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Multimorbidity of non-communicable diseases in low-income and middle-income countries: a systematic review and meta-analysis

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ABSTRACT

Introduction Multimorbidity is a major public health challenge, with a rising prevalence in low/middle-income countries (LMICs). This review aims to systematically synthesise evidence on the prevalence, patterns and factors associated with multimorbidity of non-communicable diseases (NCDs) among adults residing in LMICs.

Methods We conducted a systematic review and meta-analysis of articles reporting prevalence, determinants, patterns of multimorbidity of NCDs among adults aged >18 years in LMICs. For the PROSPERO registered review, we searched PubMed, EMBASE and Cochrane libraries for articles published from 2009 till 30 May 2020. Studies were included if they reported original research on multimorbidity of NCDs among adults in LMICs.

Results The systematic search yielded 3272 articles; 39 articles were included, with a total of 1 220 309 participants. Most studies used self-reported data from health surveys. There was a large variation in the prevalence of multimorbidity; 0.7%–81.3% with a pooled prevalence of 36.4% (95% CI 32.2% to 40.6%). Prevalence of multimorbidity increased with age, and random effect meta-analyses showed that female sex, OR (95% CI): 1.48, 1.33 to 1.64, being well-off, 1.35 (1.02 to 1.80), and urban residence, 1.10 (1.01 to 1.20), respectively were associated with higher odds of NCD multimorbidity. The most common multimorbidity patterns included cardiometabolic and cardiorespiratory conditions.

Conclusion Multimorbidity of NCDs is an important problem in LMICs with higher prevalence among the aged, women, people who are well-off and urban dwellers. There is the need for longitudinal data to access the true direction of multimorbidity and its determinants, establish causation and identify how trends and patterns change over time.

PROSPERO registration number CRD42019133453.

Strengths and limitations of this study

- Inclusion of most studies (14/36 articles) from the WHO Study on global AGEing and adult health (SAGE) ensured standardisation of methods of measurements and data collection.
- The included studies had large sample sizes, which ensured adequate statistical power to detect even a small effect of interest.
- Recall and self-declaration bias due to self-reported outcome may result in under/over estimation of the true prevalence of multimorbidity.
- Assessment of the determinants of multimorbidity did not take the heterogeneity and clusters of conditions into consideration.
- Involving patients with varied characteristics and from a wide range of settings may contribute to substantial heterogeneity.

INTRODUCTION

Although the burden of diseases in low/middle-income countries (LMICs) has classically been infectious, changes in demographic patterns as a result of the interplay between urbanisation, life-style and culture, has led to emerging non-communicable diseases (NCDs) in LMICs.[1 2] The NCD burden is estimated to increase by 27% in the African region in the next 10 years, while Western Pacific and South-East Asia will account for the highest absolute number of deaths from NCDs.[3]

Coexistence of one or more chronic diseases in an individual is commonly denoted as multimorbidity.[4 5] With the increasing prevalence of NCDs in LMICs,[6] many of which share common risk factors, the prevalence of multimorbidity of NCDs will continue to rise. There is, however, a substantial difference in the burden of NCDs between LMICs and high-income countries (HICs) due to the difference in drivers, such as promotion of healthier lifestyles and providing equitable healthcare by instituting appropriate government policies.[7] While research investigated common pathways on NCD multimorbidity in HICs, it is unclear if this is also valid for

LIMCs.[8] It is therefore important to identify common NCD multimorbidity patterns and pathways that are specific to LMICs.

Studies undertaken so far predominantly used self-reported measures and show multimorbidity to be associated with decreased quality of life, increased healthcare utilisation and costs in primary, secondary and tertiary healthcare settings,[4 5 9–12] just as reported in HICs.[13 14] There is also limited information on the distribution of patterns of multimorbidity, their size, their drivers and their risk factors in LMICs. There are a few studies indicating that multimorbidity in LMICs is more frequent in women and that it starts at an earlier age than in HICs, but these studies are scattered.[15 16] In order to address and manage the increasing number of people with multimorbidity, it is important to assess the burden of multimorbidity as well as the combinations of NCDs and their patterns in LMICs. A recent scoping review of that summarised the prevalence and determinants of multimorbidity chronic NCDs in LMICs reported prevalence ranging from 3.2% to 90.5%.[6] This review builds on the previous scoping review by adopting systematic methods and meta-analysis to synthesise the evidence on the prevalence, patterns and factors associated with multimorbidity of NCDs among adults residing in LMICs. We further showed the prevalence and patterns of multimorbidity of NCDs according to country's income level classification by the World Bank.

METHODS

Review framework and patient and public involvement

This systematic review and meta-analysis was reported according to the recommendations outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement[17] (online supplemental file 1).

Patient and public involvement

This is a meta-analysis based on study-level data and no individual-level data were involved in the study or in defining the research question or outcome measures. It was not possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Search strategy

A structured search was done in the following databases: PubMed, EMBASE and Cochrane library for articles published in English from 2009 until April 2020. Keywords and Medical Subject Headings (MeSH) terms and their combinations used in the searches included "Multiple Chronic Conditions", "Multimorbidity", "Comorbidity", "Non-Communicable Diseases", "Developing Countries", "Cardiovascular Diseases", "Neoplasms", "Lung Diseases, Obstructive", "Diabetes Mellitus" and "Mental Disorders", "Hypertension". In addition, the reference lists and bibliographies of the included articles were examined to identify any other relevant article. The detailed search strategy is provided as online supplemental file 2.

Inclusion and exclusion criteria

Studies were included if they (i) reported original research on multimorbidity of NCDs, (ii) included adults aged 18 years and above and residing in LMICs, (iii) conducted in any of these study settings; community, residential care homes, primary care, secondary care, tertiary care and specialised care centres/institutions; or at the regional level using data from primary research, demographic and health surveys, or demographic and health surveillance systems. We defined LMICs according to the World Bank's Country and Lending Group List.[18] We excluded studies conducted in HICs. Studies published in languages other than English and studies on comorbidity (studies that recruited patients based on an index disease or primary disease of interest) were also excluded. However, we included comorbidity in the search strategy to enable us to capture and scrutinise studies that used the terms comorbidity and multimorbidity interchangeably or incorrectly.

Definition of terms/concepts

We defined multimorbidity of NCDs as co-occurrence of two or more chronic non-communicable health conditions in the same individual.[8] Prevalence of multimorbidity of NCDs was defined as the proportion of people with two or more chronic NCDs in the study population.[8] Patterns of multimorbidity NCDs were assessed by considering the frequencies and distributions of NCDs among individuals, regions and countries.

Data extraction

Two reviewers (OAA, AMF) extracted data from the included articles. In case of divergent opinions, KK-G and DB were consulted. Information extracted included author(s) name, year of publication and study country, survey/source of data, sample size, method of data collection, number of NCDs, multimorbidity definition, prevalence and factors associated with multimorbidity. The following summary measures were included: prevalence, odds ratio (OR), prevalence risk ratios and relative risk ratio with their 95% CI for the association between risk factors/determinants and NCD multimorbidity.

Quality assessment

The risk of bias in the included studies was assessed using the National Institute of Health Quality Assessment Tool for Observational Cohort and Cross-sectional Studies.[19] This tool was used to appraise the reliability, validity, generalisability and overall quality of the included studies using 14 criteria. This included clearly stated research question and objective, clearly specified study population, adequate participation rate, similar subject selection/recruitment and uniform application of eligibility to all participants, sample size estimation, exposure measurement before outcome, sufficient time frame to detect an association, examination of different levels of exposure,

multiply exposure measurement over time, valid outcome assessment, detection bias, loss to follow-up and adjustment of confounding variables. The tool provides general guidance to determine the overall quality of the studies and to grade their level of quality as good, fair or poor.

Data synthesis and analysis

Studies that provided sufficient data were used in the meta-analyses using Cochrane Review Manager (RevMan) software.[20] For multi-country studies with sufficient analysis of country level data, findings from individual countries were included separately in the meta-analyses. Findings of the remaining studies were presented in a narrative format. We pooled the OR (95% CI) for the association between sex, education, income, residence (rural/urban) and multimorbidity. A pooled OR of the association between age and multimorbidity was not estimated due to the variation in reference age categories whereas smoking, physical activity and alcohol consumption were not meta-analysed due to the limited number of studies that reported on them. The log OR and SEs were combined in RevMan using the generic inverse-variance.[21 22] We performed a random effect analysis, and heterogeneity was assessed using the Cochrane's Q and degree of inconsistency (I^2).[23] The pooled prevalence of multimorbidity was estimated using Open Meta (analyst) software.[24] The pooled prevalence was further stratified according to different regions in LMICs. The robustness of the pooled estimates was assessed by conducting a leave-one-out sensitivity analysis.[25] All analyses were considered statistically significant at the two-sided 5% level ($p<0.05$).

RESULTS

The electronic database and reference list search yielded 3272 articles, while 3134 articles remained after removal of duplicates. After the title and abstract screening, 68 articles were deemed potentially relevant. Twenty-nine articles were further excluded because they were conducted on communicable diseases (n=18), in non-LMICs (n=2), had poor quality (n=1) or based on other reasons such as presence of an index disease, or assessed multimorbidity in all ages without a separate report for adult above 18 years (n=8). We included 39 studies for the current review (figure 1). Some of the studies reported results from multiple countries, which were included individually in the analyses. For example, Bao *et al*[26] included analyses from seven countries; Cuba, Dominican Republic, Puerto Rico, Peru, Venezuela, Mexico, China. Agrawal and Agrawal,[27] Garin *et al*[28] and Christian *et al*[29] each reported findings from six countries; China, India, Mexico, Russia, South Africa and Ghana. Zhou *et al*[30] reported findings from India, China, and Bangladesh while Kunna *et al*[31] assessed multimorbidity in China and India. Table 1 shows all the countries or regions where multimorbidity of NCDs were conducted.

All included articles were cross-sectional except two studies that were cohort studies.[26 32] A total of 1 220 309 individuals were included and the sample size ranged from 389[33] to 60 202.[34 35] NCDs were assessed through self-report in all included studies, or in combination with a health insurance database,[32] or medication use and clinical test. One study assessed based on the Anatomical Therapeutic Chemical Classification System. The number of self-reported NCDs ranged from 3 to 22. All studies defined multimorbidity as coexistence of two or more chronic NCDs, except one study which defined multimorbidity as a count of 21 chronic health conditions[36] (table 1).

Most of the studies were of good quality. Three included articles were judged to be of fair quality.[26 32 37] One study was excluded because of having a small sample size, and a lack of data or non-robust methods.[38] Twenty-one of the included studies did not give information about missing data handling[4 26 29–31 33 34 36 39–52] (online supplemental file 3).

The overall prevalence of multimorbidity of NCD varied from 0.7% (in a population aged ≥20 years in a rural community in Western India) to 81.3% (in an elderly population aged ≥60 years in Southern Brazil).[40 47] A study that assessed prevalence of multimorbidity among adults ≥18 years in 27 LMICs using the World Health Surveys reported a mean prevalence ranging from 1.7% (95% CI 1.4 to 2.0) in Myanmar to 15.2% (95% CI 14.3 to 16.0) in Nepal.[16] In studies that combined self-reported diseases with symptom based diagnosis, medication use/medical card review, prevalence varied between 4.0% and 72% in people ≥18 years.[36 53] The overall prevalence of multimorbidity was 36.4% (95% CI 32.2% to 40.6%) as shown in figure 2. In a subgroup analysis, the pooled prevalence according to the countries' income levels was 39.3% (95% CI 34.5% to 44.1%) for upper middle-income countries (MICs) (online supplemental figure 1a) and 29.2% (95% CI 23.0% to 35.4%) for lower MICs (online supplemental figure 1b). We did not pool the prevalence for low-income countries (LICs) because there were only three studies, with prevalence ranging from as low as 4.0% in Malawi to 65.0% in Burkina Faso. Subgroup analysis according to the World Bank regions of LMICs was 26.2% (95% CI 18.9% to 33.5%) for sub-Saharan Africa (SSA); 29.5% (95% CI 20.9% to 38.1%) for Asia; 31.8% (95% CI 25.7% to 37.8%) for East Asia; 33.1% (95% CI 10.4% to 55.8%) for Middle-East and North Africa (MENA); for Europe and Central Asia (excluding high income) 44% (95% CI 32.7% to 55.3%) and 50.4% (95% CI 35.6% to 65.2%) for Latin America and the Caribbean (LAC). According to the leave-one-out sensitivity analysis, no single study had a substantial influence on the overall prevalence of NCD multimorbidity (online supplemental figure 2).

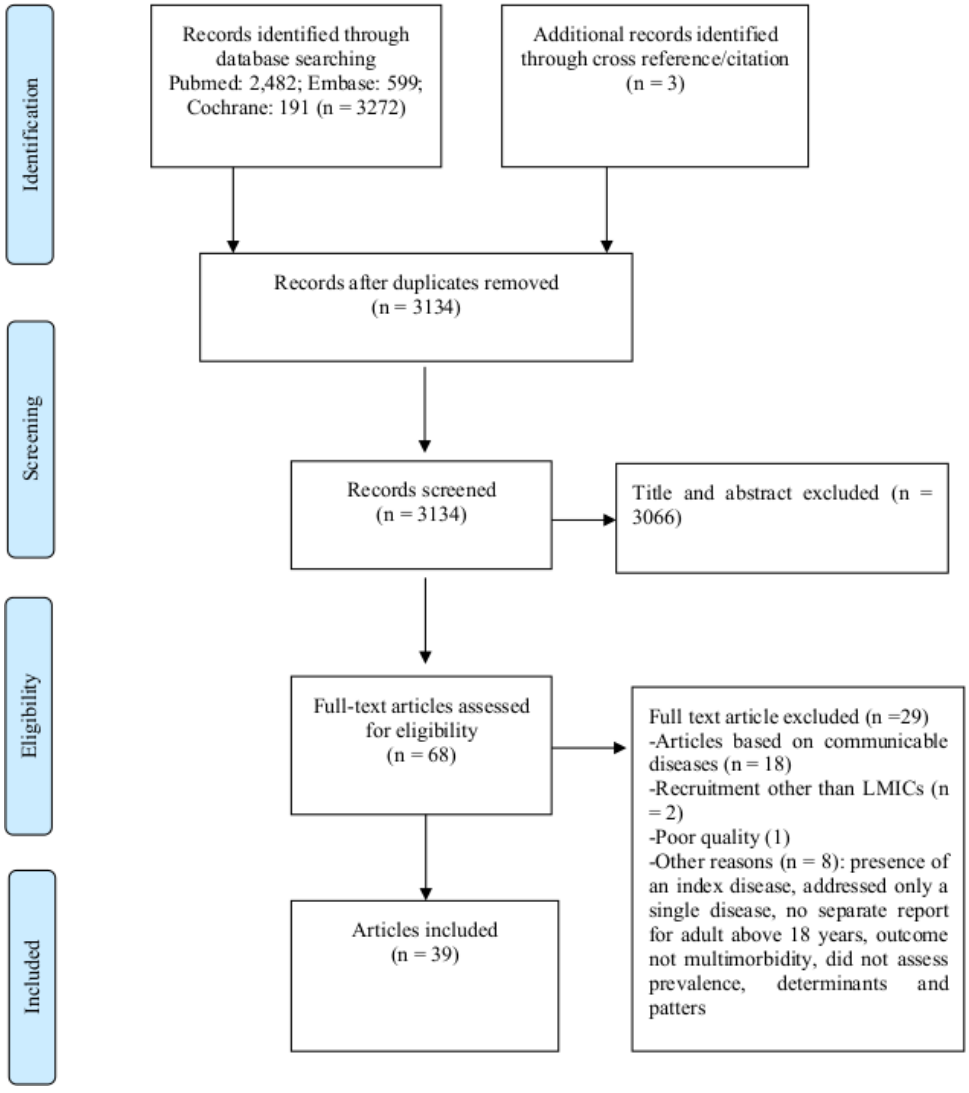

Figure 1 Flow chart for study inclusion and exclusion of studies.

Age, sex, education, wealth/income, urban/rural setting and marital status were the most studied factors associated with multimorbidity of NCDs (online supplemental table 1). ORs for the association between major predictors and multimorbidity are shown in online supplemental table 2. Age was positively associated with multimorbidity of NCDs in 22 studies, whereas 3 studies[28 48 49] found no association.

Figure 3 shows a forest plot of pooled OR for the association between major predictors and multimorbidity; details of the meta-analysis for the individual predictors are shown in online supplemental figure 3a–d). Women had significantly higher odds of multimorbidity compared with men in 11 studies,[4 9 28 34–36 48 50 54–56] whereas 8 studies showed a non-significant association[28 31 33 46 49 51 57 58] (online supplemental table 2). Fourteen studies (one study included six different country level results) were meta-analysed and the pooled OR for female sex and NCD multimorbidity was 1.48 (95% CI 1.33 to 1.64) (figure 3, online supplemental figure 3a). The association between education and multimorbidity was assessed in 31 studies. In most studies, the risk of multimorbidity was higher among those with a lower educational status,[4 16 28 34–36 43 51] while four studies reported a lower risk of lower education statu.[45 50 53 57] A meta-analysis of 13 studies (one study included six different country level results; one study included results for males and females) showed an OR of 1.22 (95% CI 1.00 to 1.49) for those with no formal education or lower educational attainment (figure 3, online supplemental figure 3b).

The association between socioeconomic status (income/wealth) and multimorbidity was determined in 14 studies; 7 studies found an association with higher odds/risk/prevalence of multimorbidity for people in the most well-off class,[9 28 31 45 48 50 53] while in 3 studies the odds/prevalence of multimorbidity was higher for people considered to be poor.[4 28 31] The pooled OR from 10 studies (one study included six different country level results; one study included results for males and females) showed increased odds of NCD multimorbidity among people who are well-off, OR 1.35 (95% CI 1.02 to 1.80) (figure 3, online supplemental figure 3c). There were

Table 1 Study characteristics of studies included in the systematic review

Author	Country/region	Inclusion criteria	Study design	Survey/source of data	Sampling characteristics	Field year	Sample size	Age range (years)	Data collection	No of NCDs	Multi-morbidity definition	Prevalence (%)	Quality of included studies
Afshar *et al* (27 LMICs)[16]	Africa, Central and South America, Eastern Europe and Central Asia, South Asia, South East Asia	Prevalence and determinants	Cross-sectional	WHS	Probabilistic	2001–2004	25 761	≥18	Self-report	6	≥2	Ranges from 1.7 to 15.2; Africa (3.6–11.2) Central and South America (5.7–13.4) Eastern Europe and Central Asia (7.6–15.0) South Asia (3.9–7.8) Southeast Asia (1.7–15.2) Mean global prevalence (95 CI) 7.8 (7.8 to 7.8)*	Good
Agrawal and Agrawal[27]	China	Prevalence and determinants	Cross-sectional	WHO SAGE	Probabilistic	2007–2010	China (15048); (India 12198); Mexico (2725); Russia (4946); South Africa (4227); Ghana (5571)	≥18	Self-report+medication use+SBD	9	≥2	22.0–50.0: China (22.0); India (24.0); Mexico (27.0); Russia (50.0); South Africa (32.0); Ghana (23.0)	Good
Arokiasamy *et al*[4]	China, Ghana, India, Mexico, South Africa, Russia	Prevalence and determinants	Cross-sectional	WHO SAGE	Probabilistic	2007–2010	42 236	≥18	Self-report+medication use+SBD	9	≥2	21.9	Good
Aye *et al*[54]	Myanmar	Prevalence, patterns and determinants	Cross-sectional	Household survey	Probabilistic	2016	4859	≥60	Self-report	14	≥2	33.2	Good
Bao *et al* [26]	Cuba, Dominican Republic, Puerto Rico, Peru, Venezuela, Mexico, China	Prevalence	Population based Cohort	Household survey	NR	2003–2010	15 027	≥65	Self-report+physical examination	15	≥2	Ranges from 31.0 to 68.0; China (31.0); Peru (49.0) Cuba (58.0), Venezuela (60.0), Mexico (60.0), Dominican Republic (68.0)	Fair
Chen *et al*[57]	China	Prevalence and determinants	Cross-sectional	CHARLS	Probabilistic	2011–2012	3737	≥45	Self-report	16	≥2	46.0	GOOD
Christian *et al*[29]	China, Ghana, India, Mexico, South Africa, Russia	Prevalence	Cross-sectional	WHO SAGE	Probabilistic	2007–2010	42 487	≥50	Self-report	8	≥2	Ranges from 8.8 to 50.2: Ghana (8.8), India (16), China (20.3), Mexico (20.8), South Africa (20.8%), Russia (50.2)	Good

Continued

Table 1 Continued

Author	Country/region	Inclusion criteria	Study design	Survey/source of data	Sampling characteristics	Field year	Sample size	Age range (years)	Data collection	No of NCDs	Multi-morbidity definition	Prevalence (%)	Quality of included studies
Ebrahimoghli *et al*[32]	Iran	Prevalence	Retrospective cohort study	IHIO	All beneficiaries of IHIO	2013–2016	481 733	≥18	ATC CS	18	≥2	21.5	Fair
Garin *et al*[28]	China, Ghana, India, Mexico, South Africa, Russia	Prevalence determinants and patterns	Cross-sectional	WHO SAGE	Probabilistic	2007–2010	China (13157), Ghana (4305), India (6560), Mexico (2301), South Africa (3763), Russia (3836)	≥50	Self-report +medication use +SBD	12	≥2	Ranges from 45.1 to 72.0: China (45.1), Ghana (48.3), India (57.9), Mexico (64.0), South Africa (63.4), Russia (72.0)	
Hien *et al*[33]	Burkina Faso	Prevalence and determinants	Cross-sectional	Household survey	Probabilistic	2012	389	≥60	Self-report+clinical examination+medical record review	16	≥2	65.0	Good
Jawed *et al*[55]	Pakistan	Prevalence and determinants	Cross-sectional	The IMPACT study	Probabilistic	2015–2016	1500	≥30	Self-report+medication use+SBD	16	≥2	48.6	Good
Jerliu *et al*[46]	Kosovo	Prevalence and determinants	Cross-sectional	Community survey	Probabilistic	2011	2265	≥65	Self-report	7	≥2	45.0	Good
Jovic *et al*[42]	Serbian	Prevalence, patterns	Cross-sectional	NHS-Serbia	Probabilistic	2013	13 103	≥20	Self-report	12	≥2	26.9	Good
Jankovic *et al*[43]	Serbian	Prevalence and determinants	Cross-sectional	NHS-Serbia	Probabilistic	2013	13 765	≥20	Self-report	13	≥2	30.2	Good
Khan *et al*[45]	Bangladesh	Prevalence, patterns and determinants	Cross-sectional	Household survey	Probabilistic	2014–2016	12 338	≥35	Self-report+medication use+SBD	6	≥2	8.4	Good
Khanam *et al*[48]	Bangladesh	Prevalence and determinants	Cross-sectional	HDSS	Probabilistic	2003–2004	452	≥60	Self-report+physical examination+blood test	9	≥2	53.7	Good
Kumar *et al*[47]	India	Prevalence	Cross-sectional	Household survey	NR	2012–2013	58 590	≥20	Self-report	5	≥2	0.7	Fair
Kunna *et al*[31]	China, Ghana	Prevalence and determinants	Cross-sectional	WHO SAGE	Probabilistic	2007–2010	China (11 814); Ghana (4050)	≥50	Self-report+SBD	7	≥2	China (29.7); Ghana (30.2)	Good
Koyanagi *et al*[87]	China, Ghana, India, Mexico, South Africa, Russia	Prevalence	Cross-sectional	WHO SAGE	Probabilistic	2007–2011	32 715	≥50	Self-report+SBD	10	≥2	49.8	Good
Lee *et al*[9]	China, Ghana, India, Mexico, South Africa, Russia	Prevalence and determinants	Cross-sectional	WHO SAGE	Probabilistic	2007–2010	39 213	≥18	Self-report	9	≥2	Varies from 3.9 in Ghana-33.6 in Russia	Good
Mini and Thankappan[50]	India	Prevalence, patterns and determinants	Cross-sectional	UNFPA	Probabilistic	2011	9852	≥60	Self-report	12	≥2	30.7	Good

Continued

Table 1 Continued

Author	Country/region	Inclusion criteria	Study design	Survey/source of data	Sampling characteristics	Field year	Sample size	Age range (years)	Data collection	No of NCDs	Multi-morbidity definition	Prevalence (%)	Quality of included studies
Nugraha *et al*[41]	Indonesia	Prevalence	Cross-sectional	Community survey	Probabilistic	2018	427	≥60	Self-report	15	≥2	60.7	Good
Nunes *et al*[40]	Brazil	Prevalence and patterns	Cross-sectional	Household survey	Probabilistic	2008	1593	≥60	Self-report	17	≥2	81.3	Good
Nunes *et al*[34]	Brazil	Prevalence, patterns and determinants	Cross-sectional	PNS	Probabilistic	2013	60 202	≥18	Self-report	22	≥2 or≥3	22 for ≥2 and 10.2 for ≥3	Good
Pati *et al*[58]	India	Prevalence and determinants	Cross-sectional	WHO SAGE	Probabilistic	2007	10 973	≥18	Self-report	9	≥2	8.9	Good
Pati *et al*[39]	India	Prevalence and patterns	Cross-sectional	Primary healthcare	Probabilistic		1649	≥18	Self-report	21	≥2	28.3	Good
Pengpid and Peltzer[36]	Mekong	Prevalence, determinants	Cross-sectional	Primary healthcare	Probabilistic	NR	6236	≥18	Self-report	21	≥2	72.6 (28.6 had 2, 22.4 had 3 and 21.6 had ≥24 chronic conditions)	Good
Phaswana-Mafuya *et al*[52]	South Africa	Prevalence	Cross-sectional	WHO SAGE	Probabilistic	2008	3840	≥50	Self-report	8	≥2	22.5	Good
Price *et al*[53]	Malawi	Prevalence and determinants	Cross-sectional	Household survey	No sampling: all adults	2013–2016	28 891	≥18	Self-report+medication use+patient health record+clinical test	3	≥2	4.0	Good
Rehr *et al*[51]	Northern Jordan	Prevalence, patterns and determinants	Cross-sectional	UNHCR	Probabilistic	2016	8041	≥18	Self-report	6	≥2	44.7	Good
Rzewuska *et al*[35]	Brazil	Prevalence, patterns and determinants	Cross-sectional	PNS	Probabilistic	2013	60 202	≥18	Self-report+SBD	14	≥2	24.2	Good
Sum *et al*[44]	China, Ghana, India, Mexico, South Africa, Russia	Prevalence and patterns	Cross-sectional	WHO SAGE	Probabilistic	2007–2010	41 557	≥18	Self-report+SBD	9	≥2	18.9	Good
Vadrevu[56]	India	Prevalence and determinants	Cross-sectional	Household survey	Probabilistic	2009	815	≥40	Self-report+SBD	6	≥2	44.1	Good
Vancampfort *et al*[88]	China, Ghana, India, Mexico, South Africa, Russia	Prevalence	Cross-sectional	WHO SAGE	Probabilistic	2007–2010	34 129	≥50	Self-report+SBD	11	≥2	45.5	Good
Vancampfort *et al*[89]	China, Ghana, India, Mexico, South Africa, Russia	Prevalence	Cross-sectional	WHO SAGE	Probabilistic	2007–2010	34 129	≥50	Self-report+SBD	11	≥2	45.5	Good

Continued

Table 1 Continued

Author	Country/region	Inclusion criteria	Study design	Survey/source of data	Sampling characteristics	Field year	Sample size	Age range (years)	Data collection	No of NCDs	Multi-morbidity definition	Prevalence (%)	Quality of included studies
Vancampfort *et al*[49]	China, Ghana, India, Mexico, South Africa, Russia	Prevalence and determinants	Cross-sectional	WHO SAGE	Probabilistic	2007–2010	14 585	≥65	Self-report+SBD	11	≥2	60.2	Good
Waterhouse *et al*[60]	South Africa	Prevalence	Cross-sectional	WHO SAGE	Probabilistic	2007–2008	3055	≥50	Self-report	8	≥2	13.2	Good
Woldesemayat *et al*[60]	Ethiopia	Prevalence, patterns and determinants	Cross-sectional	Healthcare	NR	2016	411	≥18	Self-report+medical card	18	≥2	17.8	Good
Zhou *et al*[30]	Bangladesh, India, China	Prevalence	Cross-sectional	WHS	Probabilistic	2002–2004	Bangladesh (5507); India (9199); China (3990)	≥18	Self-report	9	≥2	Bangladesh (28.8); India (34.4); China (14.3)	Good

*Include prevalence from 27 LMICs and 1 high-income country.
ATC CS, Anatomical Therapeutic Chemical Classification System; BDHS, Bangladesh Demographic and Health Survey; CHARLS, China Health and Population Fund; HDSS, Health and Demographic Surveillance System; IHIO, Iranian Health Insurance Organization; LMIC, low/middle-income country; NCDs, non-communicable diseases; PNS, Pesquisa Nacional de Saude (Brazilian National Health Survey); SA-NIDS, South Africa National Income Dynamics Study; SBD, symptom based diagnosis; UNHCR, United Nations High Commission for Refugees; WHO-SAGE, WHO Study on Global AGEing and adults health; WHS, World Health Survey.

significantly higher odds/risk for multimorbidity of NCDs for urban areas.[9 34 49 53 54 59] A meta-analysis of 10 studies (one study included six different country level results; two included results for males and females) showed a pooled OR of 1.10 (95% CI 1.01 to 1.20) for urban residence (figure 3, online supplemental figure 3d). There was a high degree of heterogeneity as depicted by high I^2 >90% in the various meta-analyses conducted.

Three of the seven studies that assessed the association between multimorbidity of NCDs and physical activity/exercise showed significantly higher odds for those that do little or no physical activity,[4 31 49] while the other five showed no significant relationship.[31 36 45 53 60] Eight studies examined the relationship between obesity and multimorbidity; five articles found higher a positive association between multimorbidity of NCDs and obesity.[4 27 31 45 56] In the WHO SAGE study among five LMICs, obese individuals were 2.3 times (95% CI 2.0 to 2.52) more likely to have multimorbidity compared with the non-obese when multimorbidity was compared with no disease.[4] Eight studies assessed the association between smoking and multimorbidity, with a study conducted among the elderly from seven Indian urban and rural states reporting a positive association[50] when compared with no NCD (OR: 1.22, 95% CI 1.08 to 1.37). Alcohol consumption was associated with higher odds of NCD multimorbidity.[50 53]

The patterns of reported NCD multimorbidity are shown in table 2. Seventeen studies assessed patterns of multimorbidity of NCDs using factor analysis,[28 34 35 42 54] cluster analysis[50] or descriptive methods.[39 40 44 45 51 60] Sixteen out of the 17 studies that reported on patterns of multimorbidity were conducted in MICs, while only one study was conducted in LIC. Cardiometabolic and cardiorespiratory conditions were the most identified patterns seen in MICs, while cardiovascular, musculoskeletal system diseases and endocrine system diseases were observed in the only one study in LMICs (table 2). The highest prevalence of cardiometabolic pattern was 70.3% and 60.7% among males and females aged 20–40 years, respectively in MICs. Cardiometabolic, mental and respiratory conditions were present in both men and women in two MICs studies that stratified by sex.[35 42] Mental disorder was also reported to cluster with other conditions such as cardiometabolic, respiratory and musculoskeletal conditions in studies conducted in Brazil, Serbia and a multicountry study in South Africa, Ghana, Mexico, Russia, Bangladesh, India and China.[28 34 35 39 42 44]

DISCUSSION

This systematic review with meta-analyses of 39 studies shows that the overall prevalence of NCD multimorbidity in LMICs was 36% with substantial variation between studies. Prevalence differed by region and was observed to be lowest in SSA and highest in LAC region. According to income levels of countries, the prevalence of NCD multimorbidity was higher among upper MICs and as compared with lower-middle income countries. Older age,

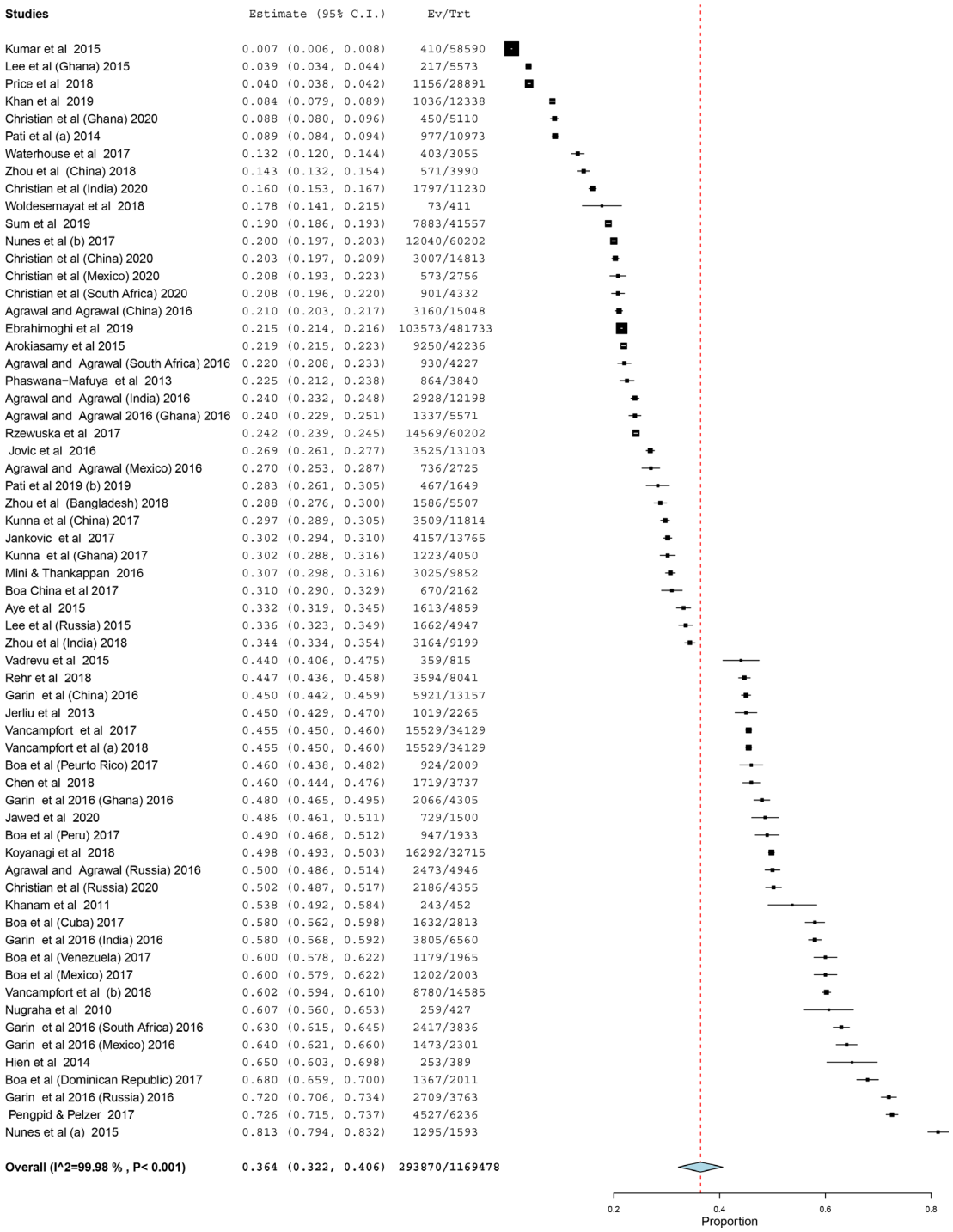

Figure 2 Forest plot of pooled prevalence of multimorbidity in low/middle-income countries.

female sex, higher income and urban residence increased the odds of having NCD multimorbidity. Cardiometabolic and cardiorespiratory patterns of multimorbidity of NCDs were most common; in addition, multimorbidity of mental disorders with respiratory, musculoskeletal and cardiometabolic conditions was observed.

An important finding from our review is the large variation in the estimates of prevalence of multimorbidity of NCDs in LMICs. This may be explained by differences in definition/measurement of multimorbidity, study populations, demographics, study settings, self-reported diseases and the number of NCDs included. Similar variation was seen in reviews that focused on South Asia[61] and HICs.[62 63] A recent scoping review of multimorbidity of chronic NCDs in LMICs also found a wide variation in the prevalence of multimorbidity in LMICs (3.2%–90.5%), depending on population age and the number of conditions considered.[6] Since prevalence estimates depend on the number and the type of chronic conditions included in the measurement of multimorbidity, there might be underreporting due to lack of data or undiagnosed conditions. To date, there is no valid standard measurement of

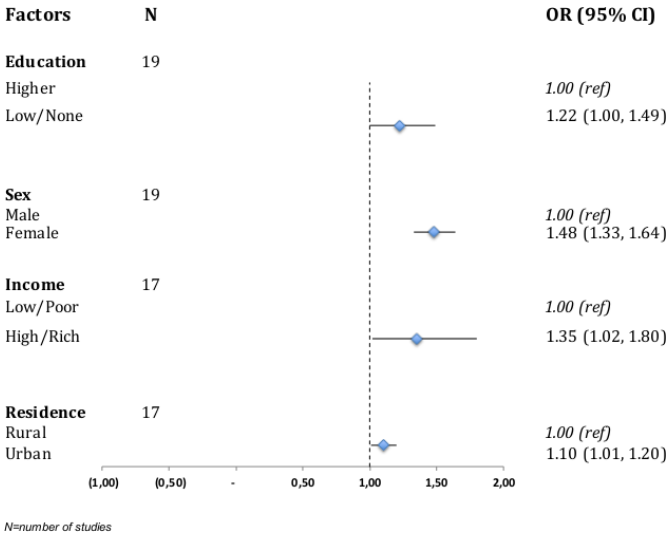

Figure 3 Forest plot of pooled ORs of factors associated with multimorbidity in low/middle-income countries.

multimorbidity indicating a need for a uniform definition and a reporting system for multimorbidity, as suggested by the Academy of Medical Science.[8]

The positive association of multimorbidity with age and female sex is consistent with a study comparing 27 LMICs and 1 HIC using the World Health Survey,[16] other reviews on multimorbidity in South Asia and LIMCs[6 39] as well as reviews from HICs.[62 63] The meta-analyses showed higher odds of multimorbidity among women compared with men. While the association between these factors and multimorbidity is inconsistently reported, the sex-related differences in multimorbidity could be related to context related proxy for behavioural characteristics such as care seeking, that might influence the detection of multimorbidity.[8] Women are more likely to have frequent healthcare consultations than men[64 65] and might be able to self-report their health status than men. In addition, sex differences in socioeconomic status could also account for the discrepancy observed. Socioeconomic status affects general health functioning, including mental and physical health. Research show that women, in general, have lower socioeconomic status than men, which is in part related to gender inequality and could negatively affect health outcomes.[66]

In LMICs, people who are well-off in terms of income seem to be most affected by multimorbidity, in contrast with evidence from HIC[8] that shows an inverse association. Few studies from HIC have, however, reported higher prevalence among people who are well-off.[9 16 59] Contextually, people who are well-off in LMICs are generally less physically active and consume more fats, salt and processed food which could partly explain the higher prevalence of NCD multimorbidity.[67] Further, they might be better educated, informed and have greater access to medical care and are more likely to receive disease diagnosis. The significantly higher odds for multimorbidity of NCDs seen in the urban areas may be due to underreporting in rural areas as a result of poorer access to healthcare and healthcare insurance.[68] In most LMICs, healthcare services are paid out of pocket for every inpatient and outpatient visit.[9] People living in rural areas are less likely to have long-term healthcare insurance and also less likely to be provided with adequate healthcare.[69] Furthermore, regional differences in lifestyle could also explain higher odds of multimorbidity of NCDs in people living in urban areas as residence in urban areas is associated with unfavourable diets and lower physical activity levels.[70 71]

This review identified various patterns of NCD multimorbidity across different regions in LMICs. Cardiometabolic and cardiorespiratory patterns of multimorbidity were most common and share major pathophysiological pathways and common risk factors such as smoking,[72 73] partly explaining their clustering together. The frequent co-occurrence of cardiometabolic conditions and mental disorders among studies in LMICs as shown in this review is consistent with findings from HICs[62 74 75] and highlights the importance of prevention and management policies addressing environmental and living conditions.[76]

Current evidence suggests a poorer health-related quality of life, worse clinical outcomes and an increased risk of premature mortality among patients with concurrent physical and mental health conditions than those who have physical conditions alone.[77–79] Individuals with concurrent physical and mental health conditions are also found to have challenges with medication adherence, compromised self-management,[80] high risk of adverse drug events,[81] higher rates of healthcare utilisation. They are however at a risk of receiving suboptimal care for coexisting health conditions, leading to poorer health outcomes and increased mortality.[82]

Strength and limitations

A strength of this review is that most of the included studies from the database search were from the WHO Study on global AGEing and adult health (SAGE), which ensured standardisation of methods of measurements and data collection. This review provides worldwide prevalence rates and predictors for multimorbidity. The standardised methods and large sample sizes of the underlying studies ensure a high qualitative standard of the report.

A main limitation of this review is that all studies included self-reported measures for data collection of multimorbidity, and very few collected physical or biochemical data. Self-reported disease is fairly accurate, and may be subject to recall and self-declaration bias, under or over reporting of outcome of interest.[83 84] This may result in under/over estimation of the true prevalence of multimorbidity. The restriction of inclusion criteria to only studies conducted in English might have also led to studies from other LMICs, especially South America where Spanish dominates, leading to potential bias in the estimates. Generally, studies that assessed determinants of multimorbidity did not take the heterogeneity and clusters of conditions into consideration. The observational studies summarised involved patients with

Table 2 Patterns of multimorbidity reported in included studies

Pattern	Study	Economy status	Diseases	Prevalence % (95% CI)
Cardiometabolic	Garin *et al*[28] (China)	MIC	Diabetes, obesity, hypertension, angina, stroke, cataract	NR
	Garin *et al*[28] (Ghana, India, Mexico)	MIC	Diabetes, obesity, hypertension	NR
	Garin *et al*[28] (Russia)	MIC	Diabetes, obesity, hypertension, angina, stroke, cataract, arthritis, edentulism, depression	NR
	Garin *et al*[28] (South Africa)	MIC	Diabetes, obesity, hypertension, angina, stroke, arthritis, edentulism	NR
	Jovic *et al*[42]	MIC	Male (age 20–44 years): Cardiometabolic Age 45–64 years: Cardiometabolic Age 65+ years: Cardiometabolic	70.3 39.2 29.5
		MIC	Female (Age 20–44 years): Cardiometabolic Age 45–64 years: Cardiometabolic Age 65+ years: Cardiometabolic	60.7 53.2 33.2
	Khan *et al*[45]	MIC	Hypertension, diabetes, CVD; Hypertension, diabetes, stroke; Hypertension, diabetes, cancer; Hypertension, CVD, stroke Diabetes, CVD, stroke Hypertension, diabetes, CVD, stroke	0.6 0.4 0.0 0.3 0.3 0.6
	Mini and Thankappan[50]	MIC	High blood pressure, diabetes	4.7
	Nunes *et al*[34]	MIC	High blood pressure, heart attack, angina, heart failure, stroke, hypercholesterolaemia, diabetes, arthritis/rheumatism	NR
	Rehr *et al*[51]	MIC	Diabetes and hypertension; Diabetes, hypertension and CVD; Hypertension and CVD; Diabetes, hypertension and thyroid disease	17.6 (15.9 to 19.5) 8.1 (6.9 to 9.7) 7.1 (5.9 to 8.4) 1.3 (0.9 to 2.0)
	Rzewuska *et al*[35]	MIC	Male and female: diabetes, stroke, cardiovascular disorders; high blood cholesterol, hypertension	NR
Cardiovascular	Aye *et al*[54]	MIC	Coronary heart disease, Heart failure	NR
	Jovic *et al*[42]	MIC	Male (age 45–64 years): cardiovascular Age >65 years: cardiovascular Female (45–64 years): cardiovascular Age >65 years: cardiovascular	22.8 28.7 29.6 18.9
	Rehr *et al*[51]	MIC	Hypertension and CVD	7.1 (5.9 to 8.4)
	Woldesemayat *et al*[60]	LIC	Cardiovascular and endocrine system diseases	2.4
Cardiorespiratory	Aye *et al*[54]	MIC	Asthma, COPD, hypertension, diabetes, stroke	NR
	Garin *et al*[28] (China)	MIC	Angina, asthma, COPD, depression, arthritis, cataract	NR
	Garin *et al*[28] (Ghana)	MIC	Angina, asthma, COPD	NR
	Garin *et al*[28] (India)	MIC	Angina, asthma, COPD, depression	NR
	Garin *et al*[28] (Mexico)	MIC	Angina, asthma, COPD, stroke, depression, arthritis, cataract	NR
	Garin *et al*[28] (South Africa)	MIC	Angina, asthma, COPD, stroke, depression, arthritis	NR
	Rehr *et al*[51]	MIC	Hypertension and chronic respiratory condition	1.3 (0.8 to 1.9)
	Khan *et al*[45]	MIC	Hypertension, diabetes, COPD	0.1

Continued

Table 2 Continued

Pattern	Study	Economy status	Diseases	Prevalence % (95% CI)
Mental	Aye *et al*[54]	MIC	Depression, mental illness	NR
Respiratory	Garin *et al*[28] (Russia)	MIC	Asthma, COPD, cataract	NR
	Jovic *et al*[42]	MIC	Male (age 45–64): respiratory Age 65+ years: respiratory Female (age 45–64 years): respiratory 16.8 Age 65+ years: respiratory	13.7 16.0 14.5
	Rzewuska *et al*[35]	MIC	Male and female: Asthma, chronic obstructive pulmonary disease	NR
Musculoskeletal	Aye *et al*[54]	MIC	Arthritis, osteoporosis	NR
Ocular+musculoskeletal +cardiorespiratory	Aye *et al*[54]	MIC	Asthma, COPD, cataract, arthritis, osteoporosis, asthma, COPD, hypertension, diabetes, stroke	NR
	Mini and Thankappan[50]	MIC	Arthritis, hypertension; Arthritis, cataract	7.5 5.3
	Nunes *et al*[40]	MIC	HBP, heart problem, eyesight problem, spinal column disease, rheumatism	10.6 to 5.5
	Pati *et al*[39]	MIC	Hypertension+APD+diabetes, Hypertension+APD+CBA; Hypertension+arthritis+diabetes; Hypertension+arthritis+CBA; APD+visual impairment+CBA; APD+visual impairment+arthritis Athritis+CBA+CLD; Athritis+CBA+visual impairment APD+hypertension/visual impairment/CBA/arthritis/diabetes/CLD/deafness Hypertension+visual impairment/CBA/visual impairment/arthritis/deafness Arthritis+visual impairment/CBA/diabetes	NR
	Sum *et al*[44]	MIC	Age 18–49 years: Hypertension+arthritis, Hypertension+angina, Hypertension+CLD, Age 50–64 years: Hypertension+arthritis, Hypertension+angina, Hypertension+CLD Age >64 years: Hypertension+arthritis, Hypertension+angina, Hypertension+CLD, Hypertension+cataract	4.99 4.13 1.90 19.08 17.08 9.79 33.77 29.73 16.44 15.27
Mental+musculoskeletal	Garin *et al*[28] (China)	MIC	Arthritis, depression, stroke, cataract	NR
	Garin *et al*[28] (Ghana)	MIC	Arthritis, depression	NR
	Garin *et al*[28] (India)	MIC	Arthritis, depression, cataract, angina	NR
	Jovic *et al*[42]	MIC	Male age ≥65 years: mechanical/mental/metabolic Female age ≥65 years: mechanical/mental/metabolic	25.8 32.3
	Nunes *et al*[34]	MIC	Arthritis/rheumatism, spinal column problem, spinal column problem, asthma/wheezy bronchitis, COPD, work-related muscle-skeletal disorders, depression, bipolar disorder, kidney problem	NR

Continued

Table 2 Continued

Pattern	Study	Economy status	Diseases	Prevalence % (95% CI)
	Rzewuska *et al*[35]	MIC	Male and female: Arthritis or rheumatism, high blood cholesterol, MSK-D related to work, any chronic back problem, chronic renal insufficiency, schizophrenia, bipolar, obsessive-compulsive disorder, depression	NR
	Sum *et al*[44]	MIC	Age: 18–49 years: Hypertension+arthritis, Hypertension+angina, Hypertension+CLD, Hypertension+depression	4.99 4.13 1.90 1.67
Cardio metabolic+musculoskeletal	Mini and Thankappan[50]	MIC	Arthritis, hypertension	7.5
	Nunes *et al*[40]	MIC	HBP, rheumatism, spinal column disease; HBP, heart problem, spinal column disease; HBP, heart problem, cognitive impairment; HBP, spinal column, falls	10.6 to 5.7
	Pati *et al*[39]	MIC	Hypertension, arthritis, diabetes/CBA	
	Woldesemayat *et al*[60]	LIC	Cardiovascular and musculoskeletal system diseases	1.2
Cardio metabolic+musculoskeletal +mental	Nunes *et al*[40]	MIC	HBP, heart problem, cognitive impairment, depression	10.6 to 5.2
	Jovic *et al*[42]	MIC	Male: Age 45–64 years: Aggregate pattern, such as degenerative joint disease/arthrosis, depression, cardiovascular, kidney disease, stroke and malignancy Female: Aged 20–44 years: non-communicable pattern such as degenerative joint disease/arthrosis, depression, cardiovascular and malignancy	24.3 13.3
Cardio+metabolic+respiratory +musculoskeletal+mental	Jovic *et al*[42]	MIC	Male: Age 20–44 years: non-communicable pattern such as degenerative joint disease/arthrosis, depression, cardiovascular, respiratory, kidney disease and malignancy	29.7
	Pati *et al*[39]	MIC	Arthritis+CBA/visual impairment/chronic lung disease	NR
	Sum *et al*[44]	MIC	Age 18–49 years: Hypertension+arthritis, Hypertension+angina, Hypertension+CLD, Hypertension+depression Age 50–64 years: Hypertension+arthritis, Hypertension+angina, Hypertension+CLD	4.99 4.13 1.90 1.67 19.08 17.08 9.79

APD, acid peptic disease; CBA, chronic back pain; CLD, chronic lung disease; COPD, chronic obstructive pulmonary disease; CRD, cardiorespiratory disease; CVD, cardiovascular disease; LIC, low-income country; MIC, middle-income country; MSK-D, musculoskeletal disorder.

varied characteristics and from a wide range of settings contributing to substantial heterogeneity, which could affect the reliability of the findings. The use of cross-sectional design in almost all studies limits the ability to assess the outcome over a longer period and therefore makes it impossible to draw a causal relationship between the various determinants and multimorbidity.[85] In the absence of intervention studies, the meta-analysis of the observational studies provides insight into the direction and strength of the association between the various risk factors and NCD multimorbidity. We did not include MeSH terms related to metabolic diseases such as obesity/overweight, metabolic syndrome and osteoarthritis mainly because they are risk factors of major NCDs. We believe, however, that our search strategy was able to cover these risk factors since most of the major NCDs are assessed together with these in most multimorbidity studies.

Implications of findings

The rising burden of multimorbidity in LMICs indicates the urgent need to strengthen the healthcare system to accommodate for the diagnosis and management of multiple chronic conditions. Available evidence shows that patients with multimorbidity have significantly higher mean outpatient and inpatient visits, resulting in higher out-of-pocket expenditure.[9 43 58] Increased healthcare utilisation among patients with multimorbidity poses challenges to the patients, health providers and the healthcare system.

Evidence from HIC shows diverse challenges when dealing with patients with multimorbidity, including the complexity of multiple guidelines which focus on the management of single conditions and challenges in delivering patient-centred care.[86] This emphasises the need to develop context-specific guidelines on how to diagnose and deal with multiple chronic conditions and to ensure better health service provision, health management and resource deployment to manage the increasing number of people with multimorbidity. Exploring the economic burden of multimorbidity across different settings and populations in LMICs will be crucial in informing policy decisions about service provision and resource allocation.

Despite the clear rise of multimorbidity in LMICs, there is a challenge in explaining the factors behind this rising burden given inconsistencies in findings. This is partly due to the lack of longitudinal studies providing strong evidence on the determinants and the differences in patterns of multimorbidity among different age groups as well as factors that influence variation in clusters of multimorbidity. The acceptance of a standard definition of multimorbidity will provide more clarity on the burden and epidemiology of multimorbidity.

CONCLUSION

In conclusion, this review shows a high burden of multimorbidity in LMICs, especially among women, the people who are well-off, and people residing in urban areas, with cardiometabolic and cardiorespiratory profiles being the most prevalent patterns of multimorbidity. There are however major gaps in epidemiological research on this topic, including the need for longitudinal data to access the true direction of the multimorbidity and its determinants, to establish causation and to identify how trends and patterns change over time.

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	7
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	7,8
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	7,8,9
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	7
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	7
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	9
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	11
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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([mh Comorbidity] OR comorbidity:ti,ab OR comorbidities:ti,ab OR polymorbidit*:ti,ab OR [mh "Multiple Chronic Conditions"] OR Multiple-Chronic NEXT Illness*:ti,ab OR Multiple-Chronic-Medical NEXT Condition*:ti,ab OR (Multiple NEXT Morbidit*):ti,ab OR Multiple-Chronic NEXT Disease*:ti,ab OR Multiple-Chronic-Health NEXT Condition*:ti,ab OR multimorbidit*:ti,ab OR multi NEXT morbidit*:ti,ab)

AND

([mh "Noncommunicable Diseases"] OR Non-communicable NEXT Disease*:ti,ab OR Noncommunicable NEXT Disease*:ti,ab OR Noninfectious NEXT Disease*:ti,ab OR Non-infectious NEXT Disease*:ti,ab OR non-communicable-chronic NEXT Disease*:ti,ab OR noncommunicable-chronic NEXT Disease*:ti,ab OR [mh "Cardiovascular Diseases"] OR cardiovascular NEXT disease*:ti,ab OR [mh "Lung Diseases, Obstructive"] OR [mh "Lung Diseases"] OR chronic NEXT obstructive:ti,ab OR asthma:ti,ab OR emphysema:ti,ab OR COPD:ti,ab OR CF:ti,ab OR cystic NEXT fibrosis:ti,ab OR bronchitis:ti,ab OR [mh "Neoplasms"] OR neoplasm:ti,ab OR neoplasms:ti,ab OR cancer:ti,ab OR cancers:ti,ab OR tumor:ti,ab OR tumors:ti,ab OR tumour:ti,ab OR tumours:ti,ab OR malignant:ti,ab OR malignancy:ti,ab OR malignancies:ti,ab OR [mh "Diabetes Mellitus"] OR diabetes:ti,ab OR diabetic:ti,ab OR [mh "Mental Disorders"] OR Mental NEXT Disorders:ti,ab OR Mental NEXT Disorder:ti,ab OR [mh "Hypertension"] OR Hypertension:ti,ab)

EMBASE

(('developing country'/exp OR 'developing countr*':ti,ab OR 'developing nation*':ti,ab OR 'developing population*':ti,ab OR 'developing econom*':ti,ab OR 'undeveloped countr*':ti,ab OR 'undeveloped nation*':ti,ab OR 'undeveloped economy':ti,ab OR 'undeveloped economies':ti,ab OR 'least developed countr*':ti,ab OR 'least developed nation*':ti,ab OR 'least developed economy':ti,ab OR 'least developed economies':ti,ab OR 'less-developed countr*':ti,ab OR 'less-developed nation*':ti,ab OR 'less-developed population':ti,ab OR 'less-developed populations':ti,ab OR 'less-developed econom*':ti,ab OR 'lesser developed countr*':ti,ab OR 'lesser developed nation*':ti,ab OR 'lesser developed population':ti,ab OR 'lesser developed populations':ti,ab OR 'lesser developed economy':ti,ab OR 'lesser developed economies':ti,ab OR 'under-developed countr*':ti,ab OR 'under-developed nation*':ti,ab OR 'underdeveloped countr*':ti,ab OR 'underdeveloped nation*':ti,ab OR 'underdeveloped population*':ti,ab OR 'underdeveloped econom*':ti,ab OR 'low income countr*':ti,ab OR 'middle income countr*':ti,ab OR 'low income nation*':ti,ab OR 'middle income nation*':ti,ab OR 'low income population*':ti,ab OR 'middle income population*':ti,ab OR 'low income econom*':ti,ab OR 'middle income econom*':ti,ab OR 'lower income countr*':ti,ab OR 'lower income nation*':ti,ab OR 'lower income population*':ti,ab OR ‘lower income economy’:ti,ab OR ‘lower income economies’:ti,ab OR 'resource limited':ti,ab OR 'low resource countr*':ti,ab OR 'lower resource countr*':ti,ab OR 'low resource nation*':ti,ab OR 'low resource population*':ti,ab OR ‘low resource economy’:ti,ab OR ‘low resource economies’:ti,ab OR 'underserved countr*':ti,ab OR 'underserved nation*':ti,ab OR 'underserved population*':ti,ab OR ‘underserved economy’:ti,ab OR ‘underserved economies’:ti,ab OR ‘under-served country’:ti,ab OR ‘under-served countries’:ti,ab OR ‘under-served nation’:ti,ab OR ‘under-served nations’:ti,ab OR ‘under-served population’:ti,ab OR ‘under-served populations’:ti,ab OR ‘underserved economy’:ti,ab OR ‘underserved economies’:ti,ab OR 'derived countr*':ti,ab OR ‘deprived nation’:ti,ab OR ‘deprived nations’:ti,ab OR 'derived population*':ti,ab OR ‘deprived economy’:ti,ab OR ‘deprived economies’:ti,ab OR 'poor countr*':ti,ab OR 'poor nation*':ti,ab OR 'poor population*':ti,ab OR 'poor econom*':ti,ab OR 'poorer countr*':ti,ab OR 'poorer nation*':ti,ab OR 'poorer population*':ti,ab OR 'poorer econom*':ti,ab OR lmic:ti,ab OR lmics:ti,ab OR lami:ti,ab OR 'transitional countr*':ti,ab OR ‘transitional nation’:ti,ab OR ‘transitional nations’:ti,ab OR 'transitional econom*':ti,ab OR 'transition countr*':ti,ab OR 'transition nation*':ti,ab OR 'transition econom*':ti,ab OR 'low resource setting*':ti,ab OR 'lower resource setting*':ti,ab OR 'middle resource setting*':ti,ab OR 'Third World*':ti,ab

OR

'south asia'/exp OR 'southeast asia'/de OR 'borneo'/exp OR 'cambodia'/exp OR 'indonesia'/exp OR 'laos'/exp OR 'myanmar'/exp OR 'papua new guinea'/exp OR 'thailand'/exp OR 'timor-leste'/exp OR 'viet nam'/exp OR 'yemen'/exp OR 'turkey (republic)'/exp OR 'iraq'/exp OR 'africa south of the sahara'/exp OR 'egypt'/exp OR 'mauritania'/exp OR 'morocco'/exp OR 'tunisia'/exp OR 'fiji'/exp OR 'philippines'/exp OR 'samoan islands'/exp OR 'tonga'/exp OR 'vanuatu'/exp OR 'kiribati'/exp OR 'armenia'/exp OR 'ukraine'/exp OR 'bolivia'/exp OR 'el salvador'/exp OR 'guatemala'/exp OR 'honduras'/exp OR 'nicaragua'/exp OR 'haiti'/exp OR 'kosovo'/exp OR 'kyrgyzstan'/exp OR 'tajikistan'/exp OR 'uzbekistan'/exp OR 'federated states of micronesia'/exp OR 'mongolia'/exp OR 'north korea'/exp OR 'sao tome and principe'/exp OR 'solomon islands'/exp OR 'syrian arab republic'/exp OR 'palestine'/exp OR 'south east asia*':ti,ab OR 'middle east*':ti,ab OR afghan*:ti,ab OR angola*:ti,ab OR armenia*:ti,ab OR

bangladesh*:ti,ab OR benin*:ti,ab OR bhutan*:ti,ab OR birma*:ti,ab OR boliv*:ti,ab OR botswan*:ti,ab OR 'burkina faso*':ti,ab OR burundi*:ti,ab OR 'cabo verde*':ti,ab OR cambod*:ti,ab OR cameroon*:ti,ab OR 'cape verd*':ti,ab OR 'central africa*':ti,ab OR chad*:ti,ab OR comoro*:ti,ab OR congo*:ti,ab OR 'cote d ivoire*':ti,ab OR djibouti*:ti,ab OR 'east africa*':ti,ab OR 'eastern africa*':ti,ab OR egypt*:ti,ab OR 'el salvador*':ti,ab OR 'equatorial guinea*':ti,ab OR eritre*:ti,ab OR ethiopia*:ti,ab OR gabon*:ti,ab OR gambia*:ti,ab OR gaza*:ti,ab OR ghan*:ti,ab OR guatemal*:ti,ab OR guinea*:ti,ab OR haiti*:ti,ab OR hondur*:ti,ab OR india*:ti,ab OR indones*:ti,ab OR 'ivory coast*':ti,ab OR kenya*:ti,ab OR kiribati*:ti,ab OR kosovo*:ti,ab OR kyrgyz*:ti,ab OR 'lao pdr*':ti,ab OR lesotho*:ti,ab OR liberia*:ti,ab OR madagascar*:ti,ab OR malaw*:ti,ab OR mali:ti,ab OR mauritan*:ti,ab OR mauriti*:ti,ab OR micronesi*:ti,ab OR mocambiqu*:ti,ab OR moldov*:ti,ab OR mongolia*:ti,ab OR morocc*:ti,ab OR mozambiqu*:ti,ab OR myanmar*:ti,ab OR namibia*:ti,ab OR nepal*:ti,ab OR nicaragua*:ti,ab OR niger*:ti,ab OR 'northern korea*':ti,ab OR 'north korea*':ti,ab OR pakistan*:ti,ab OR palestin*:ti,ab OR 'papua new guinea*':ti,ab OR philippine*:ti,ab OR principe*:ti,ab OR 'republic of korea*':ti,ab OR rhodesia*:ti,ab OR rwanda*:ti,ab OR samoa*:ti,ab OR 'sao tome*':ti,ab OR senegal*:ti,ab OR 'sierra leone*':ti,ab OR 'solomon islands*':ti,ab OR somalia*:ti,ab OR 'south africa*':ti,ab OR 'south sudan*':ti,ab OR 'southern africa*':ti,ab OR 'sri lanka*':ti,ab OR 'sub saharan africa*':ti,ab OR 'subsaharan africa*':ti,ab OR sudan*:ti,ab OR swaziland*:ti,ab OR syria*:ti,ab OR tajikist*:ti,ab OR tanzan*:ti,ab OR timor*:ti,ab OR togo*:ti,ab OR tonga*:ti,ab OR tunis*:ti,ab OR ugand*:ti,ab OR ukrain*:ti,ab OR uzbekistan*:ti,ab OR vanuatu*:ti,ab OR vietnam*:ti,ab OR 'west africa*':ti,ab OR 'west bank*':ti,ab OR 'western africa*':ti,ab OR yemen*:ti,ab OR zaire*:ti,ab OR zambia*:ti,ab OR zimbabw*:ti,ab)

AND

(‘Comorbidity’/exp OR comorbidity:ti,ab OR comorbidities:ti,ab OR polymorbidit*:ti,ab OR ‘Multiple Chronic Conditions’/exp OR ‘Multiple Chronic Illness*’:ti,ab OR ‘Multiple Chronic Medical Condition*’:ti,ab OR ‘Multiple Morbidit*’:ti,ab OR ‘Multiple Chronic Disease*’:ti,ab OR ‘Multiple Chronic Health Condition*’:ti,ab OR ‘multimorbidit*’:ti,ab OR ‘multi morbidit*’:ti,ab)

AND

(‘Noncommunicable Diseases’/exp OR ‘Non-communicable Disease*’:ti,ab OR ‘Noncommunicable Disease*’:ti,ab OR ‘Noninfectious Disease*’:ti,ab OR ‘Non infectious Disease*’:ti,ab OR ‘Noninfectious Disease’:ti,ab OR ‘Non infectious Disease’:ti,ab OR ‘non communicable chronic Disease*’:ti,ab OR ‘noncommunicable chronic Disease*’:ti,ab OR ‘Cardiovascular Diseases’/exp OR ‘cardiovascular disease*’:ti,ab OR ‘Lung Diseases, Obstructive’/exp OR ‘chronic obstructive’:ti,ab OR asthma:ti,ab OR emphysema:ti,ab OR COPD:ti,ab OR CF:ti,ab OR ‘cystic fibrosis’:ti,ab OR bronchitis:ti,ab OR ‘Neoplasms’/exp OR neoplasm:ti,ab OR neoplasms:ti,ab OR cancer:ti,ab OR cancers:ti,ab OR tumor:ti,ab OR tumors:ti,ab OR tumour:ti,ab OR tumours:ti,ab OR malignant:ti,ab OR malignancy:ti,ab OR malignancies:ti,ab OR ‘Diabetes Mellitus’/exp OR diabetes:ti,ab OR diabetic:ti,ab OR ‘Mental Disorders’/exp OR ‘Mental Disorders’:ti,ab OR ‘Mental Disorder’:ti,ab OR ‘Hypertension’/exp OR Hypertension:ti,ab))

Supplementary File 1
Quality Assessment

Name	Was the research question or objective in this paper clearly stated and appropriate	Was the study population clearly specified and defined	Was the participation rate of eligible persons at least 50%	Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	Was a sample size justification, power description, or variance and effect estimates provided?	For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants	Was the exposure(s) assessed more than once over time?	Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Were the outcome assessors blinded to the exposure status of participants	Was loss to follow-up after baseline 20% or less?	Confounding variables measured and adjusted	Quality Rating	comment
Sum et al 2019	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Afshar et al 2017	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Kumar et al 2015	Yes	Yes	NR	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	NA	Fair	Did not mention how they sampled health centres and households. No information on presence of missing data and its handling.
Mini & Thankappan 2016	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Pati et al 2014[21]	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Agrawal and Agrawal 2016	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Garin et al 2016	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Chen et al 2018	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Pengpid & Pelzer 2017	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	

Lee et al 2015	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Vancampfort et al 2018	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Arokiasamy et al	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Hien et al 2014	Yes	Yes	NR	Yes	Yes	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Islas-Granillo et al 2018	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Poor	Sample size is small and did not do sample size calculation, There is no year of data collection and participants were voluters and not ramdomly selected. No information on missing data handeling
Jovic et al 2016	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	NA	Good	
Jankovic et al 2017	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Price et al 2018	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Nunes et al 2017	Yes	Yes	NR	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Rzewuska et al 2017	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Kunna et al 2017	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Koyanagi et al 2018	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	NA	Good	
Woldesemayat et al 2018	Yes	Yes	Yes	Yes	yes	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Waterhouse et al 2017	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	NA	Good	
Phaswana-Mafuya et al 2013	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	NA	Good	
Vancampfort et al 2018	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Vancampfort et al 2017	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	NA	Good	
Rehr et al 2018	Yes	Yes	NR	Yes	Yes	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Jerliu et al 2013	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	No	No	NA	Yes	Good	
Zhou et al 2018	Yes	Yes	NR	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	NA	Good	
Khanam et al 2011	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Nunes et al 2015	Yes	Yes	NR	Yes	Yes	No	No	Yes	Yes	NA	Yes	No	NA	NA	Good	
Vadrevu et al 2015	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Kumar et al 2015	Yes	Yes	NR	Yes	Yes	No	No	Yes	Yes	NA	Yes	No	NA	NA	Good	
Aye et al 2019	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	

Sum et al 2019	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Boa,et al 2019	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Fair	Did not report how they sampled patient. Sample not representative of the country
Khan et al 2019	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Pati et al 2019	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	NA	Yes	No	NA	Yes	Good	
Ebrahimoghi et al 2019	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	NA	Yes	No	NA	Yes	fair	Excluded drugs that are prescribed for multiple health conditions. Thus, prevalence may be underestimated. There may be bias because some patients may receive medication that are out of IHIO coverage.
Christian et al 2020	Yes	Yes	NR	Yes	NR	No	No	Yes	Yes	NA	Yes	No	NA	Yes	GOOD	
Jawed et al 2020	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	NA	Yes	No	NA	Yes	GOOD	
Nugraha et al 2020	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	NA	Yes	No	NA	Yes	GOOD	

Supplementary Table 1: Predictors of multimorbidity reported in included studies

Author (year)	Age	Sex	Education	Wealth/Income	Working status	Region	Marital status	BMI	Physical activity	Alcohol	Smoking	Fruit and Vegetable	Dietary	Health care use	Health insurance	Self-rated living	Social activity	Skin colour	Private health plan	Quality of life	Active travel
Afshar, et al. 2017	x	x	x																		
Agrawal and Agrawal 2016								x													
Arokiasamy, et al. 2015	x	x	x	x		x	x	x	x	x	x										
Aye, et al. 2019		x	x			x				x	x						x			x	
Chen, et al. 2018	x	x	x							x	x				x	x	x				
Garin, et al. 2016	x	x	x	x		x	x														
Hien, et al. 2014	x	x	x				x														
Jankovic, et al. 2017	x		x			x	x														
Jawed, et al. 2020	x	x						x													
Jerliu, et al. 2013	x	x	x			x										x					
Khan, et al. 2019	x	x	x	x				x	x			x									
Kumar, et al. 2015	x	x	x	x			x														
Kunna, et al. 2017	x	x	x	x	x	x	x	x	x	x	x	x									
Lee, et al. 2015	x	x	x	x		x	x														
Mini & Thankappan 2016	x	x	x	x						x	x										
Nunes, et al. 2017	x	x	x	x		x	x											x	x		
Pati, et al. 2014	x	x	x	x		x	x								x						
Pengpid & Pelzer 2017	x	x	x	x		x			x			x									
Price, et al. 2018	x	x	x	x	x	x			x	x	x										
Rehr, et al. 2018	x	x	x			x															
Rzewuska, et al. 2017	x	x	x			x			x					x							
Vadrevu, et al. 2015	x	x	x		x	x	x				x	x				x					
Vancampfort, et al. 2018	x	x	x	x	x	x	x		x												x
Woldesemayat, et al. 2018	x			x				x	x	x	x										

Supplementary Table 2: Major predictors of multimorbidity reported in included studies

Author & year	Normative category	Reference category	OR/RR	Normative category	Reference category	OR/RR	Normative category	Reference category	OR/RR
	AGE			EDUCATION			INCOME		
Nunes et al. 2017	Continuous variable	NA	1.06 (1.06-1.06)	0 Year	≥ 12 years	1.34 (1.24-1.44)	Highest	Lowest	0.92 (0.84-1.01)
Vancampfort et al. 2018	Continuous variable	NA	1.01 (1.00-1.03)	≤ Pri sch	≥ Sec sch	1.03 (0.85-1.32)	Richest	Poorest	1.06 (0.75-1.45)
Woldesemayat et al. 2018	≥ 45	18–29	4.40 (2.20-8.80)	NA	NA	NA	Rich	Poor	1.20 (0.70-2.10)
Pengpid & Pelzer 2017	≥ 50	18-49	1.83 (1.52-2.21)	Grade 0-5	≥ Grade 12	3.33 (2.56-4.34)	High	Low	0.97 (0.80-1.18)
Rehr et al. 2018	≥ 60	18-39	7.34 (5.15-10.47)	No	Yes	1.75 (1.32-2.32)	NA	NA	NA
Khan et al. 2019	> 60	35-40	8.70 (6.80-11.10)	No formal	≥ Sec sch	0.55 (0.43 - 0.63)	Richest	Poorest	2.10 (1.60-27.00)
Chen et al. 2018	≥ 70	45-49	2.76 (2.03-3.76)	< Pri sch	≥ High sch	0.65 (0.46-0.98)	NA	NA	NA
Hien et al. 2014	≥ 70	60-69	1.65 (1.01-2.68)	No	Yes	0.87 (0.83-1.40)	NA	NA	NA
Lee et al. 2015	≥ 70	18-29	45.62 (27.39-75.39)	No formal	≥ High sch	1.16 (0.88-1.54)	Highest	Lowest	1.47 (1.15-1.89)
Khanam et al. 2011	≥ 70	60-69	1.29 (0.84-1.97)	Illiterate	literate	0.85 (0.54-1.32)	Richest	Poorest	1.93 (1.14-3.27)
Pati et al. 2014	≥ 70	18–29	39.15 (20.72-73.98)	< Pri sch	≥ High sch	0.87 (0.65-1.16)	High	Low	1.35 (0.94-1.95)
Jawed et al. 2020	≥ 70	30-39	1.86 (1.13-3.07)	NA	NA	NA	NA	NA	NA
Vadrevu et al. 2015	≥ 70	40-49	Male: 4.64 (1.74-12.33) Female: 4.77 (1.89-12.06)	No formal	> Sec sch	Male: 1.15 (0.50-2.70) Female: 1.19 (0.34-4.17)	Rich	Poor	Male: 1.08 (0.54-2.12) Female: 1.16 (0.61-2.22)
Jankovic et al. 2017	≥ 70	20-29	Male: 130.46 (75.69-224.86) Female: 166.47 (108.09-256.40)	< Sec sch	≥ Sec sch	Male: 1.27 (1.00-1.60) Female: 2.59 (2.05-3.27)	NA	NA	NA
***‡ Arokiasamy et al. 2015**	≥ 70	18-49	17.96 (15.90-20.55)	No formal	≥ 10 years	1.89 (1.69-2.08)	Highest	Lowest	0.87 (0.77-0.96)
*** Price et al. 2018[34]**	≥ 70	18-29	Male: 72.70 (32.89-160.70) Female: 51.76 (34.42-77.87)	No formal	≥ Sec sch	Male: 0.34 (0.23-0.53) Female: 0.68 (0.51-0.90)	Richest	Poorest	Male: 3.91 (1.91-7.98) Female: 3.96 (2.90-5.39)
Mini & Thankappan 2016	≥ 71	60-70	2.44 (2.19-2.71)	No formal	Formal	0.86 (0.77 - 0.94)	Highest	Lowest	4.68 (3.9-5.62)

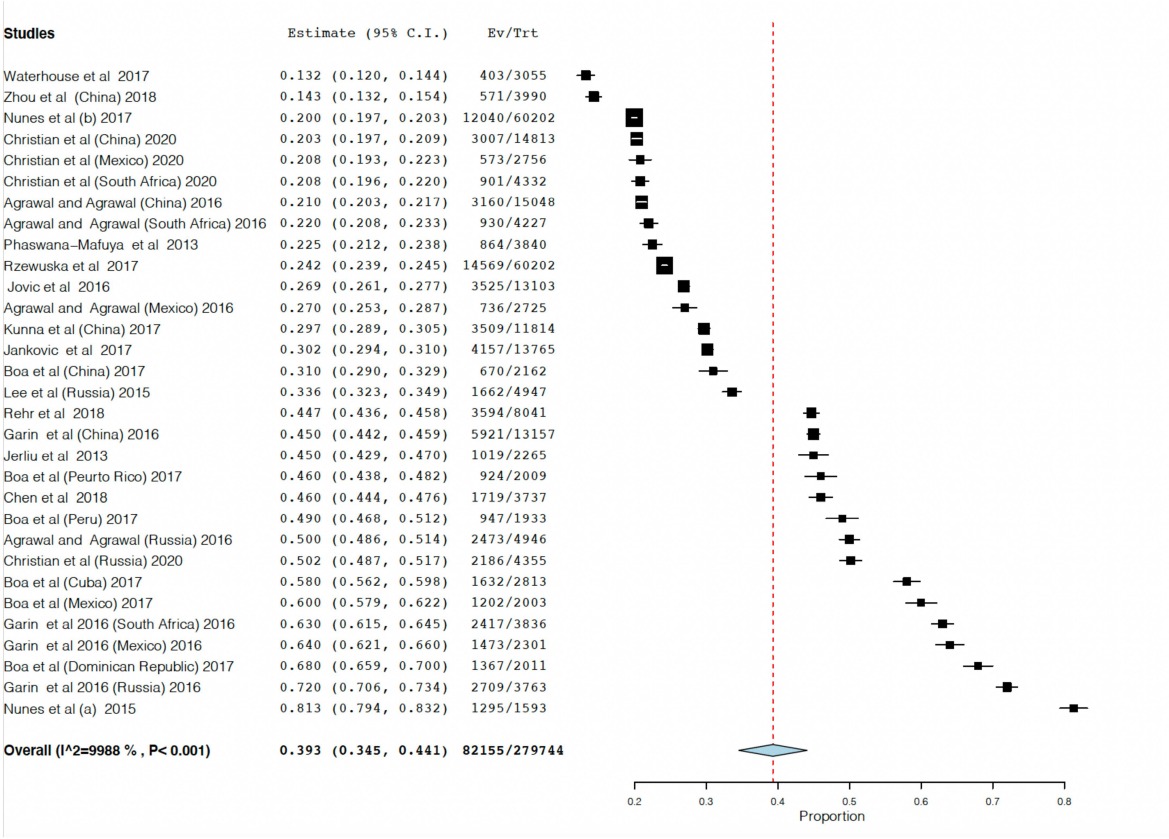
Garin et al. 2016 (China)	≥ 80	50-59	3.38 (2.76-4.14)	< Pri sch	≥ Tertiary	1.20 (0.95-1.53)	Richest	Poorest	0.75 (0.64-0.89)
Garin et al. 2016 (Ghana)	≥ 80	50-59	1.88 (1.44-2.46)	< Pri sch	≥ Tertiary	0.99 (0.64-1.51)	Richest	Poorest	1.83 (1.36-2.47)
Garin et al 2016 (India)	≥ 80	50-59	2.32 (1.54-3.51)	< Pri sch	≥ Tertiary	1.97 (1.33-2.91)	Richest	Poorest	1.06 (0.84-1.35)
Garin et al 2016 (Mexico)	≥ 80	50-59	3.57 (1.89-6.72)	< Pri sch	≥ Tertiary	1.41 (0.55-3.61)	Richest	Poorest	0.79 (0.35-1.75)
Garin et al 2016 (Russia)	≥ 80	50-59	8.73 (4.42-17.23)	< Pri sch	≥ Tertiary	2.89 (1.52-5.49)	Richest	Poorest	1.20 (0.62-2.35)
Garin et al. 2016 (South Africa)	≥ 80	50-59	0.75 (0.45-1.25)	< Pri sch	≥ Tertiary	1.66 (0.89-3.11)	Richest	Poorest	1.89 (1.14-3.13)
† Kunna et al. 2017 (China)	≥ 80	50-59	0.36 ($p < 0.0001$)	University	No formal	- 0.05 ($p \geq 0.05$)	Poorest	Richest	0.10 ($p < 0.0001$)
† Kunna et al. 2017 (Ghana)	≥ 80	50-59	0.10 ($p \leq 0.0001$)	University	No formal	- 0.03 ($p \geq 0.05$)	Poorest	Richest	- 0.11 ($p \leq 0.5$)
Jerliu et al. 2013	≥ 85	65-74	1.81 (1.36-2.39)	0 year	≥ 9 years	1.33 (0.88-2.03)	NA	NA	NA
***Rzewuska et al. 2017**	≥ 85	18-24	6.82 (5.65-9.00)	No formal	Completed superior	1.20 (1.10-1.31)	NA	NA	NA
Afshar et al. 2017 (Africa)	NA	NA	NA	< Pri sch	≥ High sch	1.25 ($p > 0.05$)	NA	NA	NA
Afshar et al. 2017 (Central & South America)	NA	NA	NA	< Pri sch	≥ High sch	1.25 ($p > 0.05$)	NA	NA	NA
Afshar et al. 2017 (Eastern Europe & Central Asia)	NA	NA	NA	< Pri sch	≥ High sch	1.11 ($p > 0.05$)	NA	NA	NA
Afshar et al. 2017 (South Asia)	NA	NA	NA	< Pri sch	≥ High sch	1.66 ($p < 0.001$)	NA	NA	NA
Afshar et al. 2017 (South East Asia)	NA	NA	NA	< Pri sch	≥ High sch	1.00 ($p > 0.05$)	NA	NA	NA
*** Aye et al. 2019**	NA	NA	NA	Illiterate	Graduate	0.48 (0.22-1.05)	NA	NA	NA
	REGION			**SEX**			**MARITAL STATUS**		
Nunes et al. 2017	Urban	Rural	1.14 (1.09-1.25)	Female	Male	1.85 (1.77-1.94)	NA	NA	NA
Pengpid & Pelzer 2017	Urban	Rural	0.81 (0.66-0.98)	Female	Male	2.19 (1.77-2.71)	NA	NA	NA
Rehr et al. 2018	Urban	Rural	1.14 (0.93-1.4)	Female	Male	1.21 (0.97-1.52)	NA	NA	NA
Jerliu et al. 2013	Urban	Rural	1.06 (0.85-1.32)	Female	Male	1.23 (0.98-1.54)	NA	NA	NA
Vancampfort et al. 2018	Urban	Rural	1.37 (1.02-1.84)	Female	Male	1.20 (1.00-1.45)	NA	NA	NA
Pati et al. 2014	Urban	Rural	1.03 (0.79-1.34)	Female	Male	1.19 (0.97-1.47)	Unmarried	Married	0.95 (0.75-1.21)

Garin et al. 2016 (China)	Urban	Rural	1.17 (1.00-1.36)	Female	Male	1.46 (1.35-1.56)	Unmarried	Married	1.12 (0.61-2.03)
Garin et al. 2016 (Ghana)	Urban	Rural	1.29 (1.05-1.58)	Female	Male	1.48 (1.25-1.76)	Unmarried	Married	0.63 (0.32-1.23)
Garin et al. 2016 (India)	Urban	Rural	1.01 (0.79-1.29)	Female	Male	1.42 (1.23-1.64)	Unmarried	Married	1.33 (0.66-2.66)
Garin et al. 2016 (Mexico)	Urban	Rural	1.16 (0.68-1.98)	Female	Male	4.50 (2.43-8.34)	Unmarried	Married	0.26 (0.09-0.73)
Garin et al. 2016 (Russia)	Urban	Rural	0.90 (0.57-1.41)	Female	Male	1.57 (1.01-2.44)	Unmarried	Married	0.74 (0.35-1.56)
Garin et al. 2016 (South Africa)	Urban	Rural	1.46 (1.10-1.93)	Female	Male	1.66 (0.89-3.11)	Unmarried	Married	1.22 (0.84-1.76)
Lee et al. 2015	Urban	Rural	1.55 (1.30-1.85)	Female	Male	1.39 (1.17-1.64)	Unmarried	Married	1.05 (0.89-1.23)
Vadrevu et al. 2015	Urban	Rural	Male: 0.87 (0.81-0.95) Female: 0.93 (0.87-1.00)	Female	Male	1.20 (1.10-1.40)	Unmarried	Married	Male: 0.54 (0.23-1.25) Female: 1.38 (0.79-2.42)
Jankovic et al. 2017	Urban	Rural	Male: 1.19 (1.02-1.39) Female: 1.01 (0.87-1.18)	NA	NA	NA	Unmarried	Married	Male: 1.05 (0.88-1.25) Female: 1.01 (0.86-1.19)
*** Price et al. 2018**	Urban	Rural	Male: 1.91 (1.31-2.78) Female: 1.43 (1.17-1.74)	NA	NA	NA	NA	NA	NA
***Aye et al. 2019**	Urban	Rural	1.28 (1.02-1.61)	Female	Male	2.14 (1.63-2.82)	NA	NA	NA
‡ Arokiasamy et al. 2015	Urban	Rural	1.05 (0.99-1.13)	Female	Male	1.26 (1.17-1.35)	Unmarried	Married	0.86 (0.56-0.71)
† Kunna et al. 2017 (China)	Rural	Urban	0.04 ($p \geq 0.05$)	Female	Male	0.08 ($p \leq 0.05$)	Unmarried	Married	0.12 ($p \leq 0.0001$)
† Kunna et al. 2017 (Ghana)	Rural	Urban	- 0.04 ($p \geq 0.05$)	Female	Male	0.05 ($p \geq 0.05$)	Unmarried	Married	0.03 ($p \geq 0.05$)
Mini & Thankappan 2016	NA	NA	NA	Female	Male	1.51 (1.35-1.69)			
Khanam et al. 2011	NA	NA	NA	Female	Male	3.32 (1.88-5.86)	Unmarried	Married	0.83 (0.47-1.47)
Hien et al. 2014	NA	NA	NA	Female	Male	1.24 (0.66-2.32)	Unmarried	Married	0.65 (0.33-1.25)
Chen et al. 2018	NA	NA	NA	Female	Male	1.20 (0.98-1.49)	NA	NA	NA
Jawed et al. 2020	NA	NA	NA	Female	Male	1.41 (1.12-1.78)	NA	NA	NA
*** Rzewuska et al. 2017**	NA	NA	NA	Female	Male	1.36 (1.29-1.43)	NA	NA	NA
	SMOKING			**PHYSICAL ACTIVITY/EXCERCISE**			**BODY MASS INDEX**		
Chen et al. 2018	Yes	No	1.29 (0.98-1.70)	NA	NA	NA	NA	NA	NA
Mini & Thankappan 2016	Yes	No	1.22 (1.08-1.37)	NA	NA	NA	NA	NA	NA
Woldesemayat et al. 2018	Yes	No	0.40 (0.10-1.67)	No	Yes	0.50 (0.30-1.00)	Obese	Normal	1.40 (0.70-2.70)
***Aye et al. 2019**	Yes	No	0.87 (0.66-1.14)	NA	NA	NA	NA	NA	NA

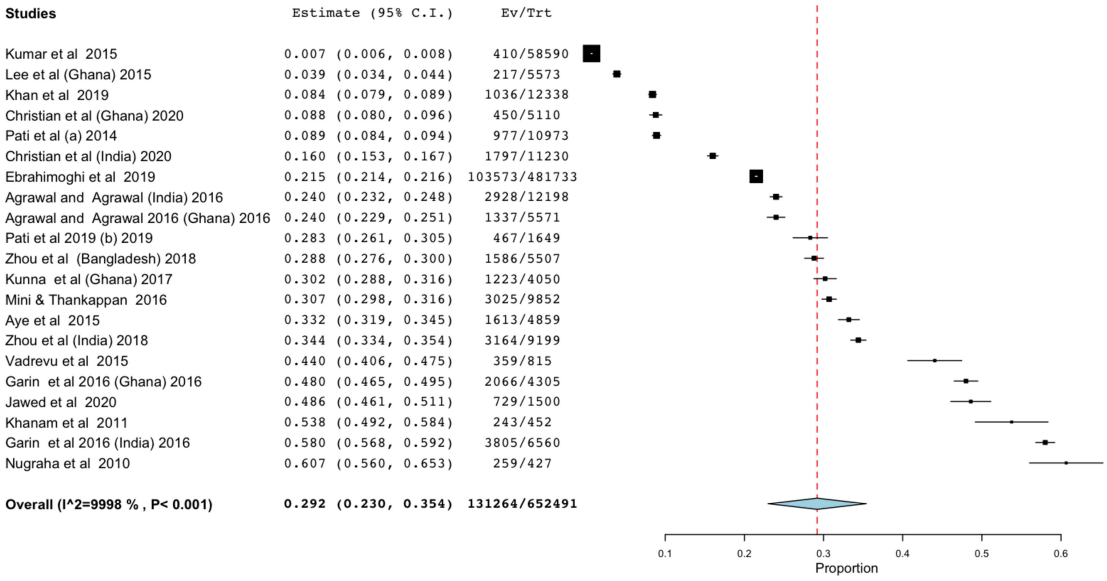
Vadrevu et al. 2015	Yes	No	Male: 1.68 (1.00-2.81) Female: 1.06 (0.08-13.31)	NA	NA	NA	Continuous variable	NA	Male: 1.14 (1.05-1.23) Female: 1.07 (1.00-1.15)
*** Price et al. 2018**	Yes	No	Male: 0.47 (0.24-0.92) Female: 0.46 (0.08-2.75)	Low	High	Male: 1.23 (1.01-1.51) Female: 1.31 (1.00-1.73)	NA	NA	NA
‡ Arokiasamy et al. 2015	Yes	No	1.00 (0.93-1.09)	Low	High	1.14 (1.07-1.23)	Obese	Normal	2.26 (2.00-2.52)
† Kunna et al. 2017 (China)	Yes	No	- 0.05 ($p \geq 0.05$)	Low	High	0.08 ($p \leq 0.0001$)	Obese	Underweight	0.51 ($p < 0.0001$)
† Kunna et al. 2017 (Ghana)	Yes	No	- 0.06 ($p \geq 0.05$)	Low	High	- 0.04 ($p \geq 0.05$)	Obese	Underweight	0.32 ($p \leq 0.0001$)
Pengpid & Pelzer 2017	NA	NA	NA	No	Yes	0.83 (0.68-1.02)	NA	NA	NA
Vancampfort et al. 2018	NA	NA	NA	Low	High	1.67 (1.36-2.05)	NA	NA	NA
Khan et al. 2019	NA	NA	NA	NA	NA	NA	Obese	Normal	2.10 (1.80-2.50)
Agrawal and Agrawal 2016	NA	NA	NA	NA	NA	NA	Obese	Normal	5.78 (3.55-9.40)
Jawed et al. 2020	NA	NA	NA	Low	High	2.00 (0.77-5.00)	Obese	Normal	1.28 (1.00-1.81)
	ALCOHOL CONSUMPTION			**FRUITS AND VEGETABLE CONSUMPTION**					
Woldesemayat et al. 2018	Yes	No	1.30 (0.60-2.90)	NA	NA	NA	NA	NA	NA
Chen et al. 2018	Yes	No	0.80 (0.63-1.02)	NA	NA	NA	NA	NA	NA
Mini & Thankappan 2016	Yes	No	1.53 (1.25-1.89)	NA	NA	NA	NA	NA	NA
***Aye et al. 2019**	Yes	No	1.51 (0.83-2.72)	NA	NA	NA	NA	NA	NA
*** Price et al. 2018**	Yes	No	Male: 0.98 (0.74-1.29) Female: 1.84 (1.42-2.38)	NA	NA	NA	NA	NA	NA
‡ Arokiasamy et al. 2015	Yes	No	1.12 (1.01-1.24)	NA	NA	NA	NA	NA	NA
† Kunna et al. 2017 (China)	Yes	No	0.05 ($p \leq 0.05$)	Insufficient	Sufficient	0.01 ($p \geq 0.05$)	NA	NA	NA
† Kunna et al. 2017 (Ghana)	Yes	No	- 0.01 ($p \geq 0.05$)	Insufficient	Sufficient	0.11 ($p \leq 0.05$)	NA	NA	NA
Khan et al. 2019	NA	NA	NA	< 3 times per week	> 4 times per week	0.77 (0.63-1.00)	NA	NA	NA
Vadrevu et al. 2015	NA	NA	NA	Insufficient	Sufficient	Male: 1.89 (1.00-3.57) Female: 0.52 (0.24-1.15)	NA	NA	NA

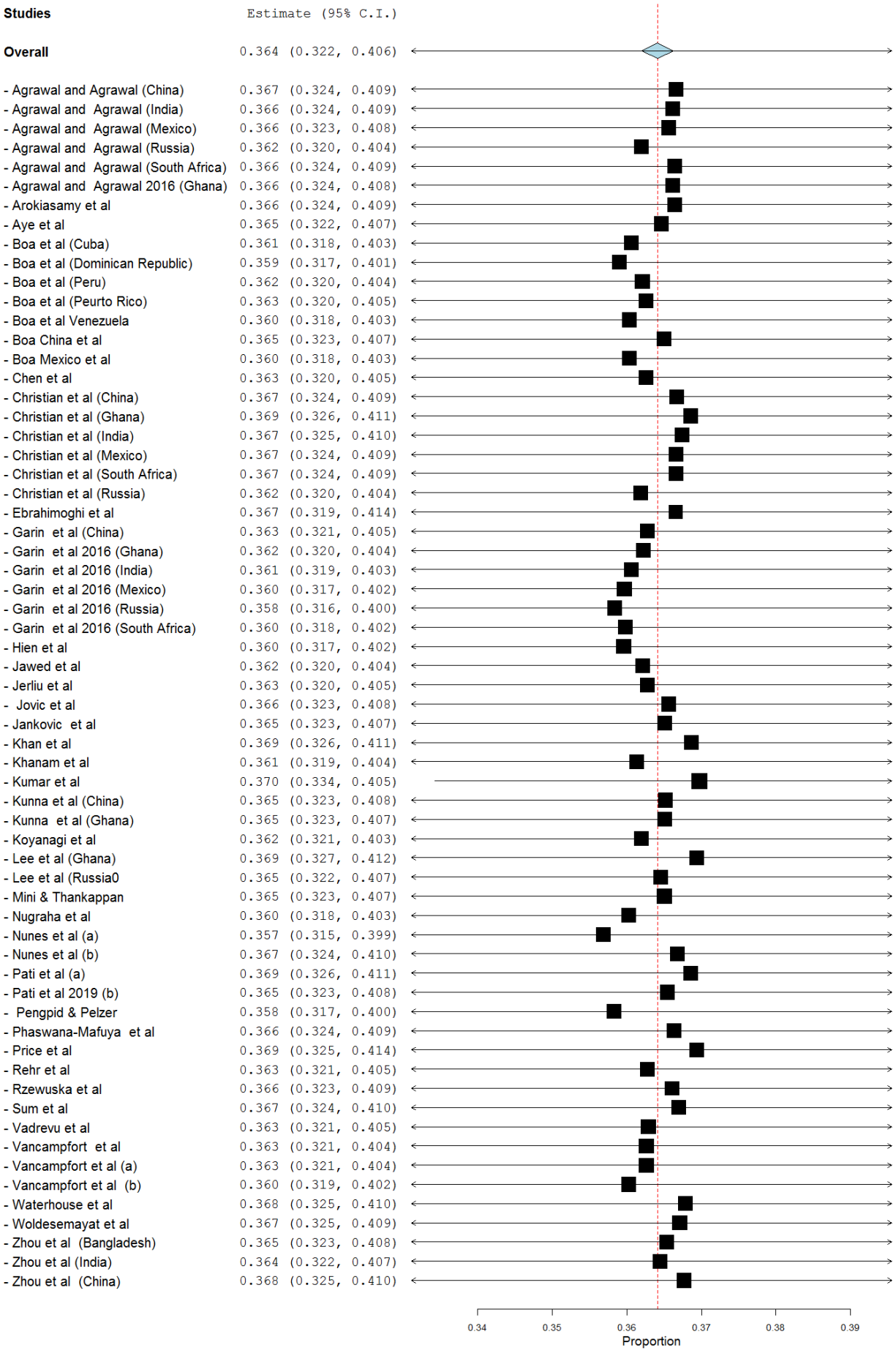
NA = Not applicable. ‡ = Relative risk ratio. † = Marginal effect. * = Prevalence risk/rate ratio. *OR = Odd ratio. Reference = reference category. LCI = Lower confidence interval. UCI = Upper confidence interval. Sch = School. Pri Sch = Primary school. Sec Sch = Secondary School.*

Supplementary Figure 1a: Pooled prevalence of multimorbidity of non-communicable diseases among upper middle-income countries

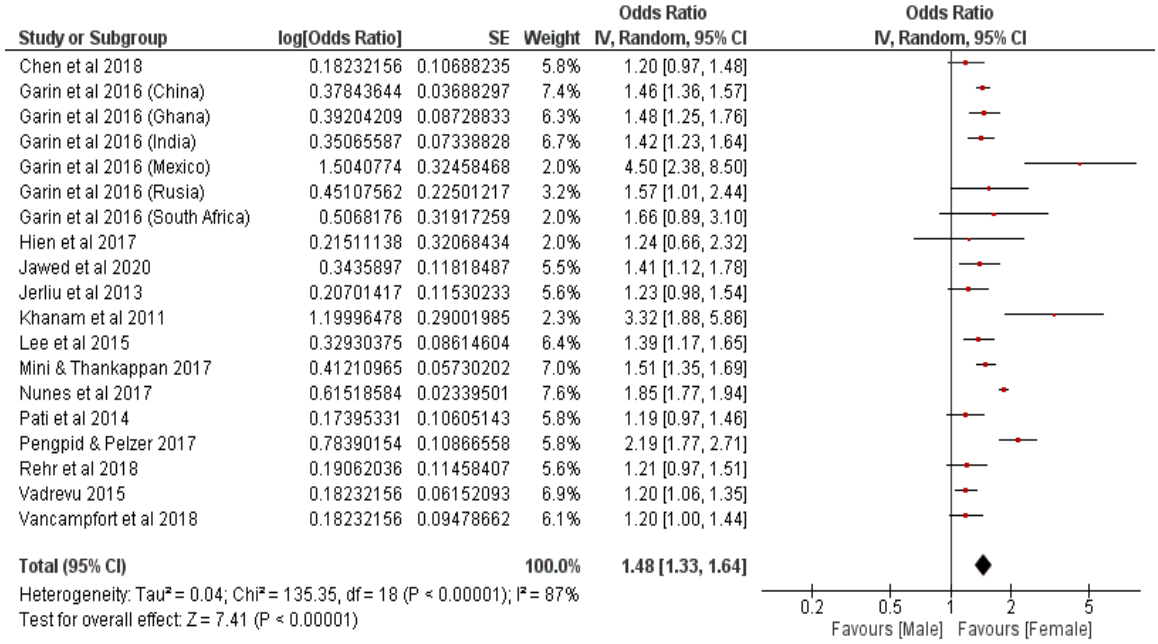


Supplementary Figure 1b: Pooled prevalence of multimorbidity of non-communicable diseases among lower middle-income countries

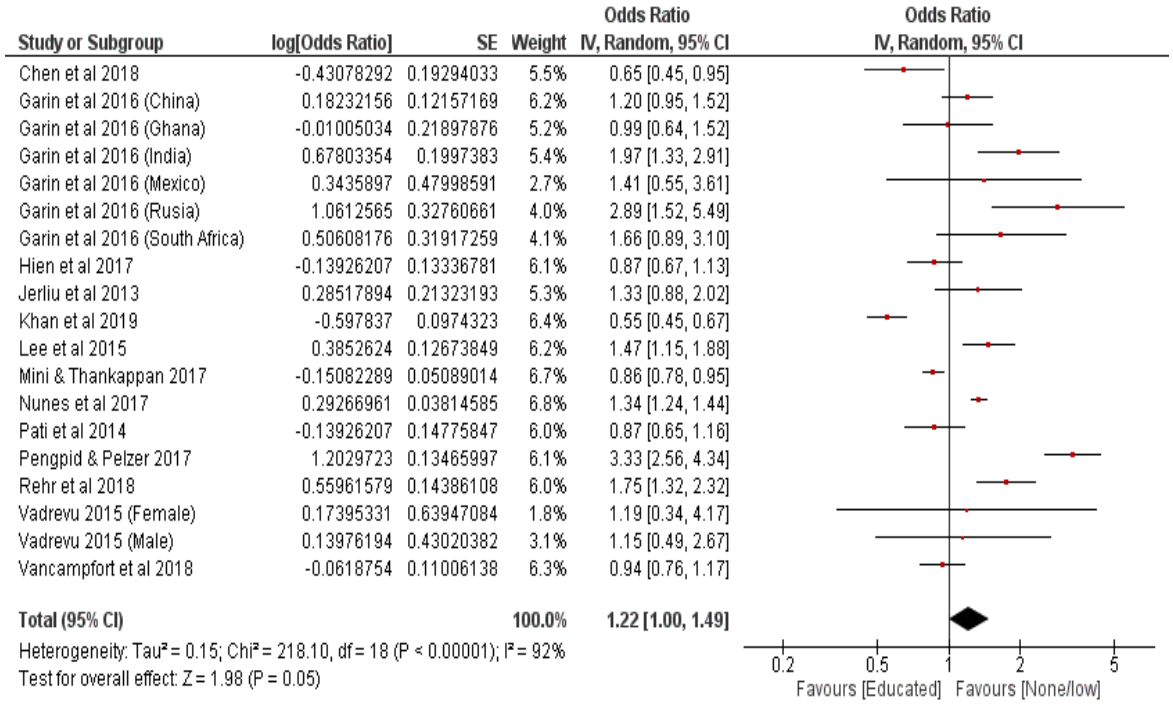



Studies
Estimate (95% C.I.)
Overall 0.364 (0.322, 0.406)
- Agrawal and Agrawal (China) 0.367 (0.324, 0.409)
- Agrawal and Agrawal (India) 0.366 (0.324, 0.409)
- Agrawal and Agrawal (Mexico) 0.366 (0.323, 0.408)
- Agrawal and Agrawal (Russia) 0.362 (0.320, 0.404)
- Agrawal and Agrawal (South Africa) 0.366 (0.324, 0.409)
- Agrawal and Agrawal 2016 (Ghana) 0.366 (0.324, 0.408)
- Arokiasamy et al 0.366 (0.324, 0.409)
- Aye et al 0.365 (0.322, 0.407)
- Boa et al (Cuba) 0.361 (0.318, 0.403)
- Boa et al (Dominican Republic) 0.359 (0.317, 0.401)
- Boa et al (Peru) 0.362 (0.320, 0.404)
- Boa et al (Peurto Rico) 0.363 (0.320, 0.405)
- Boa et al Venezuela 0.360 (0.318, 0.403)
- Boa China et al 0.365 (0.323, 0.407)
- Boa Mexico et al 0.360 (0.318, 0.403)
- Chen et al 0.363 (0.320, 0.405)
- Christian et al (China) 0.367 (0.324, 0.409)
- Christian et al (Ghana) 0.369 (0.326, 0.411)
- Christian et al (India) 0.367 (0.325, 0.410)
- Christian et al (Mexico) 0.367 (0.324, 0.409)
- Christian et al (South Africa) 0.367 (0.324, 0.409)
- Christian et al (Russia) 0.362 (0.320, 0.404)
- Ebrahimoghi et al 0.367 (0.319, 0.414)
- Garin et al (China) 0.363 (0.321, 0.405)
- Garin et al 2016 (Ghana) 0.362 (0.320, 0.404)
- Garin et al 2016 (India) 0.361 (0.319, 0.403)
- Garin et al 2016 (Mexico) 0.360 (0.317, 0.402)
- Garin et al 2016 (Russia) 0.358 (0.316, 0.400)
- Garin et al 2016 (South Africa) 0.360 (0.318, 0.402)
- Hien et al 0.360 (0.317, 0.402)
- Jawed et al 0.362 (0.320, 0.404)
- Jerliu et al 0.363 (0.320, 0.405)
- Jovic et al 0.366 (0.323, 0.408)
- Jankovic et al 0.365 (0.323, 0.407)
- Khan et al 0.369 (0.326, 0.411)
- Khanam et al 0.361 (0.319, 0.404)
- Kumar et al 0.370 (0.334, 0.405)
- Kunna et al (China) 0.365 (0.323, 0.408)
- Kunna et al (Ghana) 0.365 (0.323, 0.407)
- Koyanagi et al 0.362 (0.321, 0.403)
- Lee et al (Ghana) 0.369 (0.327, 0.412)
- Lee et al (Russia0 0.365 (0.322, 0.407)
- Mini & Thankappan 0.365 (0.323, 0.407)
- Nugraha et al 0.360 (0.318, 0.403)
- Nunes et al (a) 0.357 (0.315, 0.399)
- Nunes et al (b) 0.367 (0.324, 0.410)
- Pati et al (a) 0.369 (0.326, 0.411)
- Pati et al 2019 (b) 0.365 (0.323, 0.408)
- Pengpid & Pelzer 0.358 (0.317, 0.400)
- Phaswana-Mafuya et al 0.366 (0.324, 0.409)
- Price et al 0.369 (0.325, 0.414)
- Rehr et al 0.363 (0.321, 0.405)
- Rzewuska et al 0.366 (0.323, 0.409)
- Sum et al 0.367 (0.324, 0.410)
- Vadrevu et al 0.363 (0.321, 0.405)
- Vancampfort et al 0.363 (0.321, 0.404)
- Vancampfort et al (a) 0.363 (0.321, 0.404)
- Vancampfort et al (b) 0.360 (0.319, 0.402)
- Waterhouse et al 0.368 (0.325, 0.410)
- Woldesemayat et al 0.367 (0.325, 0.409)
- Zhou et al (Bangladesh) 0.365 (0.323, 0.408)
- Zhou et al (India) 0.364 (0.322, 0.407)
- Zhou et al (China) 0.368 (0.325, 0.410)
0.34
0.35
0.36
0.37
0.38
0.39
Proportion

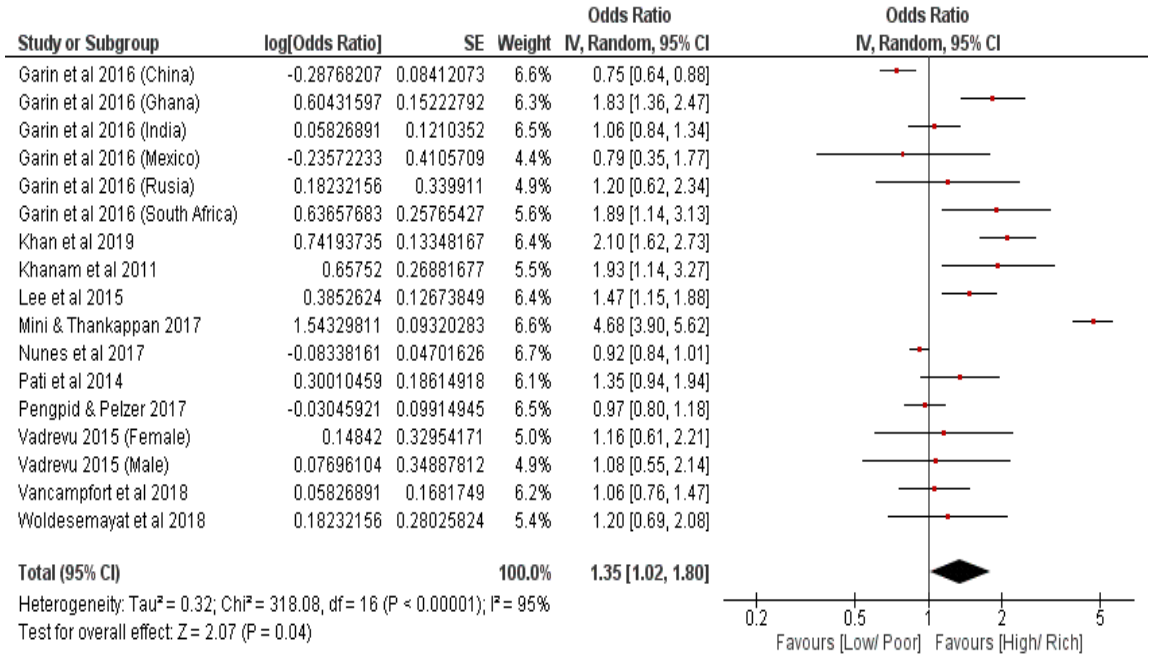
Supplementary Figure 3a: Forest plot of studies reporting odds ratios for the association between sex and multimorbidity



Supplementary Figure 3b: Forest plot of studies reporting odds ratios for the association between education and multimorbidity



Supplementary Figure 3c: Forest plot of studies reporting odds ratios for the association between income/wealth and multimorbidity



Supplementary Figure 3d: Forest plot of studies reporting odds ratios for the association between region/residence and multimorbidity