $\mathrm{G}=$ Ghana; $\mathrm{I}=$ India; $\mathrm{M}=$ Mexico; $\mathrm{P}=$ Poland; $\mathrm{R}=$ Russia; SA = South Africa; S = Spain. COURAGE Collaborative Research on Ageing in Europe; SAGE Study on Global AGEing and Adult Health.
comparisons. We included 9 of the top 10 conditions used in previous studies on multimorbidity patterns with the exception of malignancies (12), for which we had no data. Future studies
would benefit from the inclusion of other conditions such as anemia, malignancies, or renal diseases (12). Furthermore, we had no information on HIV infection which is now considered a chronic condition following the advent of antiretroviral therapy (9). The inclusion of this condition would probably have resulted in higher rates of multimorbidity in areas with high HIV prevalence such as South Africa. Next, although self-reporting of diseases has been shown to demonstrate good agreement with medical records in developed countries, in settings with limited access to health care systems, underreporting of diagnosis may be a problem. In the latter settings, individuals may be less aware of their illness or may only have them detected when they are severe. Consequently, we used a symptom-based algorithm for some conditions in addition to the self-reported medical diagnoses. This may have led to higher sensitivity at the expense of lower specificity. However, the algorithms used were validated or in line with current guidelines and some biomarkers (blood pressure, weight, and height) were also assessed with appropriate devices. Thus, we believe that the use of the algorithms was necessary and justifiable to address our study question. Finally, further studies are needed to explore the impact of polypharmacy and patients' degree of control over each condition, for which we had no information, on the multimorbidity patterns.

## Conclusions

Multimorbidity has become one of the greatest challenges for health care systems. Poor clinical outcomes, including high mortality and disability rates, are strongly associated with multimorbidity. The relationship between multiple chronic conditions and health costs is almost exponential, due to excessive use and fragmentation of care. Access to treatment, polypharmacy, poor self-management, lifestyle changes, and patients' ability to cope with this burden are the issues that should be considered when developing health care policies. The importance of implementing guidelines that consider multiple co-occurring chronic conditions rather than focusing on single diseases has also been highlighted.

Understanding the interactions between chronic diseases is a crucial first step toward a more realistic and comprehensive approach to guiding policy and establishing new clinical guidelines. Some of the multimorbidity patterns are common across countries, probably due to shared underlying biological processes or risk factors. Better understanding of these issues may facilitate the implementation of general approaches in diverse settings and the study of these interactions in the future.

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[^0]:    Notes: Data are $n(\%)$ unless otherwise stated. Unweighted frequencies, weighted means, and proportions are displayed. COPD = chronic obstructive pulmonary disease.
    *Divorced includes separated/widowed.

[^1]:    Notes: Data are odds ratios ( $95 \%$ confidence interval) adjusted for all covariates in the model.

