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Rurality associated with a higher prevalence of multimorbidity in middle-aged and elderly Chinese: findings from the China Health and Retirement Longitudinal Study (2015-2016)

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[Title page]

Title of the article: Rurality associated with higher prevalence of multimorbidity in middle-aged and elderly Chinese: findings from the China Health and Retirement Longitudinal Study (2015-2016)

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Abstract

Background

Epidemiological evidence about multimorbidity in low- and middle-income countries is lacking. We aimed to estimate the prevalence of multimorbidity among middle-aged and older adults in rural and urban China.

Methods

We used a cross-sectional design and data from a nationally representative survey conducted in 2015–2016 among Chinese people aged 45 years or older involving 19,656 participants. Multimorbidity was measured with a cut-off point of having two or more among 14 chronic illnesses. 13 of them were based on self-reported physician diagnosis. In addition, depressive disorders were assessed with the 10-item Center for Epidemiologic Studies Depression Scale (CES-D 10). The weighted prevalence of multimorbidity was calculated, with a non-response adjustment. Multivariate logistic regression was applied to analyze the relationships between covariates and multimorbidity.

Findings

Multimorbidity was highly prevalent (54.3%) among the studied population. Contrary to previous studies, we found the prevalence of multimorbidity to be higher among the rural dwellers (58.3%) than among the urban population (50.4%). After adjustment for covariates, rural residents had 7.5% higher odds (95% CI of odds ratio: [1.003, 1.151]) of having multimorbidity than their urban counterparts. Above 70% of chronic patients above 45 years old have multimorbidity, while 80.6%-97.9% of patients with any of the 14 chronic illnesses have multimorbidity.

Interpretation

Future health system development in China should transform from preventing and controlling non-communicable diseases as individual diseases to addressing people's comprehensive health needs under multimorbidity. The rural population should be prioritized as they suffered more from multimorbidity than the urban population.

[Article summary]

Strengths and limitations of this study

- This is the first study showing that rurality is associated with higher prevalence of middle-aged and elderly Chinese.
- We used nationally representative sample of the people above the age of 45 in China.
- In our measurement of multimorbidity, we have included depression, a highly prevalent and important mental health condition in China but ignored in previous studies.
- We used self-reported measurement for 13 of the 14 chronic illnesses studied, which is likely to cause underreporting as previous studies using administrative data reported higher prevalence of multimorbidity.
- The lower accessibility to health care for chronic illnesses for rural population than for urban population means that the study has probably underestimated the prevalence of multimorbidity rural population.

[Main text]

1. Introduction:

As global life expectance rises, there is an increasing number of middle-aged and elderly with chronic illnesses. The co-occurrence of two or more chronic illnesses within a person is defined as multimorbidity.[1] Multimorbidity is a strong predictor of mortality.[2] It is also associated with reduced functional independence, [3,4] poor quality of life and well-being. [5,6] Multimorbidity also accounts for a disproportionately large share of health care utilizations and expenditures. [7,8] The implications go beyond extra spending. As most health systems were designed based on single diseases, issues, such as poly-pharmacy, pose enormous challenges for care coordination and patients' self-management. [9]

Epidemiological evidence about the situation in low- and middle-income countries is lacking. [10] We conducted a systematic literature search on PubMed and Web of Science for published papers on prevalence of multimorbidity in China on 31 January 2020. We used search terms related to multimorbidity, prevalence and China and did not apply language restrictions. Our search resulted in one systematic review published in 2015 and three more recent papers. Previous work predominantly focused on urban populations. However, the poorer access to quality care than that enjoyed by their urban counterparts [24] means the rural population with chronic illnesses were at a higher risk of developing multimorbidity. The only two papers reporting national prevalence of multimorbidity had serious flaws in neglecting depression[11,12], a most prevalent mental health condition among Chinese [13] and a condition widely used in previous international multimorbidity studies. [14,15].

While lack of scholarly focus on rural multimorbidity hinders the development of equity- and needs-oriented health policies, the neglect of depression means substantial underestimation of the prevalence of multimorbidity and its consequences for health and wellbeing. To address this important gap in knowledge, this paper aimed to provide an estimation of national prevalence of multimorbidity among adults above 45 years old in China with a particular focus on the urban-rural disparity.

2. Methods

Study design and participants

The study used a cross-sectional design and data from the China Health and Retirement Longitudinal Study (CHARLS). The survey is nationally representative and longitudinal, covering adults aged 45 years or older. It includes assessments of social, economic and health circumstances of community residents. The detailed cohort profile was previously published. The participants of CHARLS closely resembled the Chinese national census population in terms of demographic characteristics.[16]

We used data from the latest wave of CHARLS collected in 2015-2016. All participants provided written informed consent, and survey protocols were approved by the Ethics Review Board at Peking University.[16] Of the 19,656 participants, a total of 2751 (14.0%) contained missing observations in variables. In the dataset, a survey weight variable was created using household and individual non-response adjustment.

Measurement of multimorbidity

In line with previous systematic review and studies done in China,[7,14,15] we used a disease count approach

to measure multimorbidity. Following suggested cut-off point, a binary variable of coexistence of two or more chronic diseases/conditions within one individual constituted our main indication of multimorbidity. Partly due to the data restriction, the selection and definition of morbidities varies across previous multimorbidity studies, and no uniform operational measurement exists. We sought to include morbidities that were prevalent, which resulted in a list of 14 chronic illnesses. 13 chronic illnesses (hypertension, diabetes, cancer, lung disease, heart problem, stroke, arthritis, dyslipidemia, liver disease, kidney disease, stomach disease, asthma and memory problem) were assessed based on self-reported diagnosis by a doctor. In addition, depressive disorders were assessed with 10-item Center for Epidemiologic Studies Depression Scale (CES-D 10). In a sensitive analysis, an ordinal measure of multimorbidity (absence or single illness, two illnesses, three illnesses, four illnesses, five illnesses or more) was considered.

Covariates

Demographic and socioeconomic status covariates for this study included age (45-54 years old, 55-64 years old, 65-74 years old, 75 years and above), sex (male or female), educational attainment (illiterate, partial primary school, completed primary school, middle school, and high school or above), marital status (married, otherwise), smoking status (current, former or never), alcohol drinking status (current, former or never), health insurance status (covered or not) and urbanity (urban or rural according to the household registration or *hukou*).

Statistical analysis

Frequencies (percentage) were reported to summarize the distribution of participants' characteristics. Weighted prevalence of individual chronic diseases and multimorbidity was calculated with adjustment of the survey weight. The distribution of multimorbidity by subpopulations was examined by stratified analysis of urbanity, sex and age groups. Multivariate logistic regression was applied to analyze the associations between covariates and the binary outcome of multimorbidity. A sensitivity analysis was conducted using ordered logit regressions to analyze the relationship between the same covariates and the ordinal outcome of multimorbidity.

Results

Table 1 presents the characteristics of the study population and their weighted prevalence of multimorbidity. Among the 19,656 participants, the mean age was 60.2 years, 51.3% were female, and 59.8% were from rural areas. 54.3% of the weighted sample had multimorbidity. Among the remainder, about half (22.8% of the sample) had only one of the 14 conditions, while the other half (22.9%) had none. The prevalence of multimorbidity generally increased as people aged.

Table 1. Characteristics of study population and weighted prevalence of multimorbidity

	N	(%)	Weighted Prevalence †		
			No illness	One illness	Multi-morbidities (≥2)
Total	19,656	(100%)	22.9%	22.8%	54.3%
Age (year)					
45-54	6792	(34.6%)	35.0%	26.3%	38.7%
55-64	6604	(33.6%)	19.3%	23.2%	57.6%
65-74	4310	(21.9%)	13.7%	19.1%	67.1%
≥75	1950	(9.9%)	13.5%	17.6%	68.9%
Sex					
Male	9573	(48.7%)	25.7%	23.9%	50.4%
Female	10083	(51.3%)	20.3%	21.7%	58.0%
Educational level					
Illiterate	4985	(25.4%)	15.8%	22.5%	61.7%
Part of primary school	3252	(16.6%)	14.8%	20.0%	65.2%
Primary school	5352	(27.3%)	32.7%	22.8%	44.5%
Junior middle school	3804	(19.4%)	21.4%	24.0%	54.5%
Senior middle school or above	2237	(11.4%)	25.9%	24.4%	49.7%
Unknown*	26	(0.1%)			
Marital status					
Not in marriage	2666	(13.6%)	15.6%	17.8%	66.6%
Married	16989	(86.4%)	24.2%	23.6%	52.2%
Unknown*	1	(0.0%)			
Smoking					
Current	5568	(28.4%)	25.6%	24.3%	50.1%
Former	3112	(15.9%)	17.8%	20.6%	61.5%
Never	10929	(55.7%)	22.8%	22.7%	54.5%
Unknown*	47	(0.2%)			
Alcohol consumption					
Current	6947	(35.5%)	27.7%	24.8%	47.6%
Former	2213	(11.3%)	13.8%	19.5%	66.7%
Never	10427	(53.2%)	21.3%	22.1%	56.6%
Unknown*	69	(0.4%)			
Health insurance status					
Covered	15406	(90.9%)	16.2%	22.0%	61.7%
Not covered	1549	(9.1%)	20.3%	21.9%	57.7%
Unknown*	2701	(13.7%)			
Urbanity					
Urban	7908	(40.2%)	26.7%	23.0%	50.4%
Rural	11748	(59.8%)	19.2%	22.6%	58.3%

Note: † Individual weight with household and individual non-response adjustment was used to calculate the weighted prevalence. * "Unknown" means that no response from the interviewed participants was recorded for the question.

Figure 1 shows the weighted proportion of population subgroups by number of chronic illnesses, urbanity, sex and age. Except for male above 75 years old, prevalence of multimorbidity was consistently higher among rural population in all age groups in both sexes. Women, no matter urban or rural, were more likely to suffer from multimorbidity in all age groups. People in general were more likely to have more chronic illnesses as they aged. The trends became inconsistent when people became older than 75 years. Detailed prevalence is provided in Appendix Table 1.

[Please insert the image of Figure 1 here.]

Figure 1. Weighted percentage of population subgroups by number of chronic illness, urbanity, sex and age

Table 2 presents the factors associated with multimorbidity. In the multivariate logistic model, older age, being female, not in marriage, without education level of middle school or above, former smoking and alcohol drinking, health insurance coverage, and rural *hukou* were significantly associated with higher odds of having multimorbidity. In particular, after adjusting for age, sex, education, marital status, smoking, alcohol consumption, and insurance coverage, rural residents had 7.5% higher odds (95% CI of odds ratio: [1.003,1.151]) of having multimorbidity than urban residents. In the sensitivity analysis, multivariate ordered logistic model using an ordinal measure of multimorbidity yields similar pattern that rural residents had 6.4% higher likelihood (95% CI of odds ratio: [1.003,1.128]) of having multimorbidity compared with urban residents, adjusted for the same covariates (Appendix Table 2).

Table 2. Odds ratios (OR) for multimorbidity by age, sex, marital status, education, former smoking and alcohol consumption, health insurance status and urbanity

	Logistic Model	
	Odds Ratio	95% CI
Age (year)		
45-54	Reference	
55-64	1.546	[1.428,1.674]
65-74	2.177	[1.982,2.392]
≥75	1.908	[1.676,2.173]
Sex		
Male	Reference	
Female	1.649	[1.484,1.832]
Educational level		
Illiterate	Reference	
Part of primary school	1.150	[1.039,1.274]
Primary school	1.077	[0.974,1.190]
Junior middle school	0.932	[0.840,1.034]
Senior middle school or above	0.838	[0.742,0.947]
Marital status		
Not in marriage	Reference	
Married	0.843	[0.761,0.934]
Smoking		
Current	Reference	

Former	1.478	[1.336,1.634]
Never	0.956	[0.862,1.061]
Alcohol consumption		
Current	Reference	
Former	1.769	[1.575,1.987]
Never	1.061	[0.980,1.150]
Insurance coverage		
Covered	Reference	
Not covered	0.816	[0.730,0.912]
Urbanity		
Urban	Reference	
Rural	1.075	[1.003,1.151]
N	16905	

Note: Logistic model was applied for binary outcome which refers to 1 as coexistence of two or more chronic diseases and/or conditions within one person.

Table 3 reports the prevalence of multimorbidity among patients with one of the 14 conditions. It shows that both urban and rural population with chronic illnesses are predominantly having multimorbidity (80.6%-97.6% in urban population, 84.5%-97.9% in rural population). While prevalence of chronic conditions ranked differently among urban and rural residents, rural patients with one of 13 chronic illnesses studied were more likely to have multimorbidity than urban patients.

Table 3. Prevalence of multimorbidity among patients with one of 14 chronic illnesses

Chronic diseases	Prevalence	Prevalence of multimorbidity		
		Total	Urban	Rural
Arthritis	42.8%	86.7%	86.6%	86.7%
Hypertension	34.6%	86.9%	85.7%	88.1%
Depressive disorders	31.1%	83.0%	80.6%	84.5%
Stomach disease	31.0%	87.3%	84.8%	89.1%
Dyslipidemia	19.8%	91.4%	89.8%	94.2%
Heart problem	18.8%	94.4%	93.3%	95.8%
Lung disease	15.0%	92.8%	92.4%	93.1%
Diabetes	10.9%	94.0%	93.1%	95.4%
Kidney disease	10.2%	94.4%	95.2%	93.7%
Liver disease	7.4%	91.8%	90.2%	93.6%
Asthma	6.0%	97.6%	97.6%	97.7%
Heart problem	3.8%	96.6%	95.4%	97.9%
Memory problem	2.8%	94.6%	94.1%	95.1%
Cancer	1.9%	87.2%	85.2%	89.4%

Note: Individual weight with household and individual non-response adjustment was used to calculate prevalence.

3. Discussion

Our study using nationally representative data revealed a high prevalence (54.3%) of multimorbidity among middle-aged or elderly adults in China. Extrapolating this figure to the entire national population of adults aged 45 or above, we estimate that there are over 240 million middle-aged or elderly Chinese with multimorbidity.[17] Our estimation of multimorbidity prevalence in China is higher than a previous estimation (42.4%) using a similar dataset. The main reason for the difference seems to be our inclusion of depression. As 24.7% of urban residents and 36.8% of rural residents above the age of 45 had depressive symptoms, depression is indeed a highly prevalent condition that merits inclusion in disease counts for multimorbidity. We also found that women were more likely to be multimorbid. In addition, multimorbidity is associated with a range of social and behavioral factors, such as lower education status, former smoking and alcohol consumption, being unmarried or divorced and lacking health insurance coverage. Most people with chronic illnesses are likely to be multimorbid. In other words, chronic illnesses rarely exist in a person as a single morbidity.

We found the prevalence of multimorbidity to be higher among the rural dwellers (58.3%) than among the urban population (50.4%) in 2015. This revised previous finding that urban residents (43%) are more likely to have multimorbidity than rural population (41%).[11] The higher prevalence of multimorbidity among rural residents than among urban residents is shown in almost all age groups in both sexes. Again, our inclusion of depression seemed to be the main reason that resulted in the higher prevalence among rural population in China. We have further shown that multimorbidity is more prevalent among rural patients with 13 of the 14 chronic illnesses studied than their urban counterparts.

Our findings have some important implications. First, given the prevalence of the multimorbidity epidemic and its dominance among chronic patients, it is imperative that China move from its current hospital-centric model with fragmented care across specialties and facilities towards an approach of people-centered integrated care built on strong primary care. Second, since rural population have higher prevalence of multimorbidity, priority for health system transformation (and related research) to address multimorbidity lies in the rural areas, where the needs are the greatest and service providers are less qualified and located more sparsely. Third, within the shorter life expectancy among rural population,[18] they also seem more severely affected by multimorbidity. The impact of multimorbidity on rural people's lives therefore deserves greater attention. Digital health solutions such as telemedicine may be potentially valuable in facilitating support for front-liner providers, patients and their care-givers. Fourth, one out of four Chinese aged 45 or above were affected by chronic physical illnesses and depression, with potentially severe consequences on their wellbeing. It is particularly important that mental health be integrated at an affordable cost to primary care.

The present study has two strengths. First, we used nationally representative sample of the people above the age of 45 in China. Second, we have included depression in our measurement of multimorbidity following the practice suggested in two systematic reviews. [14,15] There are also some limitations of the study. First, we used self-reported measurement for 13 of the 14 chronic illnesses studied. This is likely to cause underreporting as previous studies using administrative data reported higher prevalence of

multimorbidity.[19-21] Second, despite China's recent health system development which extended essential health care coverage to all its population, health care for chronic illnesses is still less accessible for rural population [22]. [24] This is likely to cause underdiagnosis of chronical illnesses in rural areas. Hence, the actual prevalence of rural multimorbidity might be even higher than the current estimate.

4. Conclusion

Our study estimated that over half of Chinese aged 45 years or above have two or more chronic medical conditions. Contrary to previous studies, we have provided clear evidence that multimorbidity is more prevalent among rural population (58.3%) than among their urban counterparts (50.4%). Above 70% of chronic patients have multimorbidity. The prevalence of multimorbidity among patients with any of the 14 chronic illnesses included in this study was even higher and ranged between 80.6% and 97.9%. Critical among the rural-urban disparity in multimorbidity prevalence are depression. Future health system development in China should transform from preventing and controlling non-communicable diseases as individual diseases to addressing people's comprehensive health need under multimorbidity. The priority for such transformation is the rural areas.

Contributorship statement

Jin Xu and Yu He did the literature review. Jin Xu and Xiaochen Ma did the study design. All authors participated in data analysis. Jin Xu and Ma Xiaochen jointly wrote the first drafts, and all authors provided comments and confirmed the finalized version.

Ethics statement

We used data from the China Health and Retirement Longitudinal Study. The survey and protocols were approved by the Peking University Ethics Review Board.

Funding statement

The study is funded by Natural Science Foundation of China (No. 71804004). The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Data sharing statement

All the data in the study are publicly available via the official website of the China Health and Retirement Longitudinal Study (http://charls.pku.edu.cn/).

Patient and Public Involvement statement

Patients and the public were not directly involved in the development of the research question or outcome measures of the study, nor were they involved in study design and execution. There are no plans to disseminate the research to study participants.

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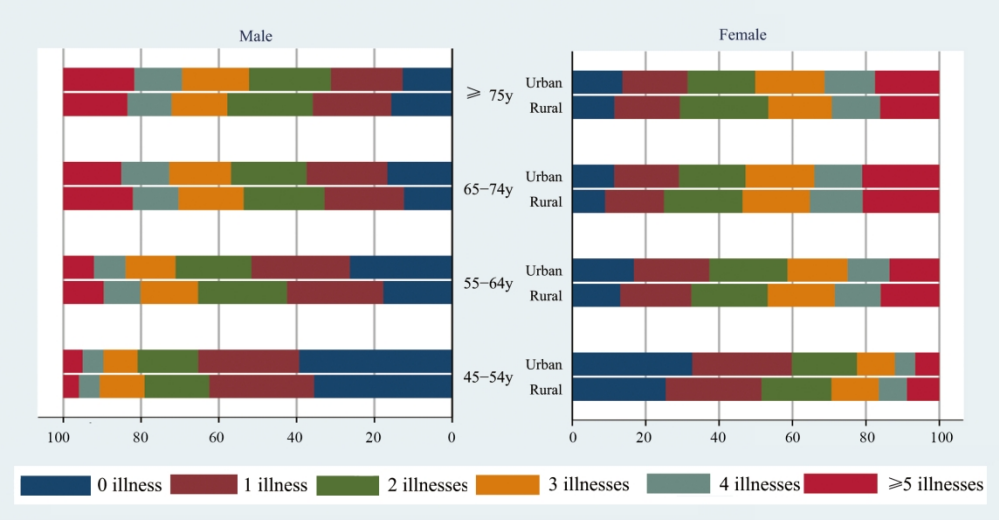

Figure 1. Weighted percentage of population subgroups by number of chronic illness, urbanity, sex and age

180x93mm (300 x 300 DPI)

Appendix Table 1. Weighted prevalence of multimorbidity by sex, urbanity and age group

Panel A. Male	45-54 years old		55-64 years old		65-74 years old		75 years and above old	
	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural
No illness	42.6%	35.3%	29.0%	17.8%	17.5%	12.3%	10.8%	14.4%
Single illness	24.6%	26.7%	25.4%	25.4%	22.8%	20.2%	16.4%	21.1%
Multimorbidity								
Two illnesses	12.9%	17.1%	17.6%	22.6%	18.3%	20.8%	19.9%	21.7%
Three illnesses	11.4%	11.7%	12.4%	15.0%	14.6%	17.5%	26.3%	15.8%
Four illnesses	4.4%	5.2%	8.8%	8.9%	11.2%	11.3%	10.2%	11.2%
Five or more illnesses	4.1%	3.9%	6.8%	10.3%	15.6%	18.0%	16.4%	15.8%
Panel B. Female	45-54 years old		55-64 years old		65-74 years old		75 years and above old	
	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural
No illness	36.9%	25.2%	17.3%	13.5%	16.7%	8.8%	16.6%	12.0%
Single illness	26.9%	27.0%	23.0%	19.0%	17.7%	15.9%	15.1%	18.4%
Multimorbidity								
Two illnesses	17.2%	19.4%	20.5%	21.7%	15.7%	21.3%	23.0%	23.4%
Three illnesses	8.9%	12.6%	16.7%	18.4%	17.1%	18.9%	18.0%	17.1%
Four illnesses	5.0%	7.6%	10.2%	12.2%	11.4%	14.0%	10.7%	13.5%
Five or more illnesses	5.1%	8.3%	12.3%	15.2%	21.4%	21.1%	16.6%	15.7%

Note: Individual weight with household and individual non-response adjustment was used to calculate the weighted prevalence.

Appendix Table 2. Odds ratios (OR) for multimorbidity by age, sex, marital status, education, former smoking and alcohol consumption, health insurance status and urbanity

	Ordered Logistic Model	
	Odds Ratio	95% CI
Age (year)		
45-54	Reference	
55-64	1.545	[1.439,1.659]
65-74	2.238	[2.064,2.426]
≥75	1.885	[1.690,2.103]
Sex	Reference	
Male	1.672	[1.527,1.830]
Female		
Educational level	Reference	
Illiterate	1.177	[1.082,1.281]
Part of primary school	1.109	[1.019,1.206]
Primary school	0.964	[0.882,1.054]
Junior middle school	0.940	[0.844,1.047]
Senior middle school or above		
Marital status	Reference	
Not in marriage	0.850	[0.782,0.924]
Married		
Smoking	Reference	
Current	1.502	[1.379,1.636]
Former	0.940	[0.859,1.029]
Never		
Alcohol consumption	Reference	
Current	1.828	[1.665,2.008]
Former	1.102	[1.028,1.181]
Never		
Health insurance status		
Covered	Reference	
Not covered	0.854	[0.776,0.941]
Urbanity		
Urban	Reference	
Rural	1.064	[1.003,1.128]
N	16905	

Note: Ordered logistic model was applied for five categories outcome which refers to absence or single illness, two illnesses, three illnesses, four illnesses, five illnesses or more.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2	Cross-sectional
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4	
Objectives	3	State specific objectives, including any prespecified hypotheses	4	
Methods				
Study design	4	Present key elements of study design early in the paper	4	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4	
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5	
Bias	9	Describe any efforts to address potential sources of bias	5	
Study size	10	Explain how the study size was arrived at	4	

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable
		(*c*) Explain how missing data were addressed	4
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	Not applicable
		(*e*) Describe any sensitivity analyses	5
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5-6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	*5-6*
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7
		(*b*) Report category boundaries when continuous variables were categorized	6-7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5	
Discussion				
Key results	18	Summarise key results with reference to study objectives	9	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9-10	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9	
Generalisability	21	Discuss the generalisability (external validity) of the study results	9	
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10	Funding Statement

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Rurality associated with a higher prevalence of multimorbidity in middle-aged and elderly Chinese: findings from the China Health and Retirement Longitudinal Study (2015-2016)

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[Title page]

Title of the article: Rurality associated with a higher prevalence of multimorbidity in middle-aged and elderly Chinese: findings from the China Health and Retirement Longitudinal Study (2015-2016)

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Abstract

Background

To address the neglect of depression in multimorbidity measurement and the lack of focus on rural population in previous literature about China, this paper aimed to estimate the prevalence of multimorbidity (including depressive disorders) among the country's rural and urban population.

Methods

We used a cross-sectional design and data from a nationally representative survey conducted in 2015–2016 among Chinese people aged 45 years or older involving 19,656 participants. Multimorbidity was measured with a cut-off point of having two or more among 14 chronic illnesses. 13 of them were based on self-reported physician diagnosis. In addition, depressive disorders were assessed with the 10-item Center for Epidemiologic Studies Depression Scale (CES-D 10). The weighted prevalence of multimorbidity was calculated, with a non-response adjustment. Multivariate logistic regression was applied to analyze the relation between covariates and multimorbidity.

Findings

Multimorbidity was highly prevalent (54.3%) among the studied population. Contrary to previous studies, we found the prevalence of multimorbidity to be higher among the rural dwellers (58.3%) than among the urban population (50.4%). After adjustment for covariates, rural residents had 7.5% higher odds (95% CI of odds ratio: [1.003, 1.151]) of having multimorbidity than their urban counterparts. Above 70% of chronic patients above 45 years old have multimorbidity, while 80.6%-97.9% of patients with any of the 14 chronic illnesses have multimorbidity.

Interpretation

Future health system development in China should transform from preventing and controlling non-communicable diseases as individual diseases to addressing people's comprehensive health needs under multimorbidity. The rural population should be prioritized as they suffered more from multimorbidity than the urban population.

[Article summary]

Strengths and limitations of this study

- This is the first study showing that rurality is associated with higher prevalence of multimorbidity in middle-aged and elderly Chinese.
- We used nationally representative sample of the people above the age of 45 in China.
- In our measurement of multimorbidity, we have included depressive disorders, a highly prevalent and important mental health condition in China but ignored in previous studies.
- We used self-reported measurement for 13 of the 14 chronic illnesses studied, which is likely to cause underreporting as previous studies using administrative data reported higher prevalence of multimorbidity.
- The lower accessibility to health care for chronic illnesses for rural population than for urban population means that the study has probably still underestimated the prevalence of multimorbidity in the rural population.

[Main text]

1. Introduction

As global life expectance rises, there is an increasing number of middle-aged and elderly with chronic disorders, both physical and mental. The co-occurrence of two or more chronic illnesses within a person is defined as multimorbidity.[1] Multimorbidity is a strong predictor of mortality.[2] It is also associated with reduced functional independence,[3,4] poor quality of life and well-being.[5,6] Multimorbidity also accounts for a disproportionately large share of health care utilizations and expenditures.[7,8] The implications go beyond extra spending. As most health systems were designed based on single diseases, issues such as poly-pharmacy pose enormous challenges for care coordination and patients' self-management.[9]

Although populations of low- and middle-income countries (LMICs) are generally younger than those in high-income countries, some major LMICs are ageing at particularly rapid paces. China is a case in point. While it took France almost 150 years for the proportion of people above 60 to increase from 10% to 20%,[10] the same proportion in China increased from 10.3% in 2000 to 17.6% in 2018 (those aged between 45 and 60 also increased from 15.4% to 23.6% during the same time).[11] The limited epidemiological evidence from LMICs gave a wide range of estimated prevalence of multimorbidity, e.g. from 9% to 83% in South Asia.[12] Given the likelihood of multimorbidity as population ages and its serious impact on health and well-being, accurate estimation of the prevalence of multimorbidity is important for LMICs like China.

Noteworthily, there is a higher percentage (20.5%) of old people (aged at or above 60) among the rural Chinese (accounting for 40.4% of all Chinese) than among their urban counterparts (16.1%),[11] likely due to emigration of younger rural adults to the urban area. As findings from a study done in South Africa suggests, multimorbidity may disproportionally affect the less well-off.[13-15] Despite improvement, quality care is less accessible in rural China compared to its urban areas[16], as most rural primary care doctors still lack a full university degree.[17] Therefore, rural adults with chronic illnesses were at a higher risk of developing multimorbidity, meaning it is important particularly to study the rural situation.

We conducted a systematic literature search for published papers on prevalence of multimorbidity in China on 31 January 2020. We used search terms related to multimorbidity, prevalence and China on PubMed and Web of Science and did not apply language restrictions. Our search resulted in one systematic review that reported findings from local areas in China and five papers that covered nation-wide prevalence. The systematic review (published in 2015) showed that most previous work about China focused on urban populations. Among the five papers, one was also restricted to urban population. The other four papers reported national prevalence of multimorbidity among middle-age and elderly Chinese.[18-21] These papers all used the same data set from the China Health and Retirement Longitudinal Study (CHARLS) and reported consistently higher prevalence of multimorbidity among urban population than rural population. Zhao et al. for example reported that rurality was associated with an odds ratio of 0.76 of multimorbidity in people above 50 years old.[21]

These studies have two important limitations. First, measurement of multimorbidity were all based on self-report. This is likely to cause underreporting which disproportionally affects rural population for whom health care is usually less accessible than urban population.[22] Second, these studies had neglected depression,[19-21] a most prevalent mental health condition among Chinese [23] and a condition widely used in previous international multimorbidity studies.[24,25] As Lei et al. reported, prevalence of depressive

symptoms in 2011/2012 was also found to be much higher among rural middle-aged and elderly (35% for men and 49% for women) than among urban ones (23% for men and 35% for women),[26] though other estimation put the range of between 6.3% to 53.6%. Given the higher prevalence of depression among females than males, neglecting depression is also problematic from a gender equity perspective.

Limited scholarly focus on rural multimorbidity, reliance on self-reported diagnosis and neglect of depression all mean potentially substantial underestimation of the prevalence of multimorbidity and its consequences for health and wellbeing, particularly among China's rural population. This knowledge gap profoundly hinders the development of equity- and needs-oriented health policies. Hence, it is important to include investigator-assessed health conditions and measurement of depression with a focus on urban-rural disparity in studies on multimorbidity in China. This paper aimed to provide an updated estimation of national prevalence of multimorbidity among middle-age and older adults in China with the inclusion of depression and through the lens of urban-rural comparison.

2. Methods

Study design and participants

The study used a cross-sectional design and data from the China Health and Retirement Longitudinal Study (CHARLS). The survey is nationally representative and longitudinal, covering adults aged 45 years or older. It includes assessments of social, economic and health circumstances of community residents. The detailed cohort profile was previously published. The participants of CHARLS closely resembled the Chinese national census population in terms of demographic characteristics.[27]

We used data from the latest wave of CHARLS collected in 2015-2016. All participants provided written informed consent, and survey protocols were approved by the Ethics Review Board at Peking University.[27] Of the 19,656 participants, a total of 2751 (14.0%) contained missing observations in variables. To address potential non-response bias, we weighed the samples using a survey weight variable provided by CHARLS, which gave sampled units (households and individuals) weights inversely proportional to their probability of having been selected and responded.[28]

Measurement of multimorbidity

In line with previous systematic review and studies done in China,[7,24,25] we used a disease count approach to measure multimorbidity. Following suggested cut-off point, a binary variable of coexistence of two or more chronic diseases/conditions within one individual constituted our main indication of multimorbidity. Partly due to the data restriction, the selection and definition of morbidities varies across previous multimorbidity studies, and no uniform operational measurement exists. We sought to include morbidities that were prevalent, which resulted in a list of 14 chronic illnesses.

Among these chronic illnesses, 13 (hypertension, diabetes, cancer, lung disease, heart problem, stroke, arthritis, dyslipidemia, liver disease, kidney disease, stomach disease, asthma and memory problem) were assessed based on self-reported diagnosis by a doctor. Participants were asked "have you been diagnosed with [conditions listed below, read by interviewers one by one] by a doctor?" Due to the recent decade of health system reform, most people in China are covered by basic social health insurance and the Essential Public Health Service Scheme that covered the screening and management (e.g. follow-up) of a range of prevalent non-communicable conditions (hypertension, diabetes, severe mental

disorders, breast cancer, etc.[29]). Regular checkup is now universally provided to all elderly above 65 years old. Most also have a community-based primary health care facility in their neighborhood. Access to care is generally good, though quality differs. On average, every Chinese visit health facilities 5.6 times per year in 2015.[30] However, continued urban-rural gaps in health service benefits and access meant that there would likely be underreporting of chronic conditions.[22,31] In addition, depressive disorders were assessed with 10-item Center for Epidemiologic Studies Depression Scale (CES-D 10). We consider the implications of using alongside self-reported physician diagnosis in the discussion section. In a sensitive analysis, an ordinal measure of multimorbidity (absence or single illness, two illnesses, three illnesses, four illnesses, five illnesses or more) was considered.

Covariates

This study used a range of demographic, socioeconomic, behavioral and health insurance covariates, including age group (45-54 years old, 55-64 years old, 65-74 years old, 75 years and above), sex (male or female), marital status (married, otherwise), educational attainment (illiterate, partial primary school, completed primary school, middle school, or high school or above), smoking (current, former or never), alcohol drinking (current, former or never), health insurance status (covered or not), and urbanity (urban vs. rural residence).

Urban or rural residence was measured based on the administrative classification of the participants' basic residing community. The basic rural resident community is a *cun* (literally meaning village), while a basic urban resident community is a *jiedao* (literally meaning street). Rural communities are usually far away from city or county centers, while urban ones are much closers. Equally important as physical distance was the fact that separated social policies applied for urban and rural communities in China. In recent years, entitlement differences between rural and urban areas regarding healthcare and social welfare are being reduced, though substantial pro-urban gaps remain.[32] In 2015, the average annual disposable income of urban residents was 31194.8 *yuan* (6.23 Chinese *yuan* = 1 US dollar in 2015), or 2.73 times that of rural residents (11421.7 *yuan*).[33]

Statistical analysis

Frequencies (percentage) are reported to summarize the distribution of participants' characteristics. Weighted prevalence of individual chronic diseases and multimorbidity was calculated with adjustment using the survey weight. The distribution of multimorbidity by subpopulations was examined by stratified analysis of urbanity, sex and age groups. Multivariate logistic regression was applied to analyze the associations between covariates and the binary outcome of multimorbidity. A sensitivity analysis was conducted using ordered logit regressions to examine the relation between the same covariates and the ordinal outcome of multimorbidity.

3. Results

Table 1 presents the characteristics of the study population and their weighted prevalence of multimorbidity. Among the 19,656 participants, the mean age was 60.2 years, 51.3% were female, and 59.8% were from rural areas. 54.3% of the weighted sample had multimorbidity. Among the remainder, about half (22.8% of the sample) had only one of the 14 conditions, while the other half (22.9%) had none. In other words, 70.4% of all chronic patients had multimorbidity. The prevalence of multimorbidity

generally increased as people aged.

Table 1. Characteristics of study population and weighted prevalence of multimorbidity

	N	(%)	Weighted Prevalence †		
			No illness	One illness	Multi-morbidities (≥2)
Total	19,656	(100%)	22.9%	22.8%	54.3%
Age (year)					
45-54	6792	(34.6%)	35.0%	26.3%	38.7%
55-64	6604	(33.6%)	19.3%	23.2%	57.6%
65-74	4310	(21.9%)	13.7%	19.1%	67.1%
≥75	1950	(9.9%)	13.5%	17.6%	68.9%
Sex					
Male	9573	(48.7%)	25.7%	23.9%	50.4%
Female	10083	(51.3%)	20.3%	21.7%	58.0%
Educational level					
Illiterate	4985	(25.4%)	15.8%	22.5%	61.7%
Part of primary school	3252	(16.6%)	14.8%	20.0%	65.2%
Primary school	5352	(27.3%)	32.7%	22.8%	44.5%
Junior middle school	3804	(19.4%)	21.4%	24.0%	54.5%
Senior middle school or above	2237	(11.4%)	25.9%	24.4%	49.7%
Unknown*	26	(0.1%)			
Marital status					
Not in marriage	2666	(13.6%)	15.6%	17.8%	66.6%
Married	16989	(86.4%)	24.2%	23.6%	52.2%
Unknown*	1	(0.0%)			
Smoking					
Current	5568	(28.4%)	25.6%	24.3%	50.1%
Former	3112	(15.9%)	17.8%	20.6%	61.5%
Never	10929	(55.7%)	22.8%	22.7%	54.5%
Unknown*	47	(0.2%)			
Alcohol consumption					
Current	6947	(35.5%)	27.7%	24.8%	47.6%
Former	2213	(11.3%)	13.8%	19.5%	66.7%
Never	10427	(53.2%)	21.3%	22.1%	56.6%
Unknown*	69	(0.4%)			
Health insurance status					
Covered	15406	(90.9%)	16.2%	22.0%	61.7%
Not covered	1549	(9.1%)	20.3%	21.9%	57.7%
Unknown*	2701	(13.7%)			
Urbanity					
Urban	7908	(40.2%)	26.7%	23.0%	50.4%
Rural	11748	(59.8%)	19.2%	22.6%	58.3%

Note: † Individual weight with household and individual non-response adjustment was used to calculate the weighted

prevalence. * "Unknown" means that no response from the interviewed participants was recorded for the question.

Figure 1 shows the weighted proportion of population subgroups by number of chronic illnesses, urbanity, sex and age. Except for male above 75 years old, prevalence of multimorbidity was consistently higher among rural population in all age groups in both sexes. Women, no matter urban or rural, were more likely to suffer from multimorbidity in all age groups. People in general were more likely to have more chronic illnesses as they aged. The trends became inconsistent when people became older than 75 years. Detailed prevalence is provided in Appendix Table 1.

[Please insert the image of Figure 1 here.]

Figure 1. Weighted percentage of population subgroups by number of chronic illness, urbanity, sex and age

Table 2 presents the factors associated with multimorbidity. In the multivariate logistic model, older age, being female, not in marriage, without education level of middle school or above, former smoking and alcohol drinking, health insurance coverage, and rural residence were significantly associated with higher odds of having multimorbidity. After adjusting for age, sex, education, marital status, smoking, alcohol consumption, and insurance coverage, rural residents had 7.5% higher odds (95% CI of odds ratio: [1.003,1.151]) of having multimorbidity than urban residents. In the sensitivity analysis, multivariate ordered logistic model using an ordinal measure of multimorbidity yields a similar pattern that rural residents had 6.4% higher likelihood (95% CI of odds ratio: [1.003,1.128]) of having multimorbidity compared with urban residents, adjusted for the same covariates (Appendix Table 2).

Table 2. Odds ratios (OR) for multimorbidity by age, sex, marital status, education, former smoking and alcohol consumption, health insurance status and urbanity

	Logistic Model	
	Odds Ratio	95% CI
Age (year)		
45-54	Reference	
55-64	1.546	[1.428,1.674]
65-74	2.177	[1.982,2.392]
≥75	1.908	[1.676,2.173]
Sex		
Male	Reference	
Female	1.649	[1.484,1.832]
Educational level		
Illiterate	Reference	
Part of primary school	1.150	[1.039,1.274]
Primary school	1.077	[0.974,1.190]
Junior middle school	0.932	[0.840,1.034]
Senior middle school or above	0.838	[0.742,0.947]
Marital status		
Not in marriage	Reference	
Married	0.843	[0.761,0.934]
Smoking		
Current	Reference	
Former	1.478	[1.336,1.634]
Never	0.956	[0.862,1.061]
Alcohol consumption		
Current	Reference	
Former	1.769	[1.575,1.987]
Never	1.061	[0.980,1.150]
Insurance coverage		
Covered	Reference	
Not covered	0.816	[0.730,0.912]
Urbanity		
Urban	Reference	
Rural	1.075	[1.003,1.151]
N	16905	

Note: Logistic model was applied for binary outcome which refers to 1 as coexistence of two or more chronic diseases and/or conditions within one person.

Table 3 reports the proportion of people with a given condition amongst the 14 chronic diseases, and the prevalence of multimorbidity among patients with at the given conditions. As much as 42.8% of Chinese at or above 45 years old had arthritis, which was the most prevalent condition. This was followed

by hypertension (34.6%), depressive disorders (31.1%) and stomach disease (31%). Compared to urban residents, rural population were much more likely to be affected by arthritis (rural vs urban = 48.3% vs 36.5%), depressive disorders (36.8% vs 24.7%), while urban population were more likely to have dyslipidemia (26.1% vs 14.3%).

Chronic patients from both urban and rural areas were predominantly having multimorbidity (83.6%-97.6% overall, 80.6%-97.6% in urban population, and 84.5%-97.9% in rural population). Only among kidney disease patients were urban conditional prevalence of multimorbidity higher than rural conditional prevalence of multimorbidity. For any of the remaining 13 types, rural chronic patients were more likely to have multimorbidity than urban ones. The maximal difference between rural and urban conditional prevalence of multimorbidity among chronic patients of any of the 14 types is 4.4 percentage point, observed in dyslipidemia.

Table 3. Prevalence of chronic diseases and conditional prevalence of multimorbidity among patients with at least one of 14 chronic diseases (aged at or above 45 years old)

Chronic diseases	Proportion of patients with at a given condition			Prevalence of multimorbidity among patients with the given condition		
	Total	Urban	Rural	Total	Urban	Rural
Arthritis	42.8%	36.5%	48.3%	86.7%	86.6%	86.7%
Hypertension	34.6%	37.1%	32.3%	86.9%	85.7%	88.1%
Depressive disorders	31.1%	24.7%	36.8%	83.0%	80.6%	84.5%
Stomach disease	31.0%	27.3%	34.2%	87.3%	84.8%	89.1%
Dyslipidemia	19.8%	26.1%	14.3%	91.4%	89.8%	94.2%
Heart problem	18.8%	21.8%	16.0%	94.4%	93.3%	95.8%
Lung disease	15.0%	13.7%	16.1%	92.8%	92.4%	93.1%
Diabetes	10.9%	13.9%	8.3%	94.0%	93.1%	95.4%
Kidney disease	10.2%	10.3%	10.1%	94.4%	95.2%	93.7%
Liver disease	7.4%	8.5%	6.4%	91.8%	90.2%	93.6%
Asthma	6.0%	5.3%	6.7%	97.6%	97.6%	97.7%
Stroke	3.8%	4.3%	3.4%	96.6%	95.4%	97.9%
Memory problem	2.8%	2.8%	2.9%	94.6%	94.1%	95.1%
Cancer	1.9%	2.0%	1.7%	87.2%	85.2%	89.4%

Note: Individual weight with household and individual non-response adjustment was used to calculate prevalence.

4. Discussion

Our study using nationally representative data revealed a high prevalence (54.3%) of multimorbidity among middle-aged or elderly adults in China. Extrapolating this figure to the entire national population of adults aged 45 or above, we estimate that there are over 240 million middle-aged or elderly Chinese with multimorbidity.[34] Our estimation of multimorbidity prevalence among people aged at or above 45 in China is higher than previous estimations (42.4%) using a similar dataset.[19]

The main reason for the difference seems to be our inclusion of depression. As 24.7% of urban residents and 36.8% of rural residents above the age of 45 had depressive symptoms, depression is indeed

a highly prevalent condition that merits inclusion in disease counts for multimorbidity. The level of prevalence is consistent with previous studies using a similar dataset.[26] Of note, the numbers are substantially lower compared to a nation-wide study on mental health using the World Mental Health Composite International Diagnostic Interview developed by the World Health Organization, which reported a 12-month prevalence of 3.6% among all Chinese in 2013.[23] However, the Composite International Diagnostic Interview was found to have high specificity and low sensitivity, thus the tool likely leads to substantial underestimation of the prevalence of depression.[35]

We also found that women were more likely to be multimorbid, consistent with a previous study in China.[19] It is likely due to the fact that women are better at expressing their conditions [36] and take better care of their health by checking out their illnesses with doctors.[37] In addition, multimorbidity is associated with a range of social and behavioral factors, such as lower education status, former smoking and alcohol consumption, being unmarried or divorced and lacking health insurance coverage.

Most chronic patients (70.4%) were likely to be multimorbid. People with a given condition out of our index chronic illnesses were very likely to be multimorbid (83.6%-97.6%). In other words, chronic illnesses rarely existed in a person as a single morbidity. A previous study using claims data found that 82% of all elderly patients (aged at or above 60) covered by Urban Employees Basic Medical Insurance in Beijing had multimorbidity.[38]

Given that conditional prevalence of multimorbidity is very high (i.e. above 83%) among patients with a given condition from the 14 chronic diseases, the most prevalent ones (i.e. arthritis, hypertension, depressive disorders, stomach disease, with a prevalence higher than 30%) seem to have substantially contributed to the high prevalence of multimorbidity. The list of prevalent conditions (arthritis, hypertension, depressive disorders, stomach disease, dyslipidemia, heart problem, lung disease, diabetes, and kidney disease, all with a prevalence above 10%) is very similar with the findings of a systematic review from South Asia,[12] except that the studies included in that systematic review had not counted in depressive disorders, stomach disease and dyslipidemia, which were prevalent in China, and that skin diseases, prevalent in South Asia, were left out in the survey we used.

Physical chronic diseases have also been found associated with an increased risk of depressive symptoms. A previous study using CHARLS data also reported that patients with one, two, and three or more chronic physical conditions were 21%, 66%, and 111% more likely than those without any chronic physical condition to be affected by depressive symptoms.[39] The relation seems to work both ways. Patients with baseline hypertension were more likely to have depressive symptoms than those without hypertension in follow-up surveys, particularly in rural areas.[40] Meanwhile, major depression in the previous year was also found to be associated with an increased risk of ischemic heart disease in Chinese adults, independent of other major cardiovascular risk factors. In terms of access to care, despite reforms aiming at primary care strengthening and development in programs to address non-communicable diseases, there is still much challenge in the quality of primary care that hinders control of prevalent chronic physical conditions like hypertension and diabetes in China.[31,41] Furthermore, mental health service is yet to be well integrated into China's general health system.[42] These health system constraints probably contributed to the coexistence of high prevalence of chronic physical conditions and depression.

We found the prevalence of multimorbidity to be higher among the rural dwellers (58.3%) than among the urban population (50.4%) in 2015. This revised the previously consistent finding that urban residents were more likely to have multimorbidity than rural population.[18,19,21] The higher prevalence of multimorbidity among rural residents than among urban residents was shown in almost all age groups in

both sexes in our study. The rural-urban difference seems to be driven by the high rural prevalence of arthritis, depressive disorders, stomach disease and lung disease. We have further shown that multimorbidity was more prevalent among rural patients with at least one of 13 of the 14 chronic illnesses studied than among their urban counterparts. Again, our inclusion of depression seems to be a main reason that we have found higher prevalence of multimorbidity among rural population than among urban population. Compared to urban population, rural population's lower socio-economic status, poorer childhood health, poorer social services, and poorer access to quality health services (including diagnostic testing), as well as the very nature of rural residence and lifestyle, might all have contributed to their substantially higher prevalence of depression.[26,31,39]

Our findings have some important implications. First, given the prevalence of the multimorbidity epidemic and its dominance among chronic patients, it is imperative that China move from its current hospital-centric model with fragmented care across specialties and facilities towards an approach of people-centered integrated care built on strong primary care. Second, since rural population have higher prevalence of multimorbidity, priority for health system transformation (and related research) to address multimorbidity lies in the rural areas, where the needs are the greatest and service providers are less qualified and located more sparsely. Third, within the shorter life expectancy among rural population,[43] they also seem more severely affected by multimorbidity. The impact of multimorbidity on rural people's lives therefore deserves greater attention. Fourth, one out of four Chinese aged 45 or above were affected by depression and at least one chronic physical disorder. This combination came with potentially severe consequences on their wellbeing.[6] It is particularly important that mental health be integrated at an affordable cost to primary care.

Considering the importance of primary care in addressing multiple diseases in a coordinated and continuous manner, it seems critical to strengthen primary care so that equally good-quality integrated services can be provided to both rural and urban Chinese. Meanwhile, improving physical capacity and human resources at primary care facilities may be a long-term process. Digital health solutions such as telemedicine may be potentially valuable in facilitating support for front-liner providers (by facilitating better communication and information sharing), patients and their care-givers (by providing self-management tools) [44] both in the short term and in the long run. Meanwhile, issues like cost and mobilization of health professionals need to be addressed, for digital health interventions to work at all. As the Chinese government continuously pushed forward the agenda of digital health, how digital health interventions can better address the pro-urban gaps in multimorbidity deserves greater attention. Public finance is needed to allow resources online to flow towards the remote rural areas.

The present study has two strengths. First, we used nationally representative sample of the people above the age of 45 in China. Second, we have included depression in our measurement of multimorbidity following the practice suggested in two systematic reviews.[24,25]

There are also limitations of the study. First, we used self-reported diagnosis by physicians for 13 of the 14 chronic illnesses studied. Despite China's recent health system development which extended essential health care coverage to all its population, health care for chronic illnesses is still less accessible for rural population.[31] Underdiagnosis of chronic illnesses (for example, diabetes) is likely to be higher in rural areas than in urban areas.[22] Hence, the actual urban-rural multimorbidity difference might be even larger than the current estimate.

Second, depression was measured by a scale (i.e. CES-D 10), unlike the other 13 conditions. The main reason is that depression was only available through CES-D 10. As the capacity of mental health

service is weak in China, particularly at the primary care level,[42] depression is likely underdiagnosed in China overall and particularly among rural population. A study has reported that a substantial proportion of rural Chinese women would attribute depressive disorders to social causes and not likely visit a doctor when having depressive disorders.[45] The CES-D 10 scale was validated as a screening instrument for depression [46] and appeared more suitable for our measurement of depression within the constraints of available data. Meanwhile, some had claimed that the scale has high sensitivity (low false negative) but low specificity (high false positive).[47] Hence, we might have over-estimated prevalence of depressive symptoms and its impact on overall prevalence of multimorbidity, though the effects are not likely to differ substantially across urban and rural areas.

5. Conclusion

Our study estimated that over half of Chinese aged 45 years or above have two or more chronic medical conditions. Contrary to previous studies, we have provided clear evidence that multimorbidity is more prevalent among rural population (58.3%) than among their urban counterparts (50.4%). Above 70% of chronic patients aged 45 years or above have multimorbidity. The prevalence of multimorbidity among patients with one of the 14 chronic illnesses included in this study was even higher and ranged between 80.6% and 97.9%. A critical driver of the rural-urban disparity in multimorbidity is the high prevalence of depression in rural areas. Future health system development in China should transform from preventing and controlling non-communicable diseases as individual diseases to addressing people's comprehensive health need under multimorbidity. The priority for such transformation is the rural areas.

Contributorship statement

Jin Xu and Yu He did the literature review. Jin Xu and Xiaochen Ma did the study design. All authors participated in data analysis. Jin Xu, Yu He and Xiaochen Ma jointly wrote the first draft, participated in the revision of the draft and versions of the manuscript. All authors provided comments and confirmed the finalized version.

Ethics statement

We used data from the China Health and Retirement Longitudinal Study. The survey and protocols were approved by the Peking University Ethics Review Board.

Funding statement

The study is funded by Natural Science Foundation of China (No. 71804004). The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Data sharing statement

All the data in the study are publicly available via the official website of the China Health and Retirement Longitudinal Study (http://charls.pku.edu.cn/).

Patient and Public Involvement statement

Patients and the public were not directly involved in the development of the research question or outcome measures of the study, nor were they involved in study design and execution. There are no plans to disseminate the research to study participants.

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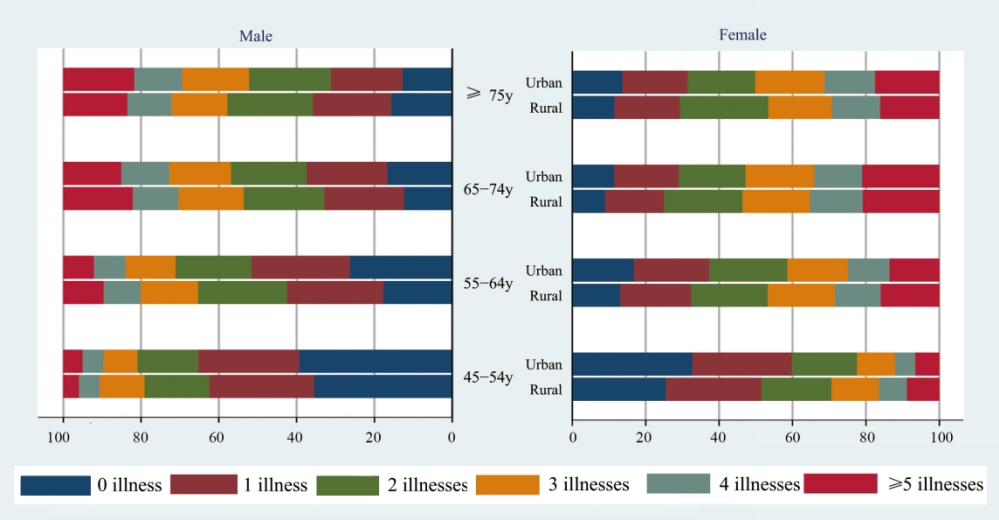

Figure 1. Weighted percentage of population subgroups by number of chronic illness, urbanity, sex and age

180x93mm (300 x 300 DPI)

Appendix Table 1. Weighted prevalence of multimorbidity by sex, urbanity and age group

Panel A. Male	45-54 years old		55-64 years old		65-74 years old		75 years and above old	
	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural
No illness	42.6%	35.3%	29.0%	17.8%	17.5%	12.3%	10.8%	14.4%
Single illness	24.6%	26.7%	25.4%	25.4%	22.8%	20.2%	16.4%	21.1%
Multimorbidity								
Two illnesses	12.9%	17.1%	17.6%	22.6%	18.3%	20.8%	19.9%	21.7%
Three illnesses	11.4%	11.7%	12.4%	15.0%	14.6%	17.5%	26.3%	15.8%
Four illnesses	4.4%	5.2%	8.8%	8.9%	11.2%	11.3%	10.2%	11.2%
Five or more illnesses	4.1%	3.9%	6.8%	10.3%	15.6%	18.0%	16.4%	15.8%
Panel B. Female	45-54 years old		55-64 years old		65-74 years old		75 years and above old	
	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural
No illness	36.9%	25.2%	17.3%	13.5%	16.7%	8.8%	16.6%	12.0%
Single illness	26.9%	27.0%	23.0%	19.0%	17.7%	15.9%	15.1%	18.4%
Multimorbidity								
Two illnesses	17.2%	19.4%	20.5%	21.7%	15.7%	21.3%	23.0%	23.4%
Three illnesses	8.9%	12.6%	16.7%	18.4%	17.1%	18.9%	18.0%	17.1%
Four illnesses	5.0%	7.6%	10.2%	12.2%	11.4%	14.0%	10.7%	13.5%
Five or more illnesses	5.1%	8.3%	12.3%	15.2%	21.4%	21.1%	16.6%	15.7%

Note: Individual weight with household and individual non-response adjustment was used to calculate the weighted prevalence.

Appendix Table 2. Odds ratios (OR) for multimorbidity by age, sex, marital status, education, former smoking and alcohol consumption, health insurance status and urbanity

	Ordered Logistic Model	
	Odds Ratio	95% CI
Age (year)		
45-54	Reference	
55-64	1.545	[1.439,1.659]
65-74	2.238	[2.064,2.426]
≥75	1.885	[1.690,2.103]
Sex	Reference	
Male	1.672	[1.527,1.830]
Female		
Educational level	Reference	
Illiterate	1.177	[1.082,1.281]
Part of primary school	1.109	[1.019,1.206]
Primary school	0.964	[0.882,1.054]
Junior middle school	0.940	[0.844,1.047]
Senior middle school or above		
Marital status	Reference	
Not in marriage	0.850	[0.782,0.924]
Married		
Smoking	Reference	
Current	1.502	[1.379,1.636]
Former	0.940	[0.859,1.029]
Never		
Alcohol consumption	Reference	
Current	1.828	[1.665,2.008]
Former	1.102	[1.028,1.181]
Never		
Health insurance status		
Covered	Reference	
Not covered	0.854	[0.776,0.941]
Urbanity		
Urban	Reference	
Rural	1.064	[1.003,1.128]
N	16905	

Note: Ordered logistic model was applied for five categories outcome which refers to absence or single illness, two illnesses, three illnesses, four illnesses, five illnesses or more.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2	Cross-sectional
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4	
Objectives	3	State specific objectives, including any prespecified hypotheses	4	
Methods				
Study design	4	Present key elements of study design early in the paper	4	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4	
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5	
Bias	9	Describe any efforts to address potential sources of bias	5	
Study size	10	Explain how the study size was arrived at	4	

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable
		(*c*) Explain how missing data were addressed	4
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	Not applicable
		(*e*) Describe any sensitivity analyses	5
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5-6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	*5-6*
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7
		(*b*) Report category boundaries when continuous variables were categorized	6-7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5	
Discussion				
Key results	18	Summarise key results with reference to study objectives	9	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9-10	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9	
Generalisability	21	Discuss the generalisability (external validity) of the study results	9	
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10	Funding Statement

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Urban-Rural Disparity in Prevalence of Multimorbidity in China: A Cross-sectional Nationally Representative Study

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Keywords:	EPIDEMIOLOGY, GERIATRIC MEDICINE, PUBLIC HEALTH, Depression & mood disorders < PSYCHIATRY

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[Title page]

Title of the article: Urban-rural disparity in prevalence of multimorbidity in China: a cross-sectional nationally representative study

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Abstract

Background

To address the neglect of depression in multimorbidity measurement and the lack of focus on rural population in previous literature about China, this paper aimed to estimate the prevalence of multimorbidity (including depressive disorders) among the country's rural and urban population.

Methods

We used a cross-sectional design and data from a nationally representative survey conducted in 2015–2016 among Chinese people aged 45 years or older involving 19,656 participants. Multimorbidity was measured with a cut-off point of having two or more among 14 chronic illnesses. 13 of them were based on self-reported physician diagnosis. In addition, depressive disorders were assessed with the 10-item Center for Epidemiologic Studies Depression Scale (CES-D 10). The weighted prevalence of multimorbidity was calculated, with a non-response adjustment. Multivariate logistic regression was applied to analyze the relation between covariates and multimorbidity.

Findings

Multimorbidity was highly prevalent (54.3%) among the studied population. Contrary to previous studies, we found the prevalence of multimorbidity to be higher among the rural dwellers (58.3%) than among the urban population (50.4%). After adjustment for covariates, rural residents had 7.5% higher odds (95% CI of odds ratio: [1.003, 1.151]) of having multimorbidity than their urban counterparts. Above 70% of chronic patients above 45 years old have multimorbidity, while 80.6%-97.9% of patients with any of the 14 chronic illnesses have multimorbidity.

Interpretation

Future health system development in China should transform from preventing and controlling non-communicable diseases as individual diseases to addressing people's comprehensive health needs under multimorbidity. The rural population should be prioritized as they suffered more from multimorbidity than the urban population.

[Article summary]

Strengths and limitations of this study

- This is the first study showing that rurality is associated with higher prevalence of multimorbidity in middle-aged and elderly Chinese.
- We used nationally representative sample of the people above the age of 45 in China.
- In our measurement of multimorbidity, we have included depressive disorders, a highly prevalent and important mental health condition in China but ignored in previous studies.
- We used self-reported measurement for 13 of the 14 chronic illnesses studied, which is likely to cause underreporting as previous studies using administrative data reported higher prevalence of multimorbidity.
- The lower accessibility to health care for chronic illnesses for rural population than for urban population means that the study has probably still underestimated the prevalence of multimorbidity in the rural population.

[Main text]

1. Introduction

As global life expectance rises, there is an increasing number of middle-aged and elderly with chronic disorders, both physical and mental. The co-occurrence of two or more chronic illnesses within a person is defined as multimorbidity.[1] Multimorbidity is a strong predictor of mortality.[2] It is also associated with reduced functional independence,[3,4] poor quality of life and well-being.[5,6] Multimorbidity also accounts for a disproportionately large share of health care utilizations and expenditures.[7,8] The implications go beyond extra spending. As most health systems were designed based on single diseases, issues such as poly-pharmacy pose enormous challenges for care coordination and patients' self-management.[9]

Although populations of low- and middle-income countries (LMICs) are generally younger than those in high-income countries, some major LMICs are ageing at particularly rapid paces. China is a case in point. While it took France almost 150 years for the proportion of people above 60 to increase from 10% to 20%,[10] the same proportion in China increased from 10.3% in 2000 to 17.6% in 2018 (those aged between 45 and 60 also increased from 15.4% to 23.6% during the same time).[11] The limited epidemiological evidence from LMICs gave a wide range of estimated prevalence of multimorbidity, e.g. from 9% to 83% in South Asia.[12] Given the likelihood of multimorbidity as population ages and its serious impact on health and well-being, accurate estimation of the prevalence of multimorbidity is important for LMICs like China.

Noteworthily, there is a higher percentage (20.5%) of old people (aged at or above 60) among the rural Chinese (accounting for 40.4% of all Chinese) than among their urban counterparts (16.1%),[11] likely due to emigration of younger rural adults to the urban area. As findings from a study done in South Africa suggests, multimorbidity may disproportionally affect the less well-off.[13-15] Despite improvement, quality care is less accessible in rural China compared to its urban areas[16], as most rural primary care doctors still lack a full university degree.[17] Therefore, rural adults with chronic illnesses were at a higher risk of developing multimorbidity, meaning it is important particularly to study the rural situation.

We conducted a systematic literature search for published papers on prevalence of multimorbidity in China on 31 January 2020. We used search terms related to multimorbidity, prevalence and China on PubMed and Web of Science and did not apply language restrictions. Our search resulted in one systematic review that reported findings from local areas in China and five papers that covered nation-wide prevalence. The systematic review (published in 2015) showed that most previous work about China focused on urban populations. Among the five papers, one was also restricted to urban population. The other four papers reported national prevalence of multimorbidity among middle-age and elderly Chinese.[18-21] These papers all used the same data set from the China Health and Retirement Longitudinal Study (CHARLS) and reported consistently higher prevalence of multimorbidity among urban population than rural population. Zhao et al. for example reported that rurality was associated with an odds ratio of 0.76 of multimorbidity in people above 50 years old.[21]

These studies have two important limitations. First, measurement of multimorbidity were all based on self-report. This is likely to cause underreporting which disproportionally affects rural population for whom health care is usually less accessible than urban population.[22] Second, these studies had neglected depression,[19-21] a most prevalent mental health condition among Chinese [23] and a condition widely covered in previous international multimorbidity studies.[24,25] As Lei et al. reported, prevalence of depressive symptoms in 2011/2012 was also found to be much higher among rural middle-aged and

elderly (35% for men and 49% for women) than among urban ones (23% for men and 35% for women),[26] though other estimation arrived at a range between 6.3% to 53.6%. Given the higher prevalence of depression among females than males, neglecting depression is also problematic from a gender equity perspective.

Limited scholarly focus on rural multimorbidity, reliance on self-reported diagnosis and neglect of depression all mean potentially substantial underestimation of the prevalence of multimorbidity and its consequences for health and wellbeing, particularly among China's rural population. This knowledge gap profoundly hinders the development of equity- and needs-oriented health policies. Hence, it is important to include investigator-assessed health conditions and measurement of depression with a focus on urban-rural disparity in studies on multimorbidity in China. This paper aimed to provide an updated estimation of national prevalence of multimorbidity among middle-age and older adults in China with the inclusion of depression and through the lens of urban-rural comparison.

2. Methods

Study design and participants

The study used a cross-sectional design and data from the China Health and Retirement Longitudinal Study (CHARLS). The longitudinal survey covers a nationally representative sample of adults aged 45 years or older. It includes assessments of social, economic and health circumstances of community residents. The detailed cohort profile was previously published. The participants of CHARLS closely resembled the Chinese national census population in terms of demographic characteristics.[27]

We used data from the latest wave of CHARLS collected in 2015-2016. All participants provided written informed consent, and survey protocols were approved by the Ethics Review Board at Peking University.[27] Of the 19,656 participants, a total of 2751 (14.0%) contained missing observations in variables. To address potential non-response bias, we weighed the samples using a survey weight variable provided by CHARLS, which gave sampled units (households and individuals) weights inversely proportional to their probability of having been selected and responded.[28]

Measurement of multimorbidity

In line with previous systematic review and studies done in China,[7,24,25] we used a disease count approach to measure multimorbidity. Following suggested cut-off point, a binary variable of coexistence of two or more chronic diseases/conditions within one individual constituted our main indication of multimorbidity. Partly due to the data restriction, the selection and definition of morbidities varies across previous multimorbidity studies, and no uniform operational measurement exists. We sought to include morbidities that were prevalent, which resulted in a list of 14 chronic illnesses.

Among these chronic illnesses, 13 (hypertension, diabetes, cancer, lung disease, heart problem, stroke, arthritis, dyslipidemia, liver disease, kidney disease, stomach disease, asthma and memory problem) were assessed based on self-reported diagnosis by a doctor. Participants were asked "have you been diagnosed with [conditions listed below, read by interviewers one by one] by a doctor?" Due to the health system reform in the recent decade, most people in China are covered by basic social health insurance and the Essential Public Health Service Scheme that covered the screening and management (e.g. follow-up) of a range of prevalent non-communicable conditions (hypertension, diabetes, severe mental disorders, breast cancer, etc.[29]). Regular checkup is now universally provided to all elderly above

65 years old. Most also have a community-based primary health care facility in their neighborhood. Access to care is generally good, though quality differs. On average, every Chinese visit health facilities 5.6 times per year in 2015.[30] However, continued urban-rural gaps in health service benefits and access meant that there would likely be underreporting of chronic conditions.[22,31] In addition, depressive disorders were assessed with 10-item Center for Epidemiologic Studies Depression Scale (CES-D 10). We consider the implications of using alongside self-reported physician diagnosis in the discussion section. In a sensitive analysis, an ordinal measure of multimorbidity (absence or single illness, two illnesses, three illnesses, four illnesses, five illnesses or more) was considered.

Covariates

This study collected a range of demographic, socioeconomic, behavioral and health insurance covariates, including age group (45-54 years old, 55-64 years old, 65-74 years old, 75 years and above), sex (male or female), marital status (married, otherwise), educational attainment (illiterate, partial primary school, completed primary school, middle school, or high school or above), smoking (current, former or never), alcohol drinking (current, former or never), health insurance status (covered or not), and urbanity (urban vs. rural residence).

Urban or rural residence was measured based on the administrative classification of the participants' basic residing community. The basic rural resident community is a *cun* (literally meaning village), while a basic urban resident community is a *jiedao* (literally meaning street). Rural communities are usually far away from city or county centers, while urban ones are much closers. Equally important as physical distance was the fact that separated social policies applied for urban and rural communities in China. In recent years, entitlement differences between rural and urban areas regarding healthcare and social welfare are being reduced, though substantial pro-urban gaps remain.[32] In 2015, the average annual disposable income of urban residents was 31,194.8 *yuan* (6.23 Chinese *yuan* = 1 US dollar in 2015), or 2.73 times that of rural residents (11,421.7 *yuan*).[33]

Statistical analysis

Frequencies (percentages) are reported to summarize the distribution of participants' characteristics. Weighted prevalence of individual chronic diseases and multimorbidity was calculated with adjustment using the survey weight. The distribution of multimorbidity by subpopulations was examined by stratified analysis of urbanity, sex and age groups. Multivariate logistic regression was applied to analyze the associations between covariates and the binary outcome of multimorbidity. A sensitivity analysis was conducted using ordered logit regressions to examine the relation between the same covariates and the ordinal outcome of multimorbidity.

3. Results

Table 1 presents the characteristics of the study population and their weighted prevalence of multimorbidity. Among the 19,656 participants, the mean age was 60.2 years, 51.3% were female, and 59.8% were from rural areas. 54.3% of the weighted sample had multimorbidity. Among the remainder, about half (22.8% of the sample) had only one of the 14 conditions, while the other half (22.9%) had none. In other words, 70.4% of all chronic patients had multimorbidity. The prevalence of multimorbidity generally increased as people aged.

Table 1. Characteristics of study population and weighted prevalence of multimorbidity

	N	(%)	Weighted Prevalence †		
			No illness	One illness	Multi-morbidities (≥2)
Total	19,656	(100%)	22.9%	22.8%	54.3%
Age (year)					
45-54	6792	(34.6%)	35.0%	26.3%	38.7%
55-64	6604	(33.6%)	19.3%	23.2%	57.6%
65-74	4310	(21.9%)	13.7%	19.1%	67.1%
≥75	1950	(9.9%)	13.5%	17.6%	68.9%
Sex					
Male	9573	(48.7%)	25.7%	23.9%	50.4%
Female	10083	(51.3%)	20.3%	21.7%	58.0%
Educational level					
Illiterate	4985	(25.4%)	15.8%	22.5%	61.7%
Part of primary school	3252	(16.6%)	14.8%	20.0%	65.2%
Primary school	5352	(27.3%)	32.7%	22.8%	44.5%
Junior middle school	3804	(19.4%)	21.4%	24.0%	54.5%
Senior middle school or above	2237	(11.4%)	25.9%	24.4%	49.7%
Unknown*	26	(0.1%)			
Marital status					
Not in marriage	2666	(13.6%)	15.6%	17.8%	66.6%
Married	16989	(86.4%)	24.2%	23.6%	52.2%
Unknown*	1	(0.0%)			
Smoking					
Current	5568	(28.4%)	25.6%	24.3%	50.1%
Former	3112	(15.9%)	17.8%	20.6%	61.5%
Never	10929	(55.7%)	22.8%	22.7%	54.5%
Unknown*	47	(0.2%)			
Alcohol consumption					
Current	6947	(35.5%)	27.7%	24.8%	47.6%
Former	2213	(11.3%)	13.8%	19.5%	66.7%
Never	10427	(53.2%)	21.3%	22.1%	56.6%
Unknown*	69	(0.4%)			
Health insurance status					
Covered	15406	(90.9%)	16.2%	22.0%	61.7%
Not covered	1549	(9.1%)	20.3%	21.9%	57.7%
Unknown*	2701	(13.7%)			
Urbanity					
Urban	7908	(40.2%)	26.7%	23.0%	50.4%
Rural	11748	(59.8%)	19.2%	22.6%	58.3%

Note: † Individual weight with household and individual non-response adjustment was used to calculate the weighted prevalence. * "Unknown" means that no response from the interviewed participants was recorded for the question.

Figure 1 shows the weighted proportion of population subgroups by number of chronic illnesses, urbanity, sex and age. Except for male above 75 years old, prevalence of multimorbidity was consistently higher among rural population in all age groups in both sexes. Women, no matter urban or rural, were more likely to suffer from multimorbidity in all age groups. People in general were more likely to have more chronic illnesses as they aged. The trends became inconsistent when people became older than 75 years. Detailed prevalence is provided in Appendix Table 1.

[Please insert the image of Figure 1 here.]

Figure 1. Weighted percentage of population subgroups by number of chronic illness, urbanity, sex and age

Table 2 presents the factors associated with multimorbidity. In the multivariate logistic model, older age, being female, not in marriage, without education level of middle school or above, former smoking and alcohol drinking, health insurance coverage, and rural residence were significantly associated with higher odds of having multimorbidity. After adjusting for age, sex, education, marital status, smoking, alcohol consumption, and insurance coverage, rural residents had 7.5% higher odds (95% CI of odds ratio: [1.003,1.151]) of having multimorbidity than urban residents. In the sensitivity analysis, multivariate ordered logistic model using an ordinal measure of multimorbidity yields a similar pattern that rural residents had 6.4% higher odds (95% CI of odds ratio: [1.003,1.128]) of having multimorbidity compared with urban residents, adjusted for the same covariates (Appendix Table 2).

Table 2. Odds ratios (OR) for multimorbidity by age, sex, marital status, education, former smoking and alcohol consumption, health insurance status and urbanity

	Logistic Model	
	Odds Ratio	95% CI
Age (year)		
45-54	Reference	
55-64	1.546	[1.428,1.674]
65-74	2.177	[1.982,2.392]
≥75	1.908	[1.676,2.173]
Sex		
Male	Reference	
Female	1.649	[1.484,1.832]
Educational level		
Illiterate	Reference	
Part of primary school	1.150	[1.039,1.274]
Primary school	1.077	[0.974,1.190]
Junior middle school	0.932	[0.840,1.034]
Senior middle school or above	0.838	[0.742,0.947]
Marital status		
Not in marriage	Reference	
Married	0.843	[0.761,0.934]
Smoking		
Current	Reference	
Former	1.478	[1.336,1.634]
Never	0.956	[0.862,1.061]
Alcohol consumption		
Current	Reference	
Former	1.769	[1.575,1.987]
Never	1.061	[0.980,1.150]
Insurance coverage		
Covered	Reference	
Not covered	0.816	[0.730,0.912]
Urbanity		
Urban	Reference	
Rural	1.075	[1.003,1.151]
N	16905	

Note: Logistic model was applied for binary outcome which refers to 1 as coexistence of two or more chronic diseases and/or conditions within one person.

Table 3 reports the proportion of people with a given condition amongst the 14 chronic diseases, and the prevalence of multimorbidity among patients with the given conditions. As much as 42.8% of Chinese at or above 45 years old had arthritis, which was the most prevalent condition. This was followed by hypertension (34.6%), depressive disorders (31.1%) and stomach disease (31%). Compared to urban

residents, rural population were much more likely to be affected by arthritis (rural vs urban = 48.3% vs 36.5%), depressive disorders (36.8% vs 24.7%), while urban population were more likely to have dyslipidemia (26.1% vs 14.3%).

Chronic patients from both urban and rural areas were predominantly having multimorbidity (83.6%-97.6% overall, 80.6%-97.6% in urban population, and 84.5%-97.9% in rural population). Only among kidney disease patients were urban conditional prevalence of multimorbidity higher than rural conditional prevalence of multimorbidity. For any of the remaining 13 types, rural chronic patients were more likely to have multimorbidity than urban ones. The maximal difference between rural and urban conditional prevalence of multimorbidity among chronic patients of any of the 14 types was 4.4 percentage point, observed in dyslipidemia.

Table 3. Prevalence of chronic diseases and conditional prevalence of multimorbidity among patients with at least one of 14 chronic diseases (aged at or above 45 years old)

Chronic diseases	Proportion of patients with a given condition			Prevalence of multimorbidity among patients with the given condition		
	Total	Urban	Rural	Total	Urban	Rural
Arthritis	42.8%	36.5%	48.3%	86.7%	86.6%	86.7%
Hypertension	34.6%	37.1%	32.3%	86.9%	85.7%	88.1%
Depressive disorders	31.1%	24.7%	36.8%	83.0%	80.6%	84.5%
Stomach disease	31.0%	27.3%	34.2%	87.3%	84.8%	89.1%
Dyslipidemia	19.8%	26.1%	14.3%	91.4%	89.8%	94.2%
Heart problem	18.8%	21.8%	16.0%	94.4%	93.3%	95.8%
Lung disease	15.0%	13.7%	16.1%	92.8%	92.4%	93.1%
Diabetes	10.9%	13.9%	8.3%	94.0%	93.1%	95.4%
Kidney disease	10.2%	10.3%	10.1%	94.4%	95.2%	93.7%
Liver disease	7.4%	8.5%	6.4%	91.8%	90.2%	93.6%
Asthma	6.0%	5.3%	6.7%	97.6%	97.6%	97.7%
Stroke	3.8%	4.3%	3.4%	96.6%	95.4%	97.9%
Memory problem	2.8%	2.8%	2.9%	94.6%	94.1%	95.1%
Cancer	1.9%	2.0%	1.7%	87.2%	85.2%	89.4%

Note: Individual weight with household and individual non-response adjustment was used to calculate prevalence.

4. Discussion

Our study using nationally representative data revealed a high prevalence (54.3%) of multimorbidity among middle-aged or elderly adults in China. Extrapolating this figure to the entire national population of adults aged 45 or above, we estimate that there are over 240 million middle-aged or elderly Chinese with multimorbidity.[34] Our estimation of multimorbidity prevalence among people aged at or above 45 in China is higher than previous estimations (42.4%) using a similar dataset.[19]

The main reason for the difference seems to be our inclusion of depression. As 24.7% of urban residents and 36.8% of rural residents above the age of 45 had depressive symptoms, depression is indeed a highly prevalent condition that merits inclusion in disease counts for multimorbidity. The level of prevalence of depression is consistent with previous studies using a similar dataset.[26] Of note, the

numbers are substantially lower compared to a nation-wide study on mental health using the World Mental Health Composite International Diagnostic Interview developed by the World Health Organization, which reported a 12-month prevalence of 3.6% among all Chinese in 2013.[23] However, the Composite International Diagnostic Interview was found to have high specificity and low sensitivity, thus the tool likely leads to substantial underestimation of the prevalence of depression.[35]

We also found that women were more likely to be multimorbid, consistent with a previous study in China.[19] It is likely due to the fact that women are better at expressing their conditions [36] and take better care of their health by checking out their illnesses with doctors.[37] In addition, multimorbidity is associated with a range of social and behavioral factors, such as lower education status, former smoking and alcohol consumption, being unmarried or divorced and lacking health insurance coverage.

Most chronic patients (70.4%) were likely to be multimorbid. People with a given condition out of our index chronic illnesses were very likely to be multimorbid (83.6%-97.6%). In other words, chronic illnesses rarely existed in a person as a single morbidity. A previous study using claims data found that 82% of all elderly patients (aged at or above 60) covered by Urban Employees Basic Medical Insurance in Beijing had multimorbidity.[38]

Given that conditional prevalence of multimorbidity is very high (i.e. above 83%) among patients with a given condition from the 14 chronic diseases, the most prevalent ones (i.e. arthritis, hypertension, depressive disorders, stomach disease, with a prevalence higher than 30%) seem to have substantially contributed to the high prevalence of multimorbidity. The list of prevalent conditions (arthritis, hypertension, depressive disorders, stomach disease, dyslipidemia, heart problem, lung disease, diabetes, and kidney disease, all with a prevalence above 10%) is very similar with the findings of a systematic review from South Asia,[12] except that the studies included in that systematic review had not counted in depressive disorders, stomach disease and dyslipidemia, which were prevalent in China, and that skin diseases, prevalent in South Asia, were left out in the survey we used.

Physical chronic diseases have also been found associated with an increased risk of depressive symptoms. A previous study using CHARLS data also reported that patients with one, two, and three or more chronic physical conditions were 21%, 66%, and 111% more likely than those without any chronic physical condition to be affected by depressive symptoms.[39] The relation seems to work both ways. Patients with baseline hypertension were more likely to have depressive symptoms than those without hypertension in follow-up surveys, particularly in rural areas.[40] Meanwhile, major depression in the previous year was also found to be associated with an increased risk of ischemic heart disease in Chinese adults, independent of other major cardiovascular risk factors. In terms of access to care, despite reforms aiming at primary care strengthening and development in programs to address non-communicable diseases, there is still much challenge in the quality of primary care that hinders control of prevalent chronic physical conditions like hypertension and diabetes in China.[31,41] Furthermore, mental health service is yet to be well integrated into China's general health system.[42] These health system constraints probably contributed to the coexistence of high prevalence of chronic physical conditions and depression.

We found the prevalence of multimorbidity to be higher among the rural dwellers (58.3%) than among the urban population (50.4%) in 2015. This revised the previously consistent finding that urban residents were more likely to have multimorbidity than rural population.[18,19,21] The higher prevalence of multimorbidity among rural residents than among urban residents was shown in almost all age groups in both sexes in our study. The rural-urban difference seems to be driven by the high rural prevalence of arthritis, depressive disorders, stomach disease and lung disease. We have further shown that multimorbidity was more prevalent among rural patients with at least one of 13 of the 14 chronic illnesses

studied than among their urban counterparts. Again, our inclusion of depression seems to be a main reason that we have found higher prevalence of multimorbidity among rural population than among urban population. Compared to urban population, rural population's lower socio-economic status, poorer childhood health, poorer social services, and poorer access to quality health services (including diagnostic testing), as well as the very nature of rural residence and lifestyle, might all have contributed to their substantially higher prevalence of depression.[26,31,39]

Our findings have some important implications. First, given the prevalence of the multimorbidity epidemic and its dominance among chronic patients, it is imperative that China move from its current hospital-centric model with fragmented care across specialties and facilities towards an approach of people-centered integrated care built on strong primary care. Second, since rural population have higher prevalence of multimorbidity, priority for health system transformation (and related research) to address multimorbidity lies in the rural areas, where the needs are the greatest and service providers are less qualified and located more sparsely. Third, within the shorter life expectancy among rural population,[43] they also seem more severely affected by multimorbidity. The impact of multimorbidity on rural people's lives therefore deserves greater attention. Fourth, one out of four Chinese aged 45 or above were affected by depression and at least one chronic physical disorder. This combination came with potentially severe consequences on their wellbeing.[6] It is particularly important that mental health be integrated at an affordable cost to primary care.

Considering the importance of primary care in addressing multiple diseases in a coordinated and continuous manner, it seems critical to strengthen primary care so that equally good-quality integrated services can be provided to both rural and urban Chinese. Meanwhile, improving physical capacity and human resources at primary care facilities may be a long-term process. Digital health solutions such as telemedicine may be potentially valuable in facilitating support for front-liner providers (by facilitating better communication and information sharing), patients and their care-givers (by providing self-management tools) [44] both in the short term and in the long run. Meanwhile, issues like cost and mobilization of health professionals need to be addressed, for digital health interventions to work at all. As the Chinese government continuously pushed forward the agenda of digital health, how digital health interventions can better address the pro-urban gaps in multimorbidity deserves greater attention. Public finance is needed to allow resources online to flow towards the remote rural areas.

The present study has two strengths. First, we used nationally representative sample of the people above the age of 45 in China. Second, we have included depression in our measurement of multimorbidity following the practice suggested in two systematic reviews.[24,25]

There are also limitations of the study. First, we used self-reported diagnosis by physicians for 13 of the 14 chronic illnesses studied. Despite China's recent health system development which extended essential health care coverage to all its population, health care for chronic illnesses is still less accessible for rural population.[31] Underdiagnosis of chronic illnesses (for example, diabetes) is likely to be more common in rural areas than in urban areas.[22] Hence, the actual urban-rural multimorbidity difference might be even larger than the current estimate.

Second, depression was measured by a scale (i.e. CES-D 10), unlike the other 13 conditions. The main reason is that depression was only available through CES-D 10. As the capacity of mental health service is weak in China, particularly at the primary care level,[42] depression is likely underdiagnosed in China overall and particularly among rural population. A study has reported that a substantial proportion of rural Chinese women would attribute depressive disorders to social causes and were not likely to visit a doctor when having depressive disorders.[45] The CES-D 10 scale was validated as a screening

instrument for depression [46] and appeared more suitable for our measurement of depression within the constraints of available data. Meanwhile, some had claimed that the scale has high sensitivity (low false negative) but low specificity (high false positive).[47] Hence, we might have over-estimated prevalence of depressive symptoms and its impact on overall prevalence of multimorbidity, though the effects are not likely to differ substantially across urban and rural areas.

5. Conclusion

Our study estimated that over half of Chinese aged 45 years or above have two or more chronic medical conditions. Contrary to previous studies, we have provided clear evidence that multimorbidity is more prevalent among rural population (58.3%) than among their urban counterparts (50.4%). Above 70% of chronic patients aged 45 years or above have multimorbidity. The prevalence of multimorbidity among patients with one of the 14 chronic illnesses included in this study was even higher and ranged between 80.6% and 97.9%. A critical driver of the rural-urban disparity in multimorbidity is the high prevalence of depression in rural areas. Future health system development in China should transform from preventing and controlling non-communicable diseases as individual diseases to addressing people's comprehensive health need under multimorbidity. The priority for such transformation is the rural areas.

Contributorship statement

Jin Xu and Yu He did the literature review. Jin Xu and Xiaochen Ma did the study design. All authors participated in data analysis. Jin Xu, Yu He and Xiaochen Ma jointly wrote the first draft, participated in the revision of the draft and versions of the manuscript. All authors provided comments and confirmed the finalized version.

Ethics statement

We used data from the China Health and Retirement Longitudinal Study. The survey and protocols were approved by the Peking University Ethics Review Board.

Funding statement

The study is funded by Natural Science Foundation of China (No. 71804004). The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Competing interests

None declared.

Data sharing statement

All the data in the study are publicly available via the official website of the China Health and Retirement Longitudinal Study (http://charls.pku.edu.cn/).

Patient and Public Involvement statement

Patients and the public were not directly involved in the development of the research question or outcome measures of the study, nor were they involved in study design and execution. There are no plans to disseminate the research to study participants.

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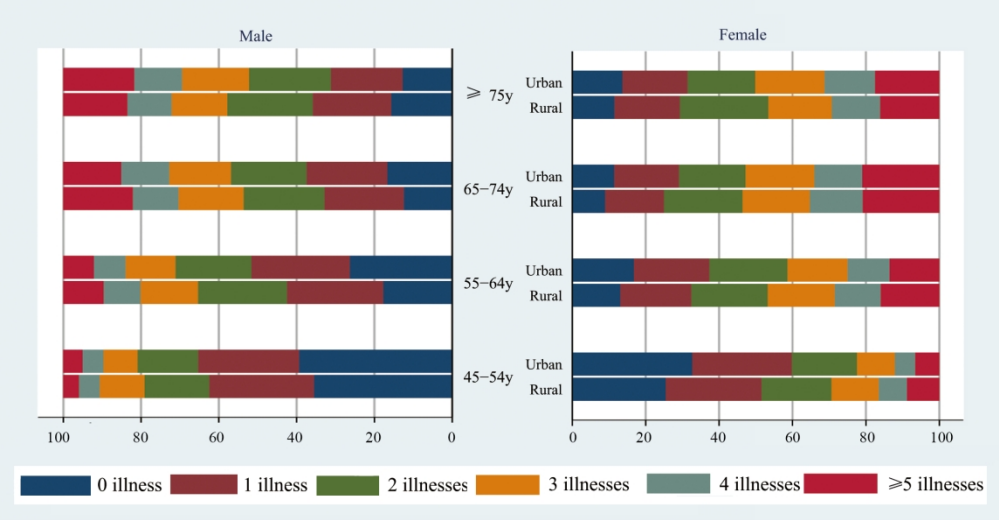

Figure 1. Weighted percentage of population subgroups by number of chronic illness, urbanity, sex and age

180x93mm (300 x 300 DPI)

Appendix Table 1. Weighted prevalence of multimorbidity by sex, urbanity and age group

Panel A. Male	45-54 years old		55-64 years old		65-74 years old		75 years and above old	
	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural
No illness	42.6%	35.3%	29.0%	17.8%	17.5%	12.3%	10.8%	14.4%
Single illness	24.6%	26.7%	25.4%	25.4%	22.8%	20.2%	16.4%	21.1%
Multimorbidity								
Two illnesses	12.9%	17.1%	17.6%	22.6%	18.3%	20.8%	19.9%	21.7%
Three illnesses	11.4%	11.7%	12.4%	15.0%	14.6%	17.5%	26.3%	15.8%
Four illnesses	4.4%	5.2%	8.8%	8.9%	11.2%	11.3%	10.2%	11.2%
Five or more illnesses	4.1%	3.9%	6.8%	10.3%	15.6%	18.0%	16.4%	15.8%
Panel B. Female	45-54 years old		55-64 years old		65-74 years old		75 years and above old	
	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural
No illness	36.9%	25.2%	17.3%	13.5%	16.7%	8.8%	16.6%	12.0%
Single illness	26.9%	27.0%	23.0%	19.0%	17.7%	15.9%	15.1%	18.4%
Multimorbidity								
Two illnesses	17.2%	19.4%	20.5%	21.7%	15.7%	21.3%	23.0%	23.4%
Three illnesses	8.9%	12.6%	16.7%	18.4%	17.1%	18.9%	18.0%	17.1%
Four illnesses	5.0%	7.6%	10.2%	12.2%	11.4%	14.0%	10.7%	13.5%
Five or more illnesses	5.1%	8.3%	12.3%	15.2%	21.4%	21.1%	16.6%	15.7%

Note: Individual weight with household and individual non-response adjustment was used to calculate the weighted prevalence.

Appendix Table 2. Odds ratios (OR) for multimorbidity by age, sex, marital status, education, former smoking and alcohol consumption, health insurance status and urbanity

	Ordered Logistic Model	
	Odds Ratio	95% CI
Age (year)		
45-54	Reference	
55-64	1.545	[1.439,1.659]
65-74	2.238	[2.064,2.426]
≥75	1.885	[1.690,2.103]
Sex	Reference	
Male	1.672	[1.527,1.830]
Female		
Educational level	Reference	
Illiterate	1.177	[1.082,1.281]
Part of primary school	1.109	[1.019,1.206]
Primary school	0.964	[0.882,1.054]
Junior middle school	0.940	[0.844,1.047]
Senior middle school or above		
Marital status	Reference	
Not in marriage	0.850	[0.782,0.924]
Married		
Smoking	Reference	
Current	1.502	[1.379,1.636]
Former	0.940	[0.859,1.029]
Never		
Alcohol consumption	Reference	
Current	1.828	[1.665,2.008]
Former	1.102	[1.028,1.181]
Never		
Health insurance status		
Covered	Reference	
Not covered	0.854	[0.776,0.941]
Urbanity		
Urban	Reference	
Rural	1.064	[1.003,1.128]
N	16905	

Note: Ordered logistic model was applied for five categories outcome which refers to absence or single illness, two illnesses, three illnesses, four illnesses, five illnesses or more.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2	Cross-sectional
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4	
Objectives	3	State specific objectives, including any prespecified hypotheses	4	
Methods				
Study design	4	Present key elements of study design early in the paper	4	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4	
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5	
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5	
Bias	9	Describe any efforts to address potential sources of bias	5	
Study size	10	Explain how the study size was arrived at	4	

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable
		(*c*) Explain how missing data were addressed	4
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	Not applicable
		(*e*) Describe any sensitivity analyses	5
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5-6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	*5-6*
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7
		(*b*) Report category boundaries when continuous variables were categorized	6-7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5	
Discussion				
Key results	18	Summarise key results with reference to study objectives	9	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9-10	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9	
Generalisability	21	Discuss the generalisability (external validity) of the study results	9	
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10	Funding Statement

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.