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Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-024268
Article Type:	Research
Date Submitted by the Author:	18-May-2018
Complete List of Authors:	zhang, ran; China Pharmaceutical University, School of International Pharmaceutical Business Lu, Yun; China Pharmaceutical University, School of International Pharmaceutical Business Shi, Liuyan; China Pharmaceutical University, School of International Pharmaceutical Business Chang, Feng; China Pharmaceutical University, School of International Pharmaceutical Business
Keywords:	multimorbidity, cross-sectional study, Prevalence, Observed-to-expected ratio, China

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Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data

Author		*E-mail*	*ORCID ID*
First author	Ran Zhang	ranzai7@126.com	0000-0002-4142-805X
Co-authors	Yun Lu	luyun20159@163.com	0000-0002-7928-7176
Co-authors	Liuyan Shi	juliasmithsly@163.com	0000-0001-6965-3235
Corresponding author	Feng Chang	cpucf@163.com	0000-0003-2689-4041

Postal address: 639 Longmian Road, Jiangning District, Nanjing, Jiangsu Province, 211198

Telephone number: +86-13805153128 (Feng Chang)

Department: School of International Pharmaceutical Business

Institution: China Pharmaceutical University

City: Nanjing, Jiangsu Province

Country: China

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ABSTRACT

Objectives: To examine the prevalence and patterns of multimorbidity among the elderly in China.

Design: The cross-sectional study.

Setting: More than 10,000 households in 28 of the 34 provinces of mainland China.

Participants: 11707 Chinese adults aged over 60.

Primary outcome measures: Prevalence and patterns of multimorbidity of these participants. Relative risks were calculated to estimate the probability of chronic conditions coexisting with other chronic diseases. Observed-to-expected ratios were used to analyze the patterns of multimorbidity.

Results: Multimorbidity was present in 43.6% respondents of the sample, with women having greater prevalence compared to men. 804 different comorbidity combinations were identified, including 76 dyad combinations and 169 triad combinations. The top 10 morbidity dyads and triads accounted for 69.01% and 47.05% of the total dyad and triad combinations respectively. Among the fourteen chronic conditions included in the study, asthma, stroke, heart attack and other six chronic conditions were the main components of multimorbidity due to their high relative risk ratios. The most frequently occurring clusters with higher O/E ratios were stroke and emotional, nervous, or psychiatric problems and memory-related diseases, emotional, nervous, or psychiatric problems and memory-related diseases and asthma, and chronic lung diseases and asthma.

Conclusions: The results of this study highlighted the high prevalence of multimorbidity in the elderly population. Further studies are required to dig into the etiology of multimorbidity and future primary healthcare policies should take multimorbidity into consideration.

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Strengths and limitations of this study

Strengths

- This is the first study to estimate the prevalence, patterns of multimorbidity among the elderly in China using data from a nationally representative survey.
- We examined the gender patterns associated with the most common clusters of chronic conditions.

Limitations

- Limitations of this study are the time lag since the data were collected from the 2015 CHARLS.
- The chronic diseases included in the study are predefined and not comprehensive enough.

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INTRODUCTION

Multimorbidity, the simultaneous occurrence of two or more chronic conditions in an individual, is increasingly becoming the norm and was reported to increase progressively with age. [1, 2] At present, with China's aging population and increasing prevalence of chronic conditions, multimorbidity among the elderly imposes an enormous societal cost due to increased mortality rates and healthcare utilization. However, to date, researches on chronic conditions in China are focused on a single disease and the coexistence of multiple chronic conditions has not been investigated systematically and thoroughly.

There are significant differences in the etiological analysis between patients with a single chronic condition and those with multimorbidity. [3] The coexistence of chronic conditions in a patient is more than a random event. It is more likely to be due to the causal relationship between diseases and the pathogenic factors they share.[4, 5] Moreover, the interactions between diseases or between disease and organism result in differences in severity of multimorbidity and functional status and prognosis of patients with multimorbidity.[6] Consequently, it is urgent for China to begin research on multimorbidity for the cost-effective treatments it may lead to.[7] The purpose of this study is therefore to determine the prevalence of multimorbidity among the elderly in China and to reveal morbidity combinations, which may benefit the design and implementation of a healthcare system directed to patients with multimorbidity.

METHODS

Data source

Data for this study were collected from the third-wave of China Health and Retirement Longitudinal Survey (CHARLS), which is the most current data available. CHARLS, a nationally representative longitudinal survey of Chinese residents aged 45 and older, was conducted by the Chinese Center for Disease Control and Prevention and Peking University to help China to adjust to rapid ageing of its population through evaluation of social, economic, and health circumstances on the community level using data collected by interviews, physical measurements and blood sample collection.[8] The national baseline survey began in 2011 and involved 17 708 respondents scattered

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in 150 county-level units, 450 village-level units, and approximately 10,000 households. Thereafter, CHARLS respondents were followed every 2 years with their informed consent and the study was approved by Peking University Biomedical Ethics Committee (IRB00001052-14013-exemption).

For the current study, we used data on gender, age and health status from the section of the general health status and disease history of senior citizens in the 2015 CHARLS, which covered the following 14 common chronic health problems: hypertension, dyslipidemia (high blood lipids or low cholesterol), diabetes or elevated blood glucose (including impaired glucose tolerance and fasting blood glucose), cancer (excluding mild skin cancer), chronic lung disease such as chronic bronchitis or emphysema, pulmonary heart disease (excluding tumor or cancer), liver disease (other than fatty liver, tumor, or cancer), heart disease (such as myocardial infarction, coronary heart disease, angina pectoris, congestive heart failure and other heart diseases), stroke, kidney disease (excluding tumors or cancer), stomach or other digestive diseases (excluding tumor or cancer), emotional and mental problems, memory-related diseases (such as Alzheimer's disease, brain atrophy, Parkinson's disease), arthritis or rheumatism, and asthma. All these data were based on self-reports.

Variables

The independent variables in the analysis were: age, sex, number of chronic diseases. Since in China people over 60 were considered as senior citizens, we only included respondents aged over 60 in the sample. In this study, multimorbidity was defined as the coexistence of more than one of the 14 chronic conditions with acute or subacute forms of certain conditions being excluded.

Statistical analysis

To detect the demographic characteristics of patients with multimorbidity, respondents were divided into two groups: those with multiple chronic conditions (MCC group) and those without multiple chronic conditions (Non-MCC group). Descriptive statistics were calculated and expressed as means (SD) and frequencies (percentage). Adjusted prevalence in the MCC group and the non-MCC group were calculated separately.

The most common clusters of chronic diseases were identified by estimating the prevalence of morbidity dyads and triads. We also calculated the relative risk of

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comorbidity for individual chronic conditions and observed-to-expected ratio (O/E ratio) for chronic condition combinations according to VAN DEN's analysis method.[9] Relative risk of comorbidity is the ratio of the number of people with a certain chronic condition who suffer from multimorbidity to the number of patients with the same disease who do not suffer from multimorbidity.[10, 11] In other words, a higher RR value means a higher probability that the disease coexists with other diseases. But it should be noted that there is no direct relationship between relative risk of comorbidity and the prevalence of diseases. [12, 13] Observed-to-expected ratios were used to estimate the conditional probability of coexistence of two or three chronic conditions. [9]

All analyses in this study was done using STATA SE(StataCorp).

p Values <0.05 were considered statistically significant.

RESULTS

Characteristics of participants

The data were gathered from the third-wave of CHARLS. After exclusion of participants with incomplete data related to these fourteen chronic conditions, 11,707 respondents with available information on related chronic diseases were included in this study. The mean age for the sample was 70.5 (range from 60 to 107) which consisted of 5,705 (48.7%) males and 5,993 (51.2%) females. The demographic characteristics of sample respondents are presented in Table 1.

Table 1 Demographic characteristics of all respondents, the MCC group and non-MCC group (adjusted for the 2015 Chinese population)

	All respondents	MCC group	Non-MCC group	P*
Number of people	11707	5107	6600	
Proportion (%)	100%	43.62%	56.38%	
Mean age				
All respondents (SD)	70.20(7.907)	70.57(7.701)	69.91(8.051)	<0.001
Male (SD)	69.97(7.575)	70.50(7.348)	69.60(7.707)	<0.001
Female (SD)	70.39(8.189)	70.62(7.892)	70.19(8.359)	<0.001
Gender（% females）	51.28%	54.41%	48.83%	<0.001
Mean number of chronic conditions				

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All respondents（SD）	1.57(1.560)	3.01(1.259)	0.45(0.498)	<0.001
Male（SD）	1.47(1.534)	2.98(1.265)	0.44(0.496)	<0.001
Female（SD）	1.65(1.581)	3.03(7.982)	0.47(0.499)	<0.001

SD = standard deviation;

p* = statistical significance of the difference between the MCC and the non-MCC sample (t-tests were performed for comparison of means, and chi-square-tests for differences between percentages)

As expected, patients in the MCC group were generally older than those belonged to the non-MCC group. The prevalence of multimorbidity of females was higher compared to men (54.41% vs 45.59%), which could be explained by the longer average life expectancy of women. [14, 15] Figure 1 shows the number and proportion of respondents over 60 according to morbidity numbers. It can be seen that among all the participants aged over 60, 43.6% suffer from multimorbidity. Considering that the prevalence of these fourteen chronic diseases in the elderly population in China has reached 69.10%, multimorbidity would be a major problem faced by the health care system.

Prevalence of chronic conditions

Adjusted prevalence of chronic conditions in the entire sample, the MCC group and the non-MCC group are shown in figure 2.The prevalence of all fourteen chronic conditions in MCC group were all over 10%, significantly higher than that in the entire sample. For instance，the prevalence of arthritis or rheumatism, hypertension, stomach or other digestive disease, heart disease and chronic lung disease in the entire sample were 38.49%, 26.41%, 24.52%, 12.32% and 12.32% respectively, compared to 65.97%, 48.82%, 45.86%, 29.00% and 24.97% in MCC group.

Table 2 shows the relative risks of comorbidity for the 14 chronic diseases. It can be seen from the table that the overall relative risks for asthma, stroke, heart disease and other six conditions were all above ten, which meant these diseases were ten times easier to coexist with other chronic conditions and lead to multimorbidity. In addition, the relative risks for certain diseases were positively associated with gender. For example, men had significantly higher relative risks for asthma yet lower relative risks

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for diabetes or high blood sugar compared to women.

Table 2 Reletive risks of multimorbidity for different chronic conditions according to gender

Chronic conditions	All respondents	Female	Male
High relative risk of multimorbidity			
Asthma	31.77	23.13	32.86
Stroke	22.60	17.94	19.82
Heart disease	18.88	15.65	14.61
Diabetes or high blood sugar	17.47	17.41	10.72
Dyslipidemia	17.05	14.42	13.54
Memory-related disease	16.61	14.07	12.58
Kidney disease	14.04	15.30	9.08
Liver disease	13.46	14.00	9.25
Chronic lung diseases	11.97	10.37	9.47
Low relative risk of multimorbidity			
Emotional, nervous, or psychiatric problems	9.00	7.14	7.62
Stomach or other digestive disease	6.96	6.00	5.30
Hypertension	6.52	5.25	5.53
Cancer or malignant tumor	5.92	5.24	3.73
Arthritis or rheumatism	4.65	3.81	3.79

Common multimorbidity combinations

804 possible comorbidity combinations were identified in the MCC group after statistical analysis, including 76 dyad combinations and 169 triad combinations. The leading 10 most frequently occurring morbidity dyads and triads were presented respectively in table 3 and table 4.

Table3 Adjusted prevalence of the 10 most common morbidity dyads

Ranking	Morbidity dyads	Prevalence			Mean Age	Proportion
		All respondents	male	female		
1	Arthritis or rheumatism and Stomach or other digestive disease	4.73%	38.63%	61.37%	69.20	23.33%
2	Arthritis or rheumatism and	2.85%	39.64%	60.36%	71.25	14.06%

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	Hypertension					
3	Arthritis or rheumatism and Chronic lung diseases	1.13%	55.30%	44.70%	71.55	5.56%
4	Hypertension and heart problems	1.03%	50.00%	50.00%	71.80	5.05%
5	Hypertension and Stomach or other digestive disease	0.89%	48.08%	51.92%	69.07	4.38%
6	Hypertension and Dyslipidemia	0.86%	48.51%	51.49%	68.58	4.25%
7	Arthritis or rheumatism and heart problems	0.76%	35.96%	64.04%	70.72	3.75%
8	Arthritis or rheumatism and Kidney disease	0.64%	58.67%	41.33%	68.24	3.16%
9	Hypertension and Diabetes or high blood sugar	0.58%	44.12%	55.88%	70.97	2.86%
10	Chronic lung diseases and Asthma	0.53%	62.90%	37.10%	71.15	2.61%

Table 4 Adjusted prevalence of the 10 most common morbidity triads

Ranking	Morbidity triads	Prevalence			Mean Age	Proportion
		All respondents	male	female		
1	Arthritis or rheumatism, Stomach or other digestive disease and Hypertension	1.19%	45.08%	54.92%	70.96	10.14%
2	Arthritis or rheumatism, Stomach or other digestive disease and Chronic lung diseases	0.82%	34.53%	65.47%	70.82	7.00%
3	Arthritis or rheumatism, Heart disease and Hypertension	0.63%	60.42%	39.58%	69.93	5.40%
4	Arthritis or rheumatism, Heart disease and Stomach or other digestive disease	0.59%	29.73%	70.27%	71.51	5.03%
5	Hypertension, Dyslipidemia and Arthritis or rheumatism	0.44%	21.74%	78.26%	70.13	3.79%

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6	Hypertension, Dyslipidemia and Heart problems	0.42%	36.54%	63.46%	71.17	3.57%
7	Arthritis or rheumatism ,Kidney disease and Stomach or other digestive disease	0.42%	42.86%	57.14%	70.14	3.57%
8	Arthritis or rheumatism, Asthma and Chronic lung diseases	0.40%	48.98%	51.02%	69.18	3.43%
9	Hypertension, Dyslipidemia and Diabetes or high blood sugar	0.35%	59.57%	40.43%	71.51	2.99%
10	Arthritis or rheumatism, Stomach or other digestive disease and Liver disease	0.53%	51.22%	48.78%	70.29	2.61%

Theoretically, there were 91 possible dyad combinations and 364 triad combinations of 14 different chronic conditions. However, only 79.12% (72 types) of the possible dyad combinations and 46.43% (169 types) of the triad combinations emerged in the sample. The 10 most frequently occurring morbidity dyads accounted for 69.01% of the 72 dyad combinations, and the proportion of the 10 most common triad combinations in the 169 triad combinations was 47.05%. Arthritis or rheumatism, which appeared five times in the top ten dyad combinations and eight times in the top ten triad combinations of chronic conditions, became the main component of the leading morbidity dyads and triads.

There were significant gender differences in the odds of these multimorbidity combinations. The number of women with triad combinations of chronic diseases were generally higher than that of men with the same morbidity triads. For example, women had significantly higher prevalence of arthritis and hypertension and hyperlipidemia than men (78.26% vs 21.74%). Among morbidity dyads, the prevalence of heart disease and arthritis or rheumatism in women was nearly two times higher than that in men while the cluster of arthritis or rheumatism and kidney disease occurred more

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frequently in men than in women. No age difference in the probability of these multimorbidity combinations was detected.

O/E ratio was also used to analyze the multimorbidity pattern. [16] The higher the value, the higher the probability of coexistence of chronic conditions. [17] Table 5 shows O/E ratios for the 10 most prevalent morbidity dyads and triads. In the midst of those triad combinations of chronic conditions, the two clusters with significantly higher O/E ratios were emotional, nervous, or psychiatric problems and stroke and memory-related disease (O/E ratio=10287.72), emotional, nervous, or psychiatric problems and memory-related disorders and asthma (O/E ratio=8498.56). These four conditions also dominated the three leading dyads with the highest O/E ratios: 97.73 for the combination of emotional and mental disorders and memory- related diseases, 23.66 for the combination of stroke and memory related disease and 19.55 for the combination of memory-related disease and asthma.

Table 5 O/E ratios for the 10 most prevalent morbidity dyads and triads

Number of chronic conditions	Ranking	Chronic conditions	O/E ratio
2	1	Chronic lung diseases and Asthma	162.15
	2	Emotional, nervous, or psychiatric problems and Memory-related disease	97.73
	3	Dyslipidemia and Diabetes or high blood sugar	38.39
	4	Heart disease and Memory-related disease	25.69
	5	Stroke and Memory-related disease	23.66
	6	Hypertension and Stroke	22.85
	7	Hypertension and Diabetes or high blood sugar	20.64
	8	Cancer or malignant tumor and Stroke	19.55
	9	Memory-related disease and Asthma	19.55
	10	Stroke and Asthma	19.55
3	1	Stroke, Emotional, nervous, or psychiatric problems and Memory-related disease	10287.72

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2	Emotional, nervous, or psychiatric problems, Memory-related disease and Asthma	8498.56
3	Emotional, nervous, or psychiatric problems, Chronic lung diseases and Asthma	2274.26
4	Heart disease, Stroke and Memory-related disease	2253.50
5	Chronic lung diseases, Heart disease and Asthma	1992.69
6	Dyslipidemia, Heart disease and Memory-related disease	1443.25
7	Hypertension, Dyslipidemia and Diabetes or high blood sugar	1398.31
8	Hypertension, Stroke and Memory-related disease	1387.35
9	Chronic lung diseases, Memory-related disease and Asthma	1376.53
10	Chronic lung diseases, Arthritis or rheumatism and Asthma	1265.95

DISCUSSION

This is the first study to estimate the prevalence, patterns of multimorbidity among the elderly in China based on the nationally representative data from CHARLS, which covered 11,707 Chinese senior citizens aged over 60. The results of the study indicated that the prevalence of the 14 chronic diseases in the elderly reached 69.10% in China, and 43.6% of the elderly population suffered from multimorbidity. The average age of the entire sample was 0.66 years higher than that of the non-MCC group and in the MCC group, the mean age of women was 0.59 years higher than that of men, which was comparable to the results of previous studies. [18-22]

The prevalence of multimorbidity estimated in this study was much lower than that from previous studies in developed countries. A study of 543 patients over 65 in Ghent, Belgium showed that the multimorbidity rate was as high as 82.6%, [23].

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Another study in Australia showed that 83.2% of the respondents suffered from multimorbidity, [24] However, it is difficult to compare the prevalence generated from different studies due to differences in the definition of multimorbidity, demographic characteristics and study methodologies. [25-29]

In line with previous studies, increased age was found to be significantly associated with higher prevalence of multimorbidity and there was also gender differences in the rates of certain clusters of chronic conditions, which is understandable in view of the distinction between female and male in terms of physiological features and lifestyles. [30, 31]

In agreement with previous reports, arthritis or rheumatism, hypertension, stomach or other digestive disease were the most common diseases in the MCC group. [10] The prevalence of these three conditions was all above 20% in the entire sample and above 45% in the MCC group. The most prevalent chronic combinations in the sample could also be found in other studies. [23]

Although, arthritis or rheumatism, a component of all the leading three morbidity dyads and triads, was also the most commonly occurring disease in multimorbidity, the relative risk of this disease was only 4.65, the lowest in the 14 chronic diseases. Moreover, arthritis or rheumatism is less common in morbidity clusters with large O/E ratios. Therefore, the frequent occurrence of arthritis or rheumatism in multimorbidity might be simply due to the high prevalence of the disease.

The relative risks for asthma, stroke, heart disease, and other six conditions were all above ten, which meant that patients with these diseases were ten times easier to be tormented by multimorbidity. These diseases also occurred at a high frequency in multimorbidity with high O/E ratios, such as the clusters of pulmonary disease and asthma, emotional and mental illness and memory-related disease, dyslipidemia and diabetes, and stroke and emotional or mental illness and memory-related disease. Patients with these diseases were vulnerable to comorbidity compared to those without these diseases and thus should be the focus of future study.

This study featured the nationally representative sample of Chinese elderly

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population, which was crucial to get an overall picture regarding multimorbidity among the elderly in China. However, there were also limitations. First, this study used data from the third wave of CHARLS, a survey which was conducted in 2015, the time lag therefore was inevitable. Second, the chronic diseases included in the study were not comprehensive enough, since only 15 chronic conditions were included in the survey. Third, the outcome was based on self-report,which may have introduced some misclassification bias. Later researches on the prevalence and patterns of multimorbidity need to be carried out in depth with a more extensive survey of chronic disease.

CONCLUSIONS

Multimorbidity still remains an underexplored area of research in China. [32]. Despite the increasing prevalence of multimorbidity, there is no specific proposals for its diagnosis and treatment. [33] This study contributes to the understanding of the prevalence and patterns of comorbidity among the elderly in China. Considering China's aging population and the high prevalence of comorbidity in senior citizens, the elderly should be prioritized in the fields of disease prevention and health promotion.

Acknowledgements The authors would like to thank the Chinese Center for Disease Control and Prevention and Peking University for China Health and Retirement Longitudinal Survey.

Contributors RZ analyzed and interpreted data, drafted the manuscript, approved the final manuscript as submitted. YL revised the manuscript for important intellectual content.LS analyzed and interpreted data and revised the manuscript for important intellectual content. FC helped on the study design and revised the manuscript on the study design and revised the manuscript.

Funding This work was funded by the National Natural Science Foundation of China (7167030838).

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Competing interests None declared.

Patient consent Obtained.

Ethics approval The original CHARLS was approved by the ethics review committee of Peking University, and all participants gave written informed consent at the time of participation

Data sharing statement No additional data are available

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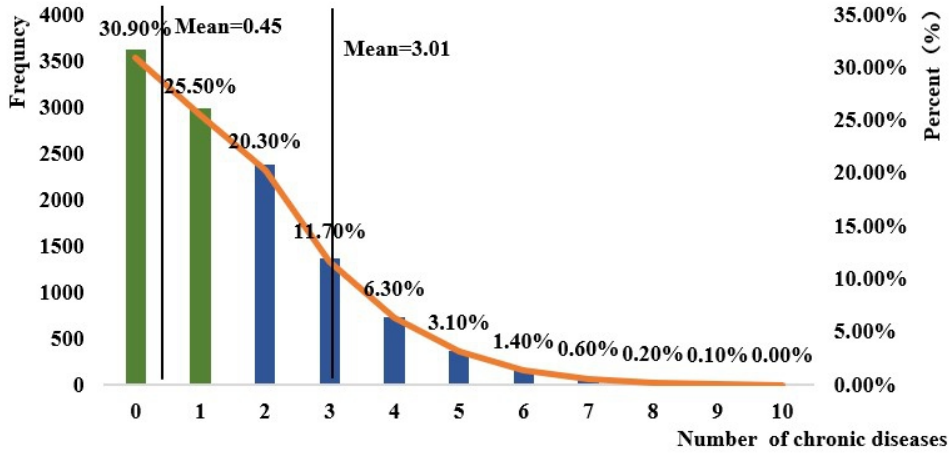

Figure 1. Frequency and percentage of people aged over 60 suffering from different diseases based on CHARLS data

211x107mm (96 x 96 DPI)

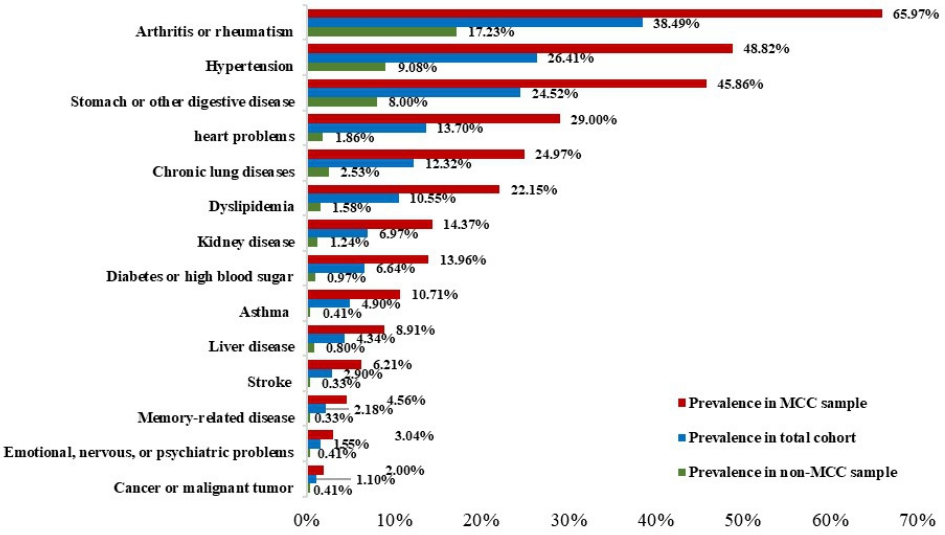

Figure 2. Prevalence rates of the chronic condition in elderly people over 60 years old based on CHARLS data.jpg

161x91mm (150 x 150 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*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 pre-specified 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	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	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
Bias	9	Describe any efforts to address potential sources of bias	Not applicable
Study size	10	Explain how the study size was arrived at	4
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	5
		(*c*) Explain how missing data were addressed	Not applicable
		(*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	5

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		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	Not applicable
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	4
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	5
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Not applicable
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Not applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	5
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
		(*b*) Report category boundaries when continuous variables were categorized	8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	10
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-12
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
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	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
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	14

*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.

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Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-024268.R1
Article Type:	Research
Date Submitted by the Author:	23-Oct-2018
Complete List of Authors:	zhang, ran; China Pharmaceutical University, School of International Pharmaceutical Business Lu, Yun; China Pharmaceutical University, School of International Pharmaceutical Business Shi, Liuyan; China Pharmaceutical University, School of International Pharmaceutical Business Zhang, SongLin; China Pharmaceutical University, School of International Pharmaceutical Business Chang, Feng; China Pharmaceutical University, School of International Pharmaceutical Business
Primary Subject Heading:	Health informatics
Secondary Subject Heading:	Public health, Qualitative research
Keywords:	multimorbidity, cross-sectional study, Prevalence, Observed-to-expected ratio, China

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Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data

Corresponding author: Feng Chang

Postal address: 639 Longmian Road, Jiangning District, Nanjing, Jiangsu Province, 211198

E-mail: cpucf@163.com

telephone number: +86-13805153128

First author: Ran Zhang

E-mail: ranzai7@126.com

Department: China Pharmaceutical University

Institution: School of International Pharmaceutical Business

City: Nanjing, Jiangsu Province

Country: China

Co-authors: Yun Lu **E-mail:** luyun20159@163.com

Co-authors: Liuyan Shi **E-mail:** juliasmithsly@163.com

Co-authors: Songlin Zhang **E-mail:** 1069822493@qq.com

Department: China Pharmaceutical University

Institution: School of International Pharmaceutical Business

City: Nanjing, Jiangsu Province

Country: China

Keywords

Multimorbidity; cross-sectional study; Prevalence; Observed-to-expected ratio; China

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Word count 3853

ABSTRACT

Objectives: Examination of the prevalence and patterns of multimorbidity among the elderly in China.

Design: Cross-sectional study.

Setting: More than 10,000 households in 28 of the 34 provinces of mainland China.

Participants: 11,707 Chinese adults aged 60 and over.

Primary outcome measures: Prevalence and patterns of multimorbidity among the participants. Relative risks were calculated to estimate the probability of up to 14 chronic conditions coexisting with each other. Observed-to-expected (O/E) ratios were used to analyze the patterns of multimorbidity.

Results: Multimorbidity was present in 43.6% of respondents from the sample population, with women having the greater prevalence compared to men. There were 804 different comorbidity combinations identified, including 76 dyad combinations and 169 triad combinations. The top 10 morbidity dyads and triads accounted for 69.01% and 47.05% of the total dyad and triad combinations observed, respectively. Among the 14 chronic conditions included in the study, asthma, stroke, heart attack and six other chronic conditions were the main components of multimorbidity due to their high relative risk ratios. The most frequently occurring clusters with higher O/E ratios were stroke along with emotional, nervous, or psychiatric problems; memory-related diseases together emotional, nervous, or psychiatric problems; and memory-related diseases and asthma accompanied by chronic lung diseases and asthma.

Conclusions: The results of this study highlight the high prevalence of multimorbidity in the elderly population in China. Further studies are required to understand the etiology of multimorbidity, and future primary healthcare policies should be made while taking

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multimorbidity into consideration.

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Strengths and limitations of this study

Strengths

- This is the first study to estimate the prevalence and patterns of multimorbidity among the elderly population in China.
- Data for this study were collected from a nationally representative longitudinal survey of 17,708 Chinese residents.

Limitations

- Only 14 predefined chronic diseases were included in the study, and these may not be comprehensive of the conditions of the population.
- The data analyzed from the CHARLS were originally collected by population self-reporting, not clinician evaluation, and could partially reflect some associated biases or confounds.
- The exclusion of incomplete data may cause a selection bias.

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INTRODUCTION

Multimorbidity, or the simultaneous occurrence of two or more chronic conditions in an individual, is becoming increasingly common, and this has been reported to increase progressively with age. [1, 2] At present, with China's aging population having an increasing prevalence of chronic conditions, multimorbidity among the elderly poses an enormous societal cost due to increased mortality rates and healthcare utilization. [3] However, to date, research on chronic conditions in China has focused on single disease states, and the coexistence of multiple chronic conditions has not been investigated systematically and thoroughly.

There is a significant difference in the etiological analysis between patients with single chronic conditions and those with multimorbidity. [4] The coexistence of chronic conditions in a patient is more than a random event, it is more typically due to the causal relationship between some diseases and shared pathogenic factors. [5, 6] Moreover, the interactions between diseases or between a disease and host result in differences in the severity of multimorbidity and functional status and prognosis of patients with multimorbidity. [7] Consequently, it is imperative to begin research on multimorbidity in China for the cost-effective treatments that the results may help to suggest. [8] The purpose of this study was therefore to determine the prevalence of multimorbidity among the elderly in China and to reveal morbidity combinations, which may benefit the design and implementation of a modified healthcare system with consideration for patients with multimorbidity.

METHODS

Data source

Data for this study were collected from the third response of the China Health and Retirement Longitudinal Survey (CHARLS), which is the most current data available. The CHARLS is a nationally representative longitudinal survey of Chinese residents aged 45

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and older that was conducted by the Chinese Center for Disease Control and Prevention, along with Peking University, to help China to adjust to the rapid aging of its population through the evaluation of social, economic, and health circumstances on the community level using data collected by interviews, physical measurements and blood sample collection. [9] The national baseline survey began in 2011 and involved 17,708 respondents from 150 county-level units, 450 village-level units, and approximately 10,000 households. Afterwards, CHARLS respondents were followed every second year, with their informed consent, and the study was approved by the Peking University Biomedical Ethics Committee (IRB00001052-14013-exemption).

Variables

The core CHARLS questionnaires included sections requesting information on demographic factors, family structure and changes, health status and functioning, healthcare and insurance, work, retirement and pension, income and consumption, and assets (individual and household). Information was collected by interview by trained staff. For the current study, the eligible and included participants were determined by being aged 60 and over, and data on gender, age and health status was used from the general health status and disease history section of senior citizens in the 2015 CHARLS data. This information included the following 14 common chronic health problems: hypertension, dyslipidemia (high blood lipids or low cholesterol), diabetes or elevated blood glucose (including impaired glucose tolerance and fasting blood glucose), cancer (excluding mild skin cancers), chronic lung disease such as chronic bronchitis or emphysema, pulmonary heart disease (excluding tumors or cancer), liver disease (other than fatty liver, tumors, or cancer), heart disease (such as myocardial infarction, coronary heart disease, angina pectoris, congestive heart failure and other heart diseases), stroke, kidney disease (excluding tumors or cancer), stomach or other digestive diseases (excluding tumors or cancer), emotional and mental problems, memory-related diseases (such as Alzheimer's disease, brain atrophy, Parkinson's disease), arthritis or rheumatism, and asthma. All these data were based on self-reports. Accordingly, multimorbidity was defined as the coexistence of more than one of the 14 chronic conditions, with acute or subacute forms of certain conditions being excluded in this study due to the CHARLS data collection protocol.

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Statistical analysis

To detect the demographic characteristics of patients with multimorbidity, respondents were divided into two groups: those with multiple chronic conditions (MCC group) and those without multiple chronic conditions (Non-MCC group). Descriptive statistics were calculated and expressed as means (SD) and frequencies (percentage). We applied the T^2 and χ^2 texts to test the differences in age, gender and the mean number of chronic conditions across different subgroups. Respective prevalence in the MCC group and the non-MCC group were calculated separately.

To determine the most common combination of chronic diseases, the prevalence of morbidity and multimorbidity dyads and triads were estimated, respectively. Next, the expected number of patients with a chronic disease were calculated, and the observed-to-expected (O/E) ratios were determined by dividing the number of patients in those groups by the expected number of patients. Observed-to-expected ratios were used to estimate the conditional probability of coexistence of two or three chronic conditions. [10] As an important indicator for assessing the correlation between diseases, the O/E ratio has been used in many areas of comorbidity. [10，11] The relative risk of comorbidity for individual chronic conditions was also calculated. Relative risk of comorbidity (RR) is the ratio of the number of people with a certain chronic condition who suffer from multimorbidity to the number of patients with the same disease who do not suffer from multimorbidity. [11, 12] In other words, a higher RR value means a higher probability that the disease coexists with other diseases. However, it should be noted that there is no direct relationship between the relative risk of comorbidity and the overall prevalence of the diseases. [13, 14]

All analyses in this study were completed using Stata softwareV.14.0 for Windows (Stata Corp). P Values <0.05 were considered to be statistically significant.

Patient and public involvement

Patients and the public were not 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 results to study participants.

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RESULTS

Characteristics of participants

The data were gathered from the third response set of CHARLS. After exclusion of participants with incomplete data (1,002) and aged under 60 (9,259), there were 11,707 respondents with available information on related chronic diseases that were included in this study. The selection process of study sample is shown in Figure 1. The demographic characteristics of sample respondents and statistical significance test results are presented in Table 1.

Overall, the mean age for the sample population was 70.5 (ranging from 60 to 107). The sample population consisted of 5,705 (48.7%) males and 6002 (51.2%) females, and 43.6% of them suffered from multimorbidity. The median of chronic conditions in the MCC group was 3.01, compared to 0.45 in the Non-MCC group. Samples in the MCC group were 0.66 year older than those belonged to the non-MCC group. Gender differences with regard to the age of samples between the MCC group and the non-MCC group (70.57 for MCC group and 69.91 for non-MCC group) were small but statistically significant ($p < 0.001$). The prevalence of multimorbidity in the female population was higher than that for the males (54.41% vs 45.59%), which is in accordance with trends reported in other available literature. [15, 16] Figure 2 shows the number and proportion of respondents over 60 according to morbidity numbers. It can be seen that among all the participants aged over 60, 43.6% suffer from multimorbidity. Considering that only 30.9% of the respondents did not have the 14 chronic diseases, and 43.7% of them had two or more chronic diseases, multimorbidity would be a major problem faced by the health care system.

Table 1. Demographic characteristics of all respondents, the MCC group and non-MCC group

	All respondents	MCC group	Non-MCC group	P*
Number of people	11707	5107	6600	
Proportion (%)	100%	43.62%	56.38%	
Mean age				

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All respondents (SD)	70.20(7.907)	70.57(7.701)	69.91(8.051)	<0.001
Male (SD)	69.97(7.575)	70.50(7.348)	69.60(7.707)	<0.001
Female (SD)	70.39(8.189)	70.62(7.892)	70.19(8.359)	<0.001
Gender（% females）	51.28%	54.41%	48.83%	<0.001
Mean number of chronic conditions				
All respondents（SD）	1.57(1.560)	3.01(1.259)	0.45(0.498)	<0.001
Male（SD）	1.47(1.534)	2.98(1.265)	0.44(0.496)	<0.001
Female（SD）	1.65(1.581)	3.03(7.982)	0.47(0.499)	<0.001

SD = standard deviation;

p* = statistical significance of the difference between the MCC and the non-MCC sample (t-tests were performed for comparison of means, and chi-square-tests for differences between percentages)

Prevalence of chronic conditions

The prevalence of chronic conditions in the entire sample, the MCC group and the non-MCC group are shown in Figure 3. The prevalence of all fourteen chronic conditions in the MCC group was significantly higher than that in the entire sample. For instance， the prevalence of arthritis or rheumatism, hypertension, stomach or other digestive disease, heart disease and chronic lung disease were 65.97%, 48.82%, 45.86%, 29.00% and 24.97% in the MCC group, compared to 38.49%, 26.41%, 24.52%, 12.32% and 12.32% in the entire sample, respectively.

Table 2 shows the relative risks of comorbidity determined for the 14 chronic diseases reported in this study. It can be seen that the overall relative risks for asthma, stroke, heart disease and six other conditions were all above 10, which meant these diseases were >10 times easier to coexist with other chronic conditions and result in multimorbidity. In addition, the relative risks for certain diseases were positively associated with gender. For example, men had significantly higher relative risks for asthma, but lower relative risks for diabetes or high blood sugar, compared to women.

Table 2 Relative risks of multimorbidity for different chronic conditions according to gender

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Chronic conditions	All respondents	95% Confidence Interval		Female	95% Confidence Interval		Male	95% Confidence Interval	
		Lower Bound	Upper Bound		Lower Bound	Upper Bound		Lower Bound	Upper Bound
High relative risk of multimorbidity									
Asthma	26.18	17.82	38.46	20.67	11.85	36.06	32.68	19.18	55.67
Stroke	18.62	12.11	28.64	21.57	10.61	43.86	17.43	10.13	29.99
Heart disease	15.56	12.99	18.63	16.48	12.80	21.21	14.26	11.02	18.46
Diabetes or high blood sugar	14.40	11.18	18.55	15.68	10.86	22.63	13.11	9.24	18.62
Dyslipidemia	14.05	11.54	17.12	15.13	11.37	20.14	12.97	9.86	17.05
Memory-related disease	13.69	8.85	21.16	34.17	12.63	92.44	9.28	5.66	15.21
Kidney disease	11.57	9.24	14.49	15.01	10.17	22.43	10.24	7.78	13.48
Liver disease	11.10	8.37	14.71	16.07	9.70	26.63	9.15	6.49	12.89
Chronic lung diseases	9.87	8.43	11.55	10.71	8.26	13.88	9.74	8.00	11.86
Low relative risk of multimorbidity									
Emotional, nervous, or psychiatric problems	7.42	4.94	11.15	6.24	3.78	10.30	9.36	4.65	18.85
Stomach or other digestive disease	5.73	5.25	6.25	6.20	5.48	7.02	5.23	4.62	5.91
Hypertension	5.38	4.96	5.84	4.90	4.40	5.47	5.92	5.24	6.69
Cancer or malignant tumor	4.88	3.20	7.45	5.33	3.06	9.29	3.99	2.07	7.72
Arthritis or rheumatism	3.83	3.61	4.05	3.70	3.43	3.99	3.91	3.59	4.26

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Common multimorbidity combinations

There were 804 possible comorbidity combinations that were identified in the MCC group after statistical analysis, including 72 dyads and 169 triads. The 10 most frequently occurring morbidity dyads and triads are presented respectively in Table 3 and Table 4.

Table3 Prevalence of the 10 most common morbidity dyads

Rank	Morbidity dyads	Prevalence			Mean Age
		All respondents	female	male	

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1	Arthritis or rheumatism and Stomach or other digestive disease	4.73%	3.56%	5.96%	69.20
2	Arthritis or rheumatism and Hypertension	2.85%	2.20%	3.53%	71.25
3	Arthritis or rheumatism and Chronic lung diseases	1.13%	1.22%	1.04%	71.55
4	Hypertension and heart problems	1.03%	1.00%	1.06%	71.80
5	Hypertension and Stomach or other digestive disease	0.89%	0.83%	0.95%	69.07
6	Hypertension and Dyslipidemia	0.86%	0.81%	0.91%	68.58
7	Arthritis or rheumatism and heart problems	0.76%	0.53%	1.00%	70.72
8	Arthritis or rheumatism and Kidney disease	0.64%	0.73%	0.54%	68.24
9	Hypertension and Diabetes or high blood sugar	0.58%	0.50%	0.67%	70.97
10	Chronic lung diseases and Asthma	0.53%	0.65%	0.40%	71.15

Table 4 Prevalence of the 10 most common morbidity triads

Rank	Morbidity triads	Prevalence			Mean Age
		All respondents	female	male	
1	Arthritis or rheumatism, Stomach or other digestive disease and Hypertension	1.19%	0.80%	1.60%	70.96
2	Arthritis or rheumatism, Stomach or other digestive disease and Chronic lung diseases	0.82%	0.97%	0.67%	70.82
3	Arthritis or rheumatism, Heart disease and Hypertension	0.63%	0.37%	0.91%	69.93
4	Arthritis or rheumatism, Heart disease and Stomach or other digestive disease	0.59%	0.25%	0.95%	71.51

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5	Hypertension, Dyslipidemia and Arthritis or rheumatism	0.44%	0.31%	0.57%	70.13
6	Hypertension, Dyslipidemia and Heart problems	0.42%	0.35%	0.49%	71.17
7	Arthritis or rheumatism, Kidney disease and Stomach or other digestive disease	0.42%	0.40%	0.44%	70.14
8	Arthritis or rheumatism, Asthma and Chronic lung diseases	0.40%	0.46%	0.33%	69.18
9	Hypertension, Dyslipidemia and Diabetes or high blood sugar	0.35%	0.35%	0.35%	71.51
10	Arthritis or rheumatism, Stomach or other digestive disease and Liver disease	0.53%	0.57%	0.49%	70.29

Theoretically, there are 91 dyad combinations and 364 triad combinations possible given the 14 different chronic conditions considered in this study. However, only 72 types (79.12%) of dyads and 169 types (46.43%) of triads emerged in the sample. The 10 most frequently occurring morbidity dyads accounted for 69.01% of the 72 dyad combinations, and the proportion of the 10 most common triad combinations in the 169 triad combinations was 47.05%. Arthritis or rheumatism, which appeared in five of the top 10 dyad combinations and eight of the top 10 triad combinations of chronic conditions, was the main component of the leading morbidity dyads and triads.

There were significant gender differences observed in the occurrences of these multimorbidity combinations. The numbers of women with triad combinations of chronic diseases were generally higher than for men with the same morbidity triads. For example, women had significantly higher prevalence of arthritis and hypertension and hyperlipidemia than men (78.26% vs 21.74%). Among morbidity dyads, the prevalence of heart disease and arthritis or rheumatism in women was nearly two times higher than that in men, while the cluster of arthritis or rheumatism and kidney disease occurred more frequently in men than in women. No age difference was detected in the probability of

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these particular multimorbidity combinations occurring.

The O/E ratio was also used to analyze the multimorbidity pattern. [17] The higher the O/E value, the higher the probability of coexistence of chronic conditions. [18] Table 5 shows O/E ratios determined for the 10 most prevalent morbidity dyads and triads. The prevalence of each conditions and the dyad and triad prevalence are presented in Annex 1. In the midst of those triad combinations of chronic conditions, the two clusters with significantly higher O/E ratios were emotional, nervous, or psychiatric problems and stroke and memory-related disease (O/E ratio = 10287.72), emotional, nervous, or psychiatric problems and memory-related disorders and asthma (O/E ratio = 8498.56). These four conditions also dominated the three leading dyads with the highest O/E ratios: 97.73 for the combination of emotional and mental disorders and memory- related diseases, 23.66 for the combination of stroke and memory related disease and 19.55 for the combination of memory-related disease and asthma.

Table 5 O/E ratios for the 10 most prevalent morbidity dyads and triads

Number of chronic conditions	Rank	Chronic conditions	O/E ratio
2	1	Chronic lung diseases and Asthma	162.15
	2	Emotional, nervous, or psychiatric problems and Memory-related disease	97.73
	3	Dyslipidemia and Diabetes or high blood sugar	38.39
	4	Heart disease and Memory-related disease	25.69
	5	Stroke and Memory-related disease	23.66
	6	Hypertension and Stroke	22.85
	7	Hypertension and Diabetes or high blood sugar	20.64
	8	Cancer or malignant tumor and Stroke	19.55
	9	Memory-related disease and Asthma	19.55

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	10	Stroke and Asthma	19.55
3	1	Stroke, Emotional, nervous, or psychiatric problems and Memory-related disease	10287.72
	2	Emotional, nervous, or psychiatric problems, Memory-related disease and Asthma	8498.56
	3	Emotional, nervous, or psychiatric problems, Chronic lung diseases and Asthma	2274.26
	4	Heart disease, Stroke and Memory-related disease	2253.50
	5	Chronic lung diseases, Heart disease and Asthma	1992.69
	6	Dyslipidemia, Heart disease and Memory-related disease	1443.25
	7	Hypertension, Dyslipidemia and Diabetes or high blood sugar	1398.31
	8	Hypertension, Stroke and Memory-related disease	1387.35
	9	Chronic lung diseases, Memory-related disease and Asthma	1376.53
	10	Chronic lung diseases, Arthritis or rheumatism and Asthma	1265.95

DISCUSSION

This is the first study to estimate the prevalence and patterns of multimorbidity among the elderly in China based on the nationally representative data from CHARLS, which covered 11,707 Chinese senior citizens of age 60 and over. The results of the study indicated that the prevalence of the 14 chronic diseases evaluated in the elderly reached 69.10% in China, and that 43.6% of the elderly population suffered from multimorbidity. The average age of the MCC group was 0.66 years higher than that of the non-MCC group and in the MCC group, the mean age of women was 0.66 years higher than that of men, which was comparable to the results of previous studies. [19-23]

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The prevalence of multimorbidity estimated in this study was much lower than that from previous studies in other developed countries. For example, a study of 543 patients over age 65 in Ghent, Belgium showed that the multimorbidity rate was as high as 82.6%, [24]. Another study in Australia showed that 83.2% of the respondents suffered from multimorbidity. [25] However, it is difficult to compare the prevalence generated from different studies due to differences in the selected definitions of multimorbidity, demographic characteristics of the samples, and different study methodologies. [26-30]

In agreement with previous reports, arthritis or rheumatism, hypertension, stomach or other digestive disease were the most common diseases in the MCC group. [11] The prevalence of these three conditions was each above 20% in the entire sample, and above 45% in the MCC group. The most prevalent chronic combinations in the sample could also be found in other studies. [24] The results of this study showed that the prevalence of arthritis or rheumatism was high and easy to coexist with other conditions. In addition to the chronic conditions mentioned above, previous studies demonstrated that women with rheumatoid arthritis might have a predisposition to gallstones which could manifest in middle or older age compared with women in the general population. This phenomenon could be related to chronic inflammation and HDL metabolism. [31]

Although arthritis or rheumatism, a component of all the leading three morbidity dyads and triads, was also the most commonly occurring disease in multimorbidity, the relative risk of this disease was only 4.65, the lowest in the 14 chronic diseases. Moreover, arthritis or rheumatism is less common in morbidity clusters with large O/E ratios. Therefore, the frequent occurrence of arthritis or rheumatism in multimorbidity might be simply due to the high prevalence of the disease.

The relative risks for asthma, stroke, heart disease, and six other conditions were all above 10, which means that patients with these diseases were 10 times more likely to be afflicted by multimorbidity. These diseases also occurred at a high frequency in

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multimorbidity with high O/E ratios, such as the clusters of pulmonary disease and asthma, emotional and mental illness and memory-related disease, dyslipidemia and diabetes, and stroke and emotional or mental illness and memory-related disease. Patients with these diseases were more likely to express comorbidity compared to those without these diseases, and thus should be the focus of future research studies.

This study featured a nationally representative sample of the Chinese elderly population, which was crucial to get an overall understanding of multimorbidity among the elderly in China. However, there were also limitations with the data sample and study. For example, this study used data from the third wave report of CHARLS, a survey which was conducted in 2015, and there is accordingly a time lag to now that exists. Additionally, the chronic diseases included in the study were not comprehensive, since only 14 chronic conditions were included in the survey. Finally, the data obtained from the survey was based on self-reporting, which may have introduced some misclassification bias or other confounds. Later research on the prevalence and patterns of multimorbidity should be carried out in-depth with a more extensive survey of chronic disease.

CONCLUSIONS

Multimorbidity remains an underexplored area of research in China. [32]. Despite the increasing prevalence of multimorbidity, there are no specific proposals for its diagnosis and treatment. [33] This study contributes to the understanding of the prevalence and patterns of comorbidity among the elderly in China. Considering China's aging population and the high prevalence of comorbidity in senior citizens, the elderly should be prioritized in the fields of disease prevention and health promotion.

Acknowledgements The authors would like to thank the Chinese Center for Disease

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Control and Prevention and Peking University for access to China Health and Retirement Longitudinal Survey data.

Contributors Ran Zhang analyzed and interpreted data, drafted the manuscript, approved the final manuscript as submitted. Yun Lu revised the manuscript for important intellectual content. Liuyan Shi analyzed and interpreted data and revised the manuscript for important intellectual content. Songlin Zhang handled and solved the data problems, analyzed and revised the data. Feng Chang helped on the study design and revised the manuscript.

Funding This work was funded by the National Natural Science Foundation of China (7167030838).

Competing interests None declared.

Patient consent Obtained.

Ethics approval The original CHARLS was approved by the ethics review committee of Peking University, and all participants gave written informed consent at the time of participation

Data sharing statement No additional data are available

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Figure 1 Flowchart for selecting the study sample from the original sample population. CHARLS, China Health and Retirement Longitudinal Survey

Figure 2 Frequency and percentage of people aged over 60 suffering from different diseases based on CHARLS data

Figure 3 Prevalence Rates of 14 common chronic diseases in Chinese people over 60 years old based on CHARLS data.

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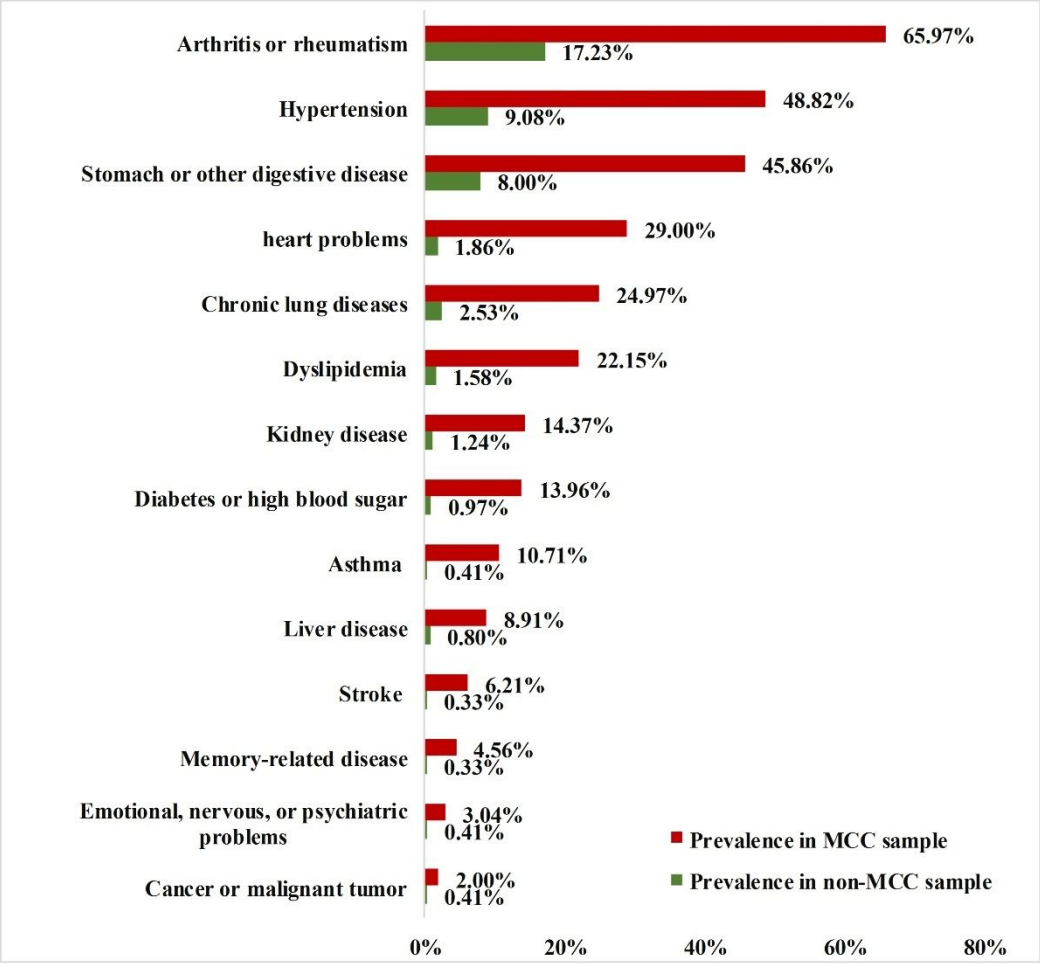

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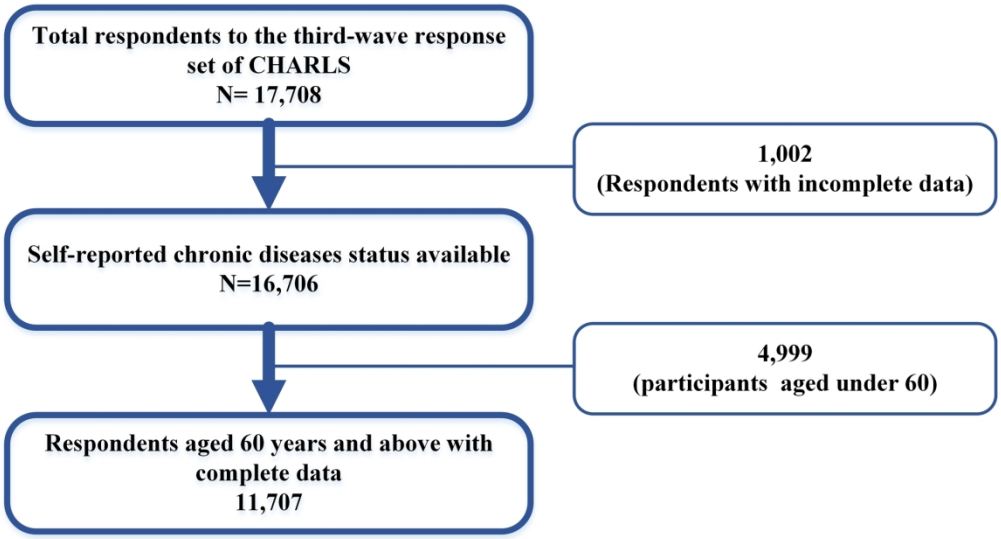

Figure 1 Flowchart for selecting the study sample from the original sample population. CHARLS, China Health and Retirement Longitudinal Survey

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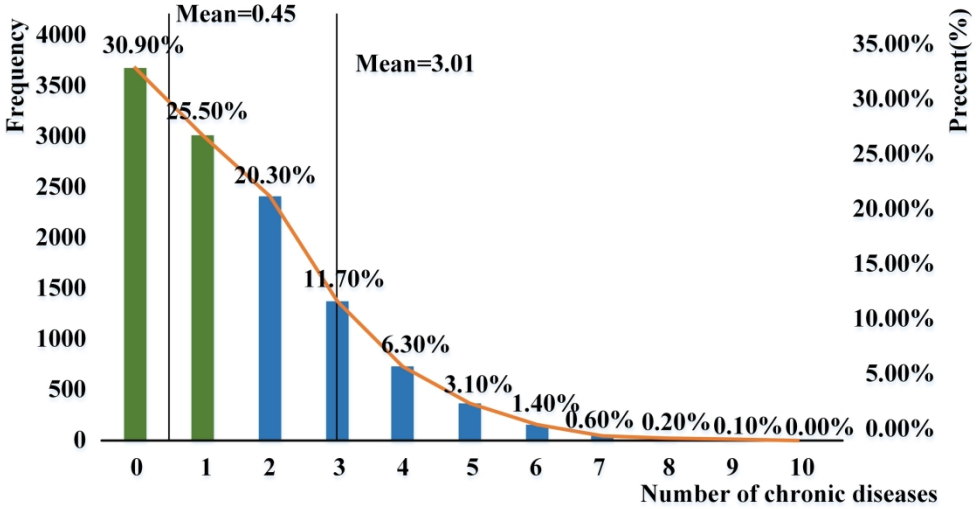

Figure 2 Frequency and percentage of people aged over 60 suffering from different diseases based on CHARLS data

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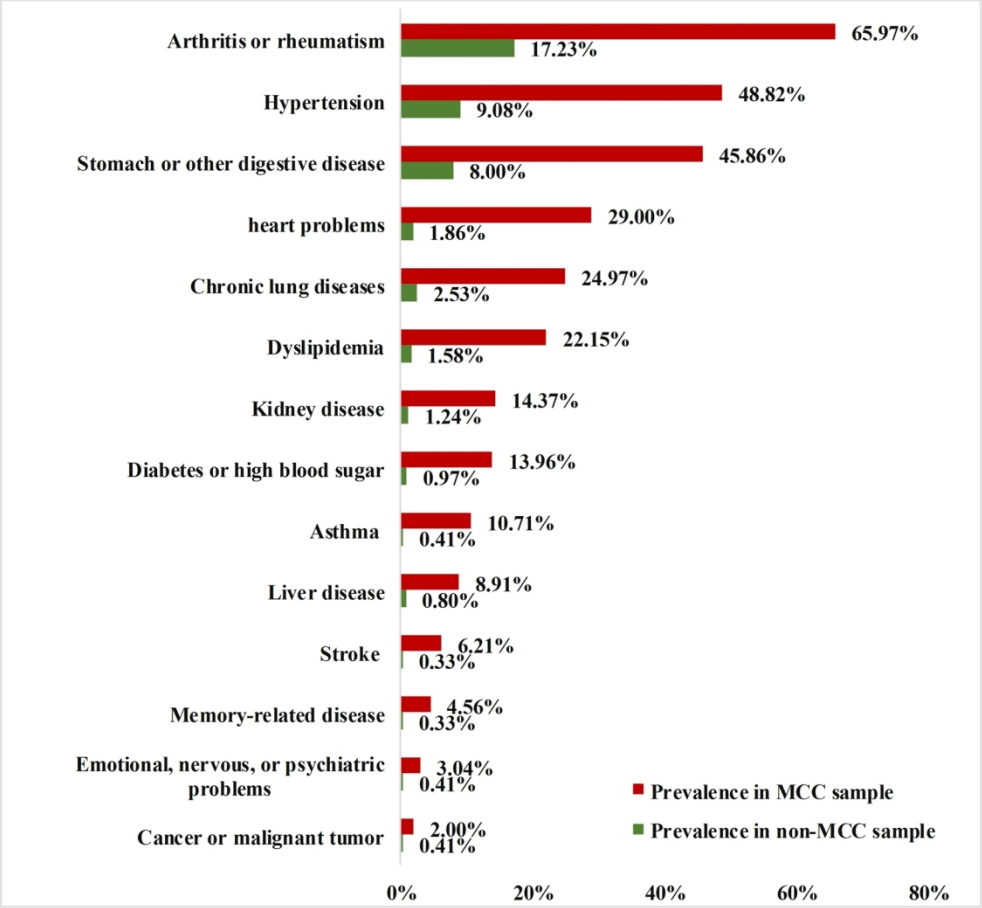

Figure 3 Prevalence Rates of chronic condition in elderly people over 60 years old based on CHARLS data

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Annex 1 O/E ratio of all binary and triads comorbidities pattern present in participants

Rank	binary comorbidities pattern	O/E ratio
1	Chronic lung diseases and Asthma	161.00
2	Emotional, nervous, or psychiatric problems and Memory-related disease	98.57
3	Dyslipidemia and Diabetes or high blood sugar	38.69
4	Heart disease and Memory-related disease	25.96
5	Stroke and Memory-related disease	24.19
6	Hypertension and Stroke	23.10
7	Hypertension and Diabetes or high blood sugar	20.77
8	Cancer or malignant tumor and Stroke	19.71
9	Memory-related disease and Asthma	19.71
10	Stroke and Asthma	19.71
11	Hypertension and Heart disease	19.07
12	Hypertension and Dyslipidemia	18.98
13	Dyslipidemia and Heart disease	17.39
14	Diabetes or high blood sugar and Heart disease	14.87
15	Diabetes or high blood sugar and Liver disease	14.40
16	Cancer or malignant tumor and Liver disease	13.65
17	Diabetes or high blood sugar and Kidney disease	13.38
18	Hypertension and Memory-related disease	13.33
19	Dyslipidemia and Cancer or malignant tumor	12.51
20	Stomach or other digestive disease and Arthritis or rheumatism	10.80
21	Liver disease and Heart disease	10.49
22	Dyslipidemia and Stroke	10.23
23	Dyslipidemia and Stomach or other digestive disease	9.81
24	Dyslipidemia and Kidney disease	9.61
25	Chronic lung diseases and Memory-related disease	9.56
26	Chronic lung diseases and Stroke	9.56
27	Kidney disease and Arthritis or rheumatism	9.42
28	Heart disease and Kidney disease	9.29
29	Chronic lung diseases and Heart disease	9.12
30	Stomach or other digestive disease and Asthma	9.03
31	Liver disease and Kidney disease	8.99
32	Kidney disease and Stomach or other digestive disease	8.92
33	Memory-related disease and Arthritis or rheumatism	8.89
34	Stroke and Arthritis or rheumatism	8.89
35	Arthritis or rheumatism and Asthma	8.77
36	Liver disease and Memory-related disease	8.38
37	Diabetes or high blood sugar and Memory-related disease	8.32
38	Diabetes or high blood sugar and Stroke	8.32
39	Chronic lung diseases and Arthritis or rheumatism	8.14
40	Heart disease and Stomach or other digestive disease	8.11

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41	Heart disease and Arthritis or rheumatism	7.45
42	Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	7.39
43	Liver disease and Stomach or other digestive disease	7.33
44	Diabetes or high blood sugar and Cancer or malignant tumor	6.78
45	Diabetes or high blood sugar and Asthma	6.78
46	Diabetes or high blood sugar and Arthritis or rheumatism	6.44
47	Liver disease and Arthritis or rheumatism	6.16
48	Chronic lung diseases and Kidney disease	5.98
49	Chronic lung diseases and Stomach or other digestive disease	5.97
50	Hypertension and Arthritis or rheumatism	5.74
51	Chronic lung diseases and Liver disease	5.52
52	Kidney disease and Emotional, nervous, or psychiatric problems	5.29
53	Kidney disease and Asthma	5.29
54	Chronic lung diseases and Emotional, nervous, or psychiatric problems	5.19
55	Dyslipidemia and Memory-related disease	5.12
56	Hypertension and Emotional, nervous, or psychiatric problems	5.07
57	Hypertension and Chronic lung diseases	5.03
58	Hypertension and Kidney disease	5.01
59	Cancer or malignant tumor and Arthritis or rheumatism	4.96
60	Cancer or malignant tumor and Stomach or other digestive disease	4.93
61	Dyslipidemia and Arthritis or rheumatism	4.75
62	Hypertension and Liver disease	4.61
63	Diabetes or high blood sugar and Chronic lung diseases	4.38
64	Heart disease and Stroke	4.33
65	Dyslipidemia and Asthma	4.17
66	Hypertension and Stomach or other digestive disease	3.85
67	Cancer or malignant tumor and Heart disease	3.53
68	Heart disease and Asthma	3.53
69	Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	3.43
70	Diabetes or high blood sugar and Stomach or other digestive disease	3.12
71	Hypertension and Cancer or malignant tumor	2.17
72	Hypertension and Asthma	2.17
73	Stomach or other digestive disease and Memory-related disease	2.02
74	Stroke and Stomach or other digestive disease	2.02
75	Dyslipidemia and Liver disease	1.77
76	Dyslipidemia and Chronic lung diseases	1.35

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Rank	triads comorbidities pattern	O/E ratio
1	Stroke, Emotional, nervous, or psychiatric problems and Memory-related disease	10491.60
2	Emotional, nervous, or psychiatric problems, Memory-related disease, Asthma,	8548.88
3	Heart disease, Stroke and Memory-related disease	2302.62
4	Chronic lung diseases, Emotional, nervous, or psychiatric problems and Asthma	2252.13
5	Chronic lung diseases, Heart disease, Asthma,	1977.13
6	Dyslipidemia, Heart disease and Memory-related disease	1461.04
7	Hypertension, Stroke and Memory-related disease	1418.54
8	Hypertension, Dyslipidemia and Diabetes or high blood sugar	1409.29
9	Chronic lung diseases, Memory-related disease and Asthma	1381.96
10	Chronic lung diseases, Arthritis or rheumatism and Asthma	1256.63
11	Dyslipidemia, Diabetes or high blood sugar and Kidney disease	1255.51
12	Cancer or malignant tumor, Chronic lung diseases and Asthma	1126.07
13	Chronic lung diseases, Kidney disease and Asthma	1112.24
14	Liver disease, Kidney disease and Asthma	974.52
15	Dyslipidemia, Diabetes or high blood sugar and Liver disease	972.21
16	Chronic lung diseases, Liver disease and Asthma	956.96
17	Dyslipidemia, Diabetes or high blood sugar and Stroke	935.99
18	Chronic lung diseases, Stomach or other digestive disease and Asthma	921.21
19	Hypertension, Dyslipidemia and Heart disease	876.36
20	Diabetes or high blood sugar, Liver disease and Kidney disease	822.11
21	Hypertension, Diabetes or high blood sugar and Stroke	812.58
22	Hypertension, Chronic lung diseases and Asthma	812.01
23	Hypertension, Dyslipidemia and Stroke	800.07
24	Dyslipidemia, Heart disease and Asthma	793.67
25	Diabetes or high blood sugar, Heart disease and Stroke	791.41
26	Hypertension, Emotional, nervous, or psychiatric problems and Memory-related disease	770.58
27	Dyslipidemia, Diabetes or high blood sugar and Cancer or malignant tumor	762.67
28	Dyslipidemia, Diabetes or high blood sugar and Emotional, nervous, or psychiatric problems	762.67
29	Dyslipidemia, Diabetes or high blood sugar and Heart disease	669.54
30	Liver disease, Heart disease and Emotional, nervous, or psychiatric problems	649.62
31	Heart disease, Kidney disease and Memory-related disease	617.74
32	Heart disease, Stroke and Kidney disease	617.74
33	Dyslipidemia, Chronic lung diseases and Asthma	584.58
34	Diabetes or high blood sugar, Liver disease and Heart disease	548.02

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35	Hypertension, Diabetes or high blood sugar and Heart disease	523.14
36	Hypertension, Heart disease and Stroke	507.36
37	Diabetes or high blood sugar, Chronic lung diseases and Asthma	474.98
38	Liver disease, Stomach or other digestive disease and Asthma	454.02
39	Stomach or other digestive disease, Emotional, nervous, or psychiatric problems and Memory-related disease	437.10
40	Hypertension, Memory-related disease, Asthma,	385.29
41	Diabetes or high blood sugar, Stomach or other digestive disease and Asthma	300.46
42	Hypertension, Dyslipidemia and Memory-related disease	300.03
43	Liver disease, Kidney disease and Arthritis or rheumatism	277.66
44	Hypertension, Heart disease and Memory-related disease	253.68
45	Dyslipidemia, Liver disease and Kidney disease	252.95
46	Hypertension, Chronic lung diseases and Stroke	249.13
47	Stroke, Memory-related disease and Arthritis or rheumatism	249.11
48	Dyslipidemia, Chronic lung diseases and Liver disease	248.40
49	Cancer or malignant tumor, Chronic lung diseases and Heart disease	247.14
50	Chronic lung diseases, Heart disease and Emotional, nervous, or psychiatric problems	247.14
51	Hypertension, Dyslipidemia and Asthma	244.47
52	Cancer or malignant tumor, Heart disease and Stomach or other digestive disease	234.50
53	Chronic lung diseases, Memory-related disease and Arthritis or rheumatism	229.69
54	Chronic lung diseases, Stroke and Stomach or other digestive disease	211.98
55	Hypertension, Stroke and Arthritis or rheumatism	210.41
56	Chronic lung diseases, Liver disease and Heart disease	210.03
57	Hypertension, Cancer or malignant tumor and Heart disease	206.71
58	Hypertension, Heart disease and Emotional, nervous, or psychiatric problems	206.71
59	Memory-related disease, Arthritis or rheumatism and Asthma	202.98
60	Emotional, nervous, or psychiatric problems, Memory-related disease and Arthritis or rheumatism	202.98
61	Stroke, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	202.98
62	Stroke, Kidney disease and Arthritis or rheumatism	200.49
63	Dyslipidemia, Diabetes or high blood sugar and Stomach or other digestive disease	194.98
64	Liver disease, Stomach or other digestive disease and Memory-related disease	185.73
65	Dyslipidemia, Stomach or other digestive disease and Asthma	184.90
66	Diabetes or high blood sugar, Stomach or other digestive disease and Memory-related disease	184.37
67	Diabetes or high blood sugar, Heart disease and Arthritis or rheumatism	183.74

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68	Chronic lung diseases, Stroke and Arthritis or rheumatism	164.06
69	Kidney disease, Arthritis or rheumatism and Asthma	163.36
70	Dyslipidemia, Diabetes or high blood sugar and Arthritis or rheumatism	162.98
71	Hypertension, Diabetes or high blood sugar and Memory-related disease	162.52
72	Hypertension, Dyslipidemia and Kidney disease	160.98
73	Hypertension, Heart disease and Kidney disease	158.80
74	Chronic lung diseases, Liver disease and Kidney disease	157.53
75	Dyslipidemia, Liver disease and Stomach or other digestive disease	157.13
76	Heart disease, Kidney disease and Stomach or other digestive disease	154.42
77	Cancer or malignant tumor, Liver disease and Stomach or other digestive disease	151.34
78	Liver disease, Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	151.34
79	Heart disease, Arthritis or rheumatism and Asthma	145.20
80	Stroke, Kidney disease and Stomach or other digestive disease	143.91
81	Liver disease, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	140.56
82	Diabetes or high blood sugar, Arthritis or rheumatism and Asthma	139.53
83	Hypertension, Dyslipidemia and Liver disease	138.50
84	Hypertension, Heart disease and Asthma	137.80
85	Kidney disease, Stomach or other digestive disease and Arthritis or rheumatism	136.43
86	Chronic lung diseases, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	133.68
87	Hypertension, Liver disease and Asthma	133.40
88	Hypertension, Diabetes or high blood sugar and Cancer or malignant tumor	132.42
89	Chronic lung diseases, Stomach or other digestive disease and Arthritis or rheumatism	131.24
90	Hypertension, Diabetes or high blood sugar and Kidney disease	130.80
91	Heart disease, Stomach or other digestive disease and Arthritis or rheumatism	128.06
92	Dyslipidemia, Heart disease and Stomach or other digestive disease	121.74
93	Hypertension, Heart disease and Arthritis or rheumatism	121.06
94	Stomach or other digestive disease, Arthritis or rheumatism and Asthma	118.39
95	Chronic lung diseases, Heart disease and Arthritis or rheumatism	117.36
96	Hypertension, Liver disease and Heart disease	117.11
97	Diabetes or high blood sugar, Kidney disease and Arthritis or rheumatism	114.85
98	Chronic lung diseases, Heart disease and Stomach or other digestive disease	113.73
99	Hypertension, Diabetes or high blood sugar and Liver disease	112.54
100	Diabetes or high blood sugar, Chronic lung diseases and Heart disease	104.24
101	Liver disease, Stomach or other digestive disease and Arthritis or rheumatism	104.21
102	Stroke, Stomach or other digestive disease and Arthritis or rheumatism	103.78

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103	Hypertension, Kidney disease and Emotional, nervous, or psychiatric problems	103.36
104	Chronic lung diseases, Liver disease and Arthritis or rheumatism	102.25
105	Hypertension, Dyslipidemia and Arthritis or rheumatism	100.61
106	Liver disease, Kidney disease and Stomach or other digestive disease	99.65
107	Dyslipidemia, Cancer or malignant tumor and Stomach or other digestive disease	92.45
108	Dyslipidemia, Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	92.45
109	Hypertension, Dyslipidemia and Chronic lung diseases	92.21
110	Hypertension, Chronic lung diseases and Heart disease	89.11
111	Heart disease, Stroke and Arthritis or rheumatism	89.10
112	Hypertension, Heart disease and Stomach or other digestive disease	88.07
113	Chronic lung diseases, Heart disease and Kidney disease	81.37
114	Chronic lung diseases, Kidney disease and Arthritis or rheumatism	79.23
115	Diabetes or high blood sugar, Chronic lung diseases and Arthritis or rheumatism	78.94
116	Chronic lung diseases, Kidney disease and Stomach or other digestive disease	75.82
117	Hypertension, Diabetes or high blood sugar and Arthritis or rheumatism	75.46
118	Hypertension, Dyslipidemia and Stomach or other digestive disease	75.00
119	Chronic lung diseases, Liver disease and Stomach or other digestive disease	73.39
120	Hypertension, Memory-related disease and Arthritis or rheumatism	73.19
121	Stomach or other digestive disease, Memory-related disease and Arthritis or rheumatism	72.65
122	Heart disease, Kidney disease and Arthritis or rheumatism	71.71
123	Liver disease, Arthritis or rheumatism and Asthma	70.28
124	Diabetes or high blood sugar, Cancer or malignant tumor and Arthritis or rheumatism	69.76
125	Kidney disease, Memory-related disease and Arthritis or rheumatism	66.83
126	Dyslipidemia, Heart disease and Arthritis or rheumatism	65.96
127	Diabetes or high blood sugar, Heart disease and Stomach or other digestive disease	65.94
128	Dyslipidemia, Chronic lung diseases and Heart disease	64.15
129	Hypertension, Kidney disease and Arthritis or rheumatism	63.81
130	Dyslipidemia, Stomach or other digestive disease and Arthritis or rheumatism	63.66
131	Hypertension, Chronic lung diseases and Memory-related disease	62.28
132	Dyslipidemia, Kidney disease and Stomach or other digestive disease	60.88
133	Hypertension, Stroke and Stomach or other digestive disease	59.10
134	Cancer or malignant tumor, Chronic lung diseases and Stomach or other digestive disease	57.58

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135	Cancer or malignant tumor, Chronic lung diseases and Arthritis or rheumatism	53.47
136	Hypertension, Stomach or other digestive disease and Arthritis or rheumatism	52.98
137	Dyslipidemia, Memory-related disease and Arthritis or rheumatism	52.69
138	Dyslipidemia, Stroke and Arthritis or rheumatism	52.69
139	Hypertension, Cancer or malignant tumor and Chronic lung diseases	50.75
140	Hypertension, Chronic lung diseases and Kidney disease	50.13
141	Liver disease, Heart disease and Arthritis or rheumatism	46.27
142	Hypertension, Cancer or malignant tumor and Arthritis or rheumatism	44.73
143	Hypertension, Liver disease and Kidney disease	43.92
144	Hypertension, Chronic lung diseases and Liver disease	43.13
145	Dyslipidemia, Cancer or malignant tumor and Arthritis or rheumatism	42.93
146	Dyslipidemia, Arthritis or rheumatism and Asthma	42.93
147	Hypertension, Diabetes or high blood sugar and Chronic lung diseases	42.81
148	Dyslipidemia, Kidney disease and Arthritis or rheumatism	42.40
149	Stomach or other digestive disease, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	42.28
150	Hypertension, Liver disease and Arthritis or rheumatism	41.18
151	Hypertension, Stomach or other digestive disease and Memory-related disease	39.40
152	Diabetes or high blood sugar, Stomach or other digestive disease and Arthritis or rheumatism	39.24
153	Hypertension, Arthritis or rheumatism and Asthma	37.27
154	Dyslipidemia, Liver disease and Arthritis or rheumatism	36.48
155	Heart disease, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	36.30
156	Hypertension, Chronic lung diseases and Arthritis or rheumatism	34.95
157	Dyslipidemia, Chronic lung diseases and Arthritis or rheumatism	34.70
158	Hypertension, Diabetes or high blood sugar and Stomach or other digestive disease	33.85
159	Cancer or malignant tumor, Stomach or other digestive disease and Arthritis or rheumatism	33.83
160	Liver disease, Heart disease and Stomach or other digestive disease	33.21
161	Dyslipidemia, Chronic lung diseases and Stomach or other digestive disease	29.89
162	Diabetes or high blood sugar, Liver disease and Arthritis or rheumatism	29.64
163	Hypertension, Kidney disease and Stomach or other digestive disease	26.42
164	Diabetes or high blood sugar, Chronic lung diseases and Stomach or other digestive disease	24.29
165	Hypertension, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	22.36
166	Hypertension, Liver disease and Stomach or other digestive disease	20.46

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167	Hypertension, Cancer or malignant tumor and Stomach or other digestive disease	16.05
168	Hypertension, Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	16.05
169	Hypertension, Chronic lung diseases and Stomach or other digestive disease	15.57

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Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-024268.R2
Article Type:	Research
Date Submitted by the Author:	28-Feb-2019
Complete List of Authors:	zhang, ran; China Pharmaceutical University, School of International Pharmaceutical Business Lu, Yun; China Pharmaceutical University, School of International Pharmaceutical Business Shi, Liuyan; China Pharmaceutical University, School of International Pharmaceutical Business Zhang, SongLin; China Pharmaceutical University, School of International Pharmaceutical Business Chang, Feng; China Pharmaceutical University, School of International Pharmaceutical Business
Primary Subject Heading:	Health informatics
Secondary Subject Heading:	Public health, Qualitative research
Keywords:	multimorbidity, cross-sectional study, Prevalence, Observed-to-expected ratio, China

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Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data

Author

NAME: Ran Zhang

Postal address: 639 Longmian Road, Nanjing, Jiangsu Province, CHINA

E-mail:ranzai7@126.com

Institutions: China Pharmaceutical University

City & Country: Jiangsu Province, CHINA

Telephone: +86-18115161231

Corresponding Author

NAME: Feng Chang

Postal address: 639 Longmian Road, Nanjing, Jiangsu Province, CHINA

E-mail: cpucf@163.com

Institutions: China Pharmaceutical University

City & Country: Jiangsu Province, CHINA

Telephone: +86-13805153128

Co-Authors

NAME: Yun Lu, Liuyan Shi, Songlin Zhang

Institutions: China Pharmaceutical University

City & Country: Jiangsu Province, CHINA

Keywords:

multimorbidity, Cross-sectional study, Prevalence, Observed-to-expected ratio, China

Word count: 4911

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ABSTRACT

Objectives: Examination of the prevalence and patterns of multimorbidity among the elderly in China.

Design: Cross-sectional study.

Setting: More than 10,000 households in 28 of the 34 provinces of mainland China.

Participants: 11,707 Chinese adults aged 60 and over.

Primary outcome measures: Prevalence and patterns of multimorbidity among the participants. Relative risks were calculated to estimate the probability of up to 14 chronic conditions coexisting with each other. Observed-to-expected (O/E) ratios were used to analyze the patterns of multimorbidity.

Results: Multimorbidity was present in 43.6% of respondents from the sample population, with women having the greater prevalence compared to men. There were 804 different comorbidity combinations identified, including 76 dyad combinations and 169 triad combinations. The top 10 morbidity dyads and triads accounted for 69.01% and 47.05% of the total dyad and triad combinations observed, respectively. Among the 14 chronic conditions included in the study, asthma, stroke, heart attack and six other chronic conditions were the main components of multimorbidity due to their high relative risk ratios. The most frequently occurring clusters with higher O/E ratios were stroke along with emotional, nervous, or psychiatric problems; memory-related diseases together emotional, nervous, or psychiatric problems; and memory-related diseases and asthma accompanied by chronic lung diseases and asthma.

Conclusions: The results of this study highlight the high prevalence of multimorbidity in the elderly population in China. Further studies are required to understand the etiology of multimorbidity, and future primary healthcare policies should be made while taking multimorbidity into consideration.

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Strengths and limitations of this study

Strengths

- This is the first study to estimate the prevalence and patterns of multimorbidity among the elderly population in China.
- Data for this study were collected from a nationally representative longitudinal survey of 17,708 Chinese residents.

Limitations

- Only 14 predefined chronic diseases were included in the study, and these may not be comprehensive of the conditions of the population.
- The data analyzed from the CHARLS were originally collected by population self-reporting, not clinician evaluation, and could partially reflect some associated biases or confounds.
- The exclusion of incomplete data may cause a selection bias.

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INTRODUCTION

Multimorbidity, or the simultaneous occurrence of two or more chronic conditions in an individual, is becoming increasingly common, and this has been reported to increase progressively with age. [1, 2] At present, with China's aging population having an increasing prevalence of chronic conditions, multimorbidity among the elderly poses an enormous societal cost due to increased mortality rates and healthcare utilization. [3] However, to date, research on chronic conditions in China has focused on single disease states, and the coexistence of multiple chronic conditions has not been investigated systematically and thoroughly.

There is a significant difference in the etiological analysis between patients with single chronic conditions and those with multimorbidity. [4] The coexistence of chronic conditions in a patient is more than a random event, it is more typically due to the causal relationship between some diseases and shared pathogenic factors. [5, 6] Moreover, the interactions between diseases or between a disease and host result in differences in the severity of multimorbidity and functional status and prognosis of patients with multimorbidity. [7] Consequently, it is imperative to begin research on multimorbidity in China for the cost-effective treatments that the results may help to suggest. [8] The purpose of this study was therefore to determine the prevalence of multimorbidity among the elderly in China and to reveal morbidity combinations, which may benefit the design and implementation of a modified healthcare system with consideration for patients with multimorbidity.

METHODS

Data source

Data for this study were collected from the third response of the China Health and Retirement Longitudinal Survey (CHARLS), which is the most current data available. The CHARLS is a nationally representative longitudinal survey of Chinese residents aged 45 and older that was conducted by the Chinese Center for Disease Control and Prevention, along with Peking University, to help China to adjust to the rapid aging of its population through the evaluation of social, economic, and health circumstances on

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the community level using data collected by interviews, physical measurements and blood sample collection. [9] The national baseline survey began in 2011 and involved 17,708 respondents from 150 county-level units, 450 village-level units, and approximately 10,000 households. Afterwards, CHARLS respondents were followed every second year, with their informed consent, and the study was approved by the Peking University Biomedical Ethics Committee (IRB00001052-14013-exemption).

Variables

The core CHARLS questionnaires included sections requesting information on demographic factors, family structure and changes, health status and functioning, healthcare and insurance, work, retirement and pension, income and consumption, and assets (individual and household). Information was collected by interview by trained staff. For the current study, the eligible and included participants were determined by being aged 60 and over, and data on gender, age and health status was used from the general health status and disease history section of senior citizens in the 2015 CHARLS data. This information included the following 14 common chronic health problems: hypertension, dyslipidemia (high blood lipids or low cholesterol), diabetes or elevated blood glucose (including impaired glucose tolerance and fasting blood glucose), cancer (excluding mild skin cancers), chronic lung disease such as chronic bronchitis or emphysema, pulmonary heart disease (excluding tumors or cancer), liver disease (other than fatty liver, tumors, or cancer), heart disease (such as myocardial infarction, coronary heart disease, angina pectoris, congestive heart failure and other heart diseases), stroke, kidney disease (excluding tumors or cancer), stomach or other digestive diseases (excluding tumors or cancer), emotional and mental problems, memory-related diseases (such as Alzheimer's disease, brain atrophy, Parkinson's disease), arthritis or rheumatism, and asthma. All these data were based on self-reports. Accordingly, multimorbidity was defined as the coexistence of more than one of the 14 chronic conditions, with acute or subacute forms of certain conditions being excluded in this study due to the CHARLS data collection protocol.

Statistical analysis

To detect the demographic characteristics of patients with multimorbidity, respondents were divided into two groups: those with multiple chronic conditions (MCC group) and those without multiple chronic conditions (Non-MCC group).

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Descriptive statistics were calculated and expressed as means (SD) and frequencies (percentage). We applied the T^2 and χ^2 texts to test the differences in age, gender and the mean number of chronic conditions across different subgroups. Respective prevalence in the MCC group and the non-MCC group were calculated separately. Given the exclusion of participants with incomplete data or aged under 60, a sensitivity analysis was conducted to compare the characteristics of the complete cases and the incomplete cases, which is presented in Annex 1.

To determine the most common combination of chronic diseases, the prevalence of morbidity and multimorbidity dyads and triads were estimated, respectively. Next, the expected number of patients with a chronic disease were calculated, and the observed-to-expected (O/E) ratios were determined by dividing the number of patients in those groups by the expected number of patients. Observed-to-expected ratios were used to estimate the conditional probability of coexistence of two or three chronic conditions. [10] As an important indicator for assessing the correlation between diseases, the O/E ratio has been used in many areas of comorbidity. [10， 11] The relative risk of comorbidity for individual chronic conditions was also calculated. Relative risk of comorbidity (RR) is the ratio of the number of people with a certain chronic condition who suffer from multimorbidity to the number of patients with the same disease who do not suffer from multimorbidity. [11, 12] In other words, a higher RR value means a higher probability that the disease coexists with other diseases. However, it should be noted that there is no direct relationship between the relative risk of comorbidity and the overall prevalence of the diseases. [13, 14]

All analyses in this study were completed using Stata softwareV.14.0 for Windows (Stata Corp). P Values <0.05 were considered to be statistically significant.

Patient and public involvement

Patients and the public were not 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 results to study participants.

RESULTS

Characteristics of participants

The data were gathered from the third response set of CHARLS. After exclusion

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of participants with incomplete data (1,002) or aged under 60 (9,259), there were 11,707 respondents with available information on related chronic diseases that were included in this study. The selection process of study sample is shown in Figure 1. The demographic characteristics of sample respondents and statistical significance test results are presented in Table 1.

Overall, the mean age for the sample population was 70.5 (ranging from 60 to 107). The sample population consisted of 5,705 (48.7%) males and 6002 (51.2%) females, and 43.6% of them suffered from multimorbidity. The median of chronic conditions in the MCC group was 3.01, compared to 0.45 in the Non-MCC group. Samples in the MCC group were 0.66 year older than those belonged to the non-MCC group. Gender differences with regard to the age of samples between the MCC group and the non-MCC group (70.57 for MCC group and 69.51 for non-MCC group) were small but statistically significant ($p < 0.001$). The prevalence of multimorbidity in the female population was higher than that for the males (54.41% vs 45.59%). Figure 2 shows the number and proportion of respondents over 60 according to morbidity numbers. It can be seen that among all the participants aged over 60, only 30.9% of them did not have the 14 chronic diseases and 43.6% suffer from multimorbidity.

Table 1. Demographic characteristics of all respondents, the MCC group and non-MCC group

	All respondents	**MCC group**	**Non-MCC group**	**P***
Number of people	11707	5107	6600	
Proportion (%)	100%	43.62%	56.38%	
Mean age				
All respondents (SD)	70.20(7.907)	70.57(7.701)	69.91(8.051)	<0.001
Male (SD)	69.97(7.575)	70.50(7.348)	69.60(7.707)	<0.001
Female (SD)	70.39(8.189)	70.62(7.892)	70.19(8.359)	<0.001
Gender（% females）	51.28%	54.41%	48.83%	<0.001
Mean number of chronic conditions				
All respondents（SD）	1.57(1.560)	3.01(1.259)	0.45(0.498)	<0.001
Male（SD）	1.47(1.534)	2.98(1.265)	0.44(0.496)	<0.001
Female（SD）	1.65(1.581)	3.03(7.982)	0.47(0.499)	<0.001

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SD = standard deviation;

p* = statistical significance of the difference between the MCC and the non-MCC sample (t-tests were performed for comparison of means, and chi-square-tests for differences between percentages)

Prevalence of chronic conditions

The prevalence of chronic conditions in the entire sample, the MCC group and the non-MCC group are shown in Figure 3. The prevalence of all fourteen chronic conditions in the MCC group was significantly higher than that in the entire sample. For instance， the prevalence of arthritis or rheumatism, hypertension, stomach or other digestive disease, heart disease and chronic lung disease were 65.97%, 48.82%, 45.86%, 29.00% and 24.97% in the MCC group, compared to 38.49%, 26.41%, 24.52%, 12.32% and 12.32% in the entire sample, respectively.

Table 2 shows the relative risks of comorbidity determined for the 14 chronic diseases reported in this study. It can be seen that the overall relative risks for asthma, stroke, heart disease and six other conditions were all above 10, which meant these diseases were >10 times easier to coexist with other chronic conditions and result in multimorbidity. In addition, the relative risks for certain diseases were positively associated with gender. For example, men had significantly higher relative risks for asthma, but lower relative risks for diabetes or high blood sugar, compared to women.

Table 2 Relative risks of multimorbidity for different chronic conditions according to gender

Chronic conditions	All respondents	95% Confidence Interval		Female	95% Confidence Interval		Male	95% Confidence Interval	
		Lower Bound	Upper Bound		Lower Bound	Upper Bound		Lower Bound	Upper Bound
High relative risk of multimorbidity									
Asthma	26.18	17.82	38.46	20.67	11.85	36.06	32.68	19.18	55.67
Stroke	18.62	12.11	28.64	21.57	10.61	43.86	17.43	10.13	29.99
Heart disease	15.56	12.99	18.63	16.48	12.80	21.21	14.26	11.02	18.46
Diabetes or high blood sugar	14.40	11.18	18.55	15.68	10.86	22.63	13.11	9.24	18.62

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Dyslipidemia	14.05	11.54	17.12	15.13	11.37	20.14	12.97	9.86	17.05
Memory-related disease	13.69	8.85	21.16	34.17	12.63	92.44	9.28	5.66	15.21
Kidney disease	11.57	9.24	14.49	15.01	10.17	22.43	10.24	7.78	13.48
Liver disease	11.10	8.37	14.71	16.07	9.70	26.63	9.15	6.49	12.89
Chronic lung diseases	9.87	8.43	11.55	10.71	8.26	13.88	9.74	8.00	11.86
Low relative risk of multimorbidity									
Emotional, nervous, or psychiatric problems	7.42	4.94	11.15	6.24	3.78	10.30	9.36	4.65	18.85
Stomach or other digestive disease	5.73	5.25	6.25	6.20	5.48	7.02	5.23	4.62	5.91
Hypertension	5.38	4.96	5.84	4.90	4.40	5.47	5.92	5.24	6.69
Cancer or malignant tumor	4.88	3.20	7.45	5.33	3.06	9.29	3.99	2.07	7.72
Arthritis or rheumatism	3.83	3.61	4.05	3.70	3.43	3.99	3.91	3.59	4.26

Common multimorbidity combinations

There were 804 possible comorbidity combinations that were identified in the MCC group after statistical analysis, including 72 dyads and 169 triads. The 10 most frequently occurring morbidity dyads and triads are presented respectively in Table 3 and Table 4.

Table3 Prevalence of the 10 most common morbidity dyads

Rank	Morbidity dyads	Prevalence			Mean
		All respondents	female	male	Age
1	Arthritis or rheumatism and Stomach or other digestive disease	4.73%	3.56%	5.96%	69.20
2	Arthritis or rheumatism and Hypertension	2.85%	2.20%	3.53%	71.25
3	Arthritis or rheumatism and Chronic lung diseases	1.13%	1.22%	1.04%	71.55
4	Hypertension and heart problems	1.03%	1.00%	1.06%	71.80
5	Hypertension and Stomach or other digestive disease	0.89%	0.83%	0.95%	69.07
6	Hypertension	0.86%	0.81%	0.91%	68.58

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	and Dyslipidemia				
7	Arthritis or rheumatism and heart problems	0.76%	0.53%	1.00%	70.72
8	Arthritis or rheumatism and Kidney disease	0.64%	0.73%	0.54%	68.24
9	Hypertension and Diabetes or high blood sugar	0.58%	0.50%	0.67%	70.97
10	Chronic lung diseases and Asthma	0.53%	0.65%	0.40%	71.15

Table 4 Prevalence of the 10 most common morbidity triads

Rank	Morbidity triads	Prevalence			Mean Age
		All respondents	female	male	
1	Arthritis or rheumatism, Stomach or other digestive disease and Hypertension	1.19%	0.80%	1.60%	70.96
2	Arthritis or rheumatism, Stomach or other digestive disease and Chronic lung diseases	0.82%	0.97%	0.67%	70.82
3	Arthritis or rheumatism, Heart disease and Hypertension	0.63%	0.37%	0.91%	69.93
4	Arthritis or rheumatism, Heart disease and Stomach or other digestive disease	0.59%	0.25%	0.95%	71.51
5	Hypertension, Dyslipidemia and Arthritis or rheumatism	0.44%	0.31%	0.57%	70.13
6	Hypertension, Dyslipidemia and Heart problems	0.42%	0.35%	0.49%	71.17
7	Arthritis or rheumatism, Kidney disease and Stomach or other digestive disease	0.42%	0.40%	0.44%	70.14
8	Arthritis or rheumatism, Asthma and Chronic lung diseases	0.40%	0.46%	0.33%	69.18
9	Hypertension, Dyslipidemia and Diabetes or high blood sugar	0.35%	0.35%	0.35%	71.51
10	Arthritis or rheumatism, Stomach or other digestive disease	0.53%	0.57%	0.49%	70.29

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and Liver disease

Theoretically, there are 91 dyad combinations and 364 triad combinations possible given the 14 different chronic conditions considered in this study. However, only 72 types (79.12%) of dyads and 169 types (46.43%) of triads emerged in the sample. The 10 most frequently occurring morbidity dyads accounted for 69.01% of the 72 dyad combinations, and the proportion of the 10 most common triad combinations in the 169 triad combinations was 47.05%. Arthritis or rheumatism, which appeared in five of the top 10 dyad combinations and eight of the top 10 triad combinations of chronic conditions, was the main component of the leading morbidity dyads and triads.

There were significant gender differences observed in the occurrences of these multimorbidity combinations. The numbers of women with triad combinations of chronic diseases were generally higher than for men with the same morbidity triads. For example, women had significantly higher prevalence of arthritis and hypertension and hyperlipidemia than men (78.26% vs 21.74%). Among morbidity dyads, the prevalence of heart disease and arthritis or rheumatism in women was nearly two times higher than that in men, while the cluster of arthritis or rheumatism and kidney disease occurred more frequently in men than in women. No age difference was detected in the probability of these particular multimorbidity combinations occurring.

The O/E ratio was also used to analyze the multimorbidity pattern. [15] The higher the O/E value, the higher the probability of coexistence of chronic conditions. [16] Table 5 shows O/E ratios determined for the 10 most prevalent morbidity dyads and triads. The prevalence of each conditions and the dyad and triad prevalence are presented in Annex 2. In the midst of those triad combinations of chronic conditions, the two clusters with significantly higher O/E ratios were emotional, nervous, or psychiatric problems and stroke and memory-related disease (O/E ratio = 10287.72), emotional, nervous, or psychiatric problems and memory-related disorders and asthma (O/E ratio = 8498.56). These four conditions also dominated the three leading dyads

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with the highest O/E ratios: 97.73 for the combination of emotional and mental disorders and memory- related diseases, 23.66 for the combination of stroke and memory related disease and 19.55 for the combination of memory-related disease and asthma.

Table 5 O/E ratios for the 10 most prevalent morbidity dyads and triads

Number of chronic conditions	Rank	Chronic conditions	O/E ratio
2	1	Chronic lung diseases and Asthma	162.15
	2	Emotional, nervous, or psychiatric problems and Memory-related disease	97.73
	3	Dyslipidemia and Diabetes or high blood sugar	38.39
	4	Heart disease and Memory-related disease	25.69
	5	Stroke and Memory-related disease	23.66
	6	Hypertension and Stroke	22.85
	7	Hypertension and Diabetes or high blood sugar	20.64
	8	Cancer or malignant tumor and Stroke	19.55
	9	Memory-related disease and Asthma	19.55
	10	Stroke and Asthma	19.55
3	1	Stroke, Emotional, nervous, or psychiatric problems and Memory-related disease	10287.72
	2	Emotional, nervous, or psychiatric problems, Memory-related disease and Asthma	8498.56
	3	Emotional, nervous, or psychiatric problems, Chronic lung diseases and Asthma	2274.26
	4	Heart disease, Stroke and Memory-related disease	2253.50
	5	Chronic lung diseases, Heart disease and Asthma	1992.69
	6	Dyslipidemia, Heart disease and Memory-related disease	1443.25
	7	Hypertension, Dyslipidemia and Diabetes or high blood sugar	1398.31

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8	Hypertension, Stroke and Memory-related disease	1387.35
9	Chronic lung diseases, Memory-related disease and Asthma	1376.53
10	Chronic lung diseases, Arthritis or rheumatism and Asthma	1265.95

DISCUSSION

This is the first study to estimate the prevalence and patterns of multimorbidity among the elderly in China based on the nationally representative data from CHARLS, which covered 11,707 Chinese senior citizens of age 60 and over. The results of the study indicated that 69.1% of the elderly population in China had at least one of the 14 diseases and 43.6% of them suffered from multimorbidity. The average age of the MCC group was 0.66 years higher than that of the non-MCC group and in the MCC group, the mean age of women was 0.12 years higher than that of men, which was comparable to the results of previous studies. [17-21]

The prevalence of multimorbidity estimated in this study was much lower than that from previous studies in other developed countries. For example, a study of 543 patients over age 65 in Ghent, Belgium showed that the multimorbidity rate was as high as 82.6%, [22]. Another study in Australia showed that 83.2% of the respondents suffered from multimorbidity. [23] However, it is difficult to compare the prevalence generated from different studies due to differences in the selected definitions of multimorbidity, demographic characteristics of the samples, and different study methodologies. [24-28]

In agreement with previous reports, arthritis or rheumatism, hypertension, stomach or other digestive disease were the most common diseases in the MCC group. [11] The prevalence of these three conditions was each above 20% in the entire sample, and above 45% in the MCC group. The most prevalent chronic combinations in the sample could also be found in other studies. [22] The results of this study showed that the prevalence of arthritis or rheumatism was high and easy to coexist with other conditions.

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In addition to the chronic conditions mentioned above, previous studies demonstrated that women with rheumatoid arthritis might have a predisposition to gallstones which could manifest in middle or older age compared with women in the general population. This phenomenon could be related to chronic inflammation and HDL metabolism. [29]

Although arthritis or rheumatism, a component of all the leading three morbidity dyads and triads, was also the most commonly occurring disease in multimorbidity, the relative risk of this disease was only 4.65, the lowest in the 14 chronic diseases. Moreover, arthritis or rheumatism is less common in morbidity clusters with large O/E ratios. Therefore, the frequent occurrence of arthritis or rheumatism in multimorbidity might be simply due to the high prevalence of the disease. Doctor-diagnosed arthritis is a common and disabling chronic condition in the world. During 2013 to 2015, an average of more than one in five (54.4 million) adults in the United States were diagnosed with arthritis [30]. The unadjusted prevalences of arthritis among adults with obesity, heart disease, or diabetes were 30.6%, 49.3%, and 47.1%, respectively. In adults with obesity, heart disease, or diabetes, the age-adjusted prevalences of arthritis were respectively 1.5, 1.7 and 1.9 times higher than those without these diseases. Improving the health of adults with arthritis and related comorbid conditions calls for wider dissemination and implementation of evidence-based interventions, such as self-management education and physical activity promotion [31].

The relative risks for asthma, stroke, heart disease, and six other conditions were all above 10, which means that patients with these diseases were 10 times more likely to be afflicted by multimorbidity. These diseases also occurred at a high frequency in multimorbidity with high O/E ratios, such as the clusters of pulmonary disease and asthma, emotional and mental illness and memory-related disease, dyslipidemia and diabetes, and stroke and emotional or mental illness and memory-related disease. Patients with these diseases were more likely to express comorbidity compared to those without these diseases, and thus should be the focus of future research studies.

This study featured a nationally representative sample of the Chinese elderly

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population, which was crucial to get an overall understanding of multimorbidity among the elderly in China. However, there were also limitations with the data sample and study. For example, this study used data from the third wave report of CHARLS, a survey which was conducted in 2015, and there is accordingly a time lag to now that exists. Additionally, the chronic diseases included in the study were not comprehensive, since only 14 chronic conditions were included in the survey. Finally, the data obtained from the survey was based on self-reporting, which may have introduced some misclassification bias or other confounds. Later research on the prevalence and patterns of multimorbidity should be carried out in-depth with a more extensive survey of chronic disease.

CONCLUSIONS

Multimorbidity remains an underexplored area of research in China. [32]. Despite the increasing prevalence of multimorbidity, there are no specific proposals for its diagnosis and treatment. [33] This study contributes to the understanding of the prevalence and patterns of comorbidity among the elderly in China. Considering China's aging population and the high prevalence of comorbidity in senior citizens, the elderly should be prioritized in the fields of disease prevention and health promotion.

Acknowledgements The authors would like to thank the Chinese Center for Disease Control and Prevention and Peking University for access to China Health and Retirement Longitudinal Survey data.

Contributors RZ analyzed and interpreted data, drafted the manuscript, approved the final manuscript as submitted. YL revised the manuscript for important intellectual content. YLS analyzed and interpreted data and revised the manuscript for important intellectual content. FC helped on the study design and revised the manuscript.

Funding This work was funded by the National Natural Science Foundation of China

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(7167030838).

Competing interests None declared.

Patient consent Obtained.

Ethics approval The original CHARLS was approved by the ethics review committee of Peking University, and all participants gave written informed consent at the time of participation

Data sharing statement No additional data are available

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Figure legends

Figure 1 Flowchart for selecting the study sample from the original sample population. CHARLS, China Health and Retirement Longitudinal Survey

Figure 2 Frequency and percentage of people aged over 60 suffering from different diseases based on CHARLS data

Figure 3 Prevalence Rates of chronic condition in elderly people over 60 years old based on CHARLS data

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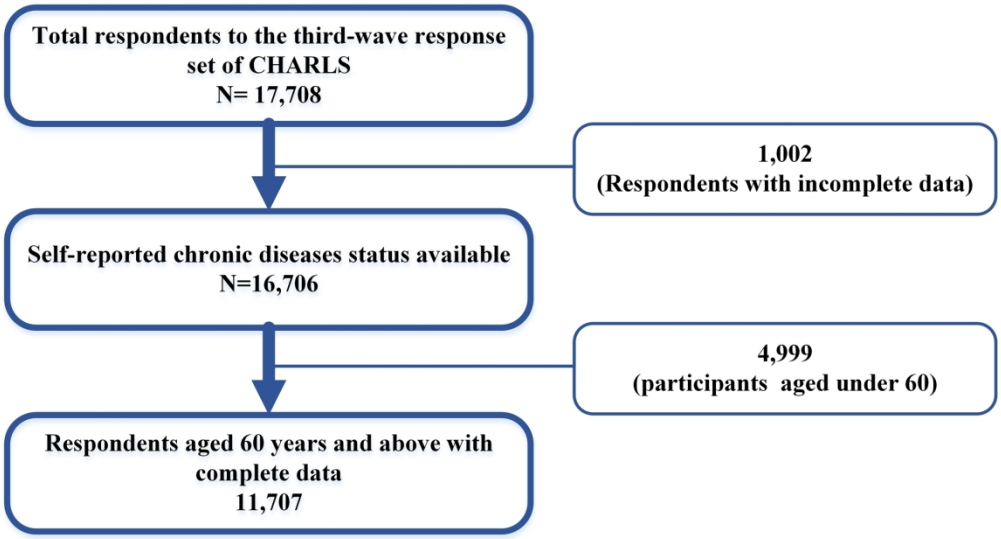

Figure 1 Flowchart for selecting the study sample from the original sample population. CHARLS, China Health and Retirement Longitudinal Survey

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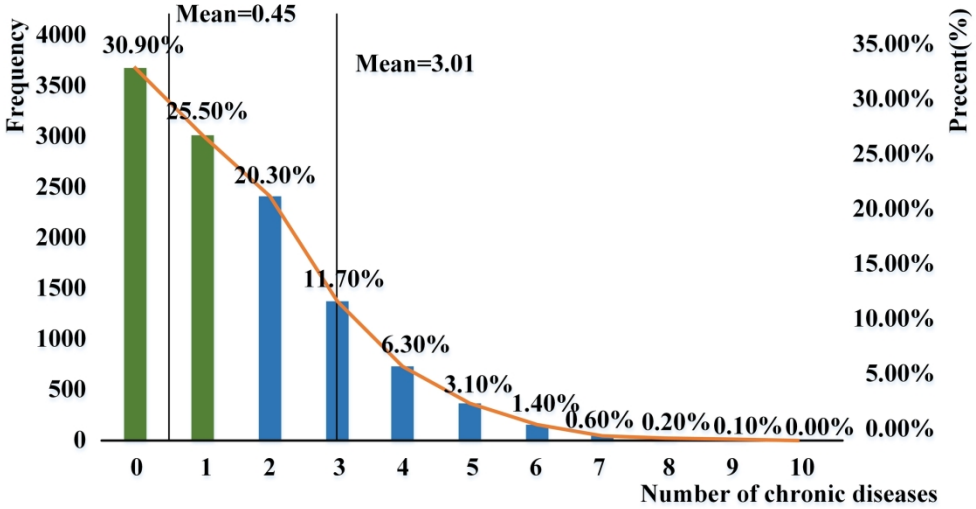

Figure 2 Frequency and percentage of people aged over 60 suffering from different diseases based on CHARLS data

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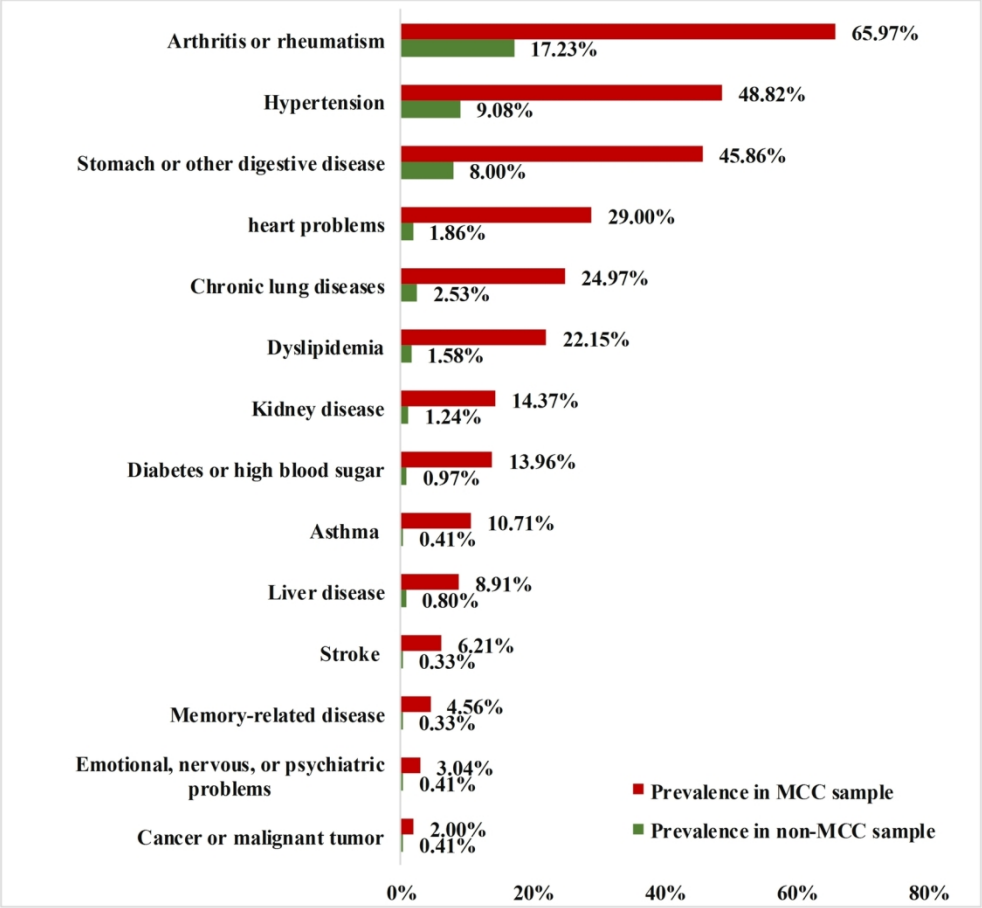

Figure 3 Prevalence Rates of chronic condition in elderly people over 60 years old based on CHARLS data

151x140mm (300 x 300 DPI)

Annex 1 Sensitivity analysis, Comparison of the characteristics of complete samples and incomplete samples

	Complete samples	**Incomplete samples**	**P***
Number of people	11707	876	
Proportion (%)	93.04%	6.96%	
Mean age All respondents (SD)	70.20(7.907)	69.60（7.824）	<0.001
Male (SD)	69.97(7.575)	69.58（7.721）	<0.001
Female (SD)	70.39(8.189)	69.62（7.973）	<0.001
Gender（% females）	51.28%	49.27%	0.193

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Annex 2 O/E ratio of all binary and triads comorbidities pattern present in participants

Rank	binary comorbidities pattern	O/E ratio
1	Chronic lung diseases and Asthma	161.00
2	Emotional, nervous, or psychiatric problems and Memory-related disease	98.57
3	Dyslipidemia and Diabetes or high blood sugar	38.69
4	Heart disease and Memory-related disease	25.96
5	Stroke and Memory-related disease	24.19
6	Hypertension and Stroke	23.10
7	Hypertension and Diabetes or high blood sugar	20.77
8	Cancer or malignant tumor and Stroke	19.71
9	Memory-related disease and Asthma	19.71
10	Stroke and Asthma	19.71
11	Hypertension and Heart disease	19.07
12	Hypertension and Dyslipidemia	18.98
13	Dyslipidemia and Heart disease	17.39
14	Diabetes or high blood sugar and Heart disease	14.87
15	Diabetes or high blood sugar and Liver disease	14.40
16	Cancer or malignant tumor and Liver disease	13.65
17	Diabetes or high blood sugar and Kidney disease	13.38
18	Hypertension and Memory-related disease	13.33
19	Dyslipidemia and Cancer or malignant tumor	12.51
20	Stomach or other digestive disease and Arthritis or rheumatism	10.80
21	Liver disease and Heart disease	10.49
22	Dyslipidemia and Stroke	10.23
23	Dyslipidemia and Stomach or other digestive disease	9.81
24	Dyslipidemia and Kidney disease	9.61
25	Chronic lung diseases and Memory-related disease	9.56
26	Chronic lung diseases and Stroke	9.56
27	Kidney disease and Arthritis or rheumatism	9.42
28	Heart disease and Kidney disease	9.29
29	Chronic lung diseases and Heart disease	9.12
30	Stomach or other digestive disease and Asthma	9.03
31	Liver disease and Kidney disease	8.99
32	Kidney disease and Stomach or other digestive disease	8.92
33	Memory-related disease and Arthritis or rheumatism	8.89
34	Stroke and Arthritis or rheumatism	8.89
35	Arthritis or rheumatism and Asthma	8.77
36	Liver disease and Memory-related disease	8.38
37	Diabetes or high blood sugar and Memory-related disease	8.32
38	Diabetes or high blood sugar and Stroke	8.32
39	Chronic lung diseases and Arthritis or rheumatism	8.14
40	Heart disease and Stomach or other digestive disease	8.11

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41	Heart disease and Arthritis or rheumatism	7.45
42	Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	7.39
43	Liver disease and Stomach or other digestive disease	7.33
44	Diabetes or high blood sugar and Cancer or malignant tumor	6.78
45	Diabetes or high blood sugar and Asthma	6.78
46	Diabetes or high blood sugar and Arthritis or rheumatism	6.44
47	Liver disease and Arthritis or rheumatism	6.16
48	Chronic lung diseases and Kidney disease	5.98
49	Chronic lung diseases and Stomach or other digestive disease	5.97
50	Hypertension and Arthritis or rheumatism	5.74
51	Chronic lung diseases and Liver disease	5.52
52	Kidney disease and Emotional, nervous, or psychiatric problems	5.29
53	Kidney disease and Asthma	5.29
54	Chronic lung diseases and Emotional, nervous, or psychiatric problems	5.19
55	Dyslipidemia and Memory-related disease	5.12
56	Hypertension and Emotional, nervous, or psychiatric problems	5.07
57	Hypertension and Chronic lung diseases	5.03
58	Hypertension and Kidney disease	5.01
59	Cancer or malignant tumor and Arthritis or rheumatism	4.96
60	Cancer or malignant tumor and Stomach or other digestive disease	4.93
61	Dyslipidemia and Arthritis or rheumatism	4.75
62	Hypertension and Liver disease	4.61
63	Diabetes or high blood sugar and Chronic lung diseases	4.38
64	Heart disease and Stroke	4.33
65	Dyslipidemia and Asthma	4.17
66	Hypertension and Stomach or other digestive disease	3.85
67	Cancer or malignant tumor and Heart disease	3.53
68	Heart disease and Asthma	3.53
69	Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	3.43
70	Diabetes or high blood sugar and Stomach or other digestive disease	3.12
71	Hypertension and Cancer or malignant tumor	2.17
72	Hypertension and Asthma	2.17
73	Stomach or other digestive disease and Memory-related disease	2.02
74	Stroke and Stomach or other digestive disease	2.02
75	Dyslipidemia and Liver disease	1.77
76	Dyslipidemia and Chronic lung diseases	1.35

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Rank	triads comorbidities pattern	O/E ratio
1	Stroke, Emotional, nervous, or psychiatric problems and Memory-related disease	10491.60
2	Emotional, nervous, or psychiatric problems, Memory-related disease, Asthma,	8548.88
3	Heart disease, Stroke and Memory-related disease	2302.62
4	Chronic lung diseases, Emotional, nervous, or psychiatric problems and Asthma	2252.13
5	Chronic lung diseases, Heart disease, Asthma,	1977.13
6	Dyslipidemia, Heart disease and Memory-related disease	1461.04
7	Hypertension, Stroke and Memory-related disease	1418.54
8	Hypertension, Dyslipidemia and Diabetes or high blood sugar	1409.29
9	Chronic lung diseases, Memory-related disease and Asthma	1381.96
10	Chronic lung diseases, Arthritis or rheumatism and Asthma	1256.63
11	Dyslipidemia, Diabetes or high blood sugar and Kidney disease	1255.51
12	Cancer or malignant tumor, Chronic lung diseases and Asthma	1126.07
13	Chronic lung diseases, Kidney disease and Asthma	1112.24
14	Liver disease, Kidney disease and Asthma	974.52
15	Dyslipidemia, Diabetes or high blood sugar and Liver disease	972.21
16	Chronic lung diseases, Liver disease and Asthma	956.96
17	Dyslipidemia, Diabetes or high blood sugar and Stroke	935.99
18	Chronic lung diseases, Stomach or other digestive disease and Asthma	921.21
19	Hypertension, Dyslipidemia and Heart disease	876.36
20	Diabetes or high blood sugar, Liver disease and Kidney disease	822.11
21	Hypertension, Diabetes or high blood sugar and Stroke	812.58
22	Hypertension, Chronic lung diseases and Asthma	812.01
23	Hypertension, Dyslipidemia and Stroke	800.07
24	Dyslipidemia, Heart disease and Asthma	793.67
25	Diabetes or high blood sugar, Heart disease and Stroke	791.41
26	Hypertension, Emotional, nervous, or psychiatric problems and Memory-related disease	770.58
27	Dyslipidemia, Diabetes or high blood sugar and Cancer or malignant tumor	762.67
28	Dyslipidemia, Diabetes or high blood sugar and Emotional, nervous, or psychiatric problems	762.67
29	Dyslipidemia, Diabetes or high blood sugar and Heart disease	669.54
30	Liver disease, Heart disease and Emotional, nervous, or psychiatric problems	649.62
31	Heart disease, Kidney disease and Memory-related disease	617.74
32	Heart disease, Stroke and Kidney disease	617.74
33	Dyslipidemia, Chronic lung diseases and Asthma	584.58
34	Diabetes or high blood sugar, Liver disease and Heart disease	548.02

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35	Hypertension, Diabetes or high blood sugar and Heart disease	523.14
36	Hypertension, Heart disease and Stroke	507.36
37	Diabetes or high blood sugar, Chronic lung diseases and Asthma	474.98
38	Liver disease, Stomach or other digestive disease and Asthma	454.02
39	Stomach or other digestive disease, Emotional, nervous, or psychiatric problems and Memory-related disease	437.10
40	Hypertension, Memory-related disease, Asthma,	385.29
41	Diabetes or high blood sugar, Stomach or other digestive disease and Asthma	300.46
42	Hypertension, Dyslipidemia and Memory-related disease	300.03
43	Liver disease, Kidney disease and Arthritis or rheumatism	277.66
44	Hypertension, Heart disease and Memory-related disease	253.68
45	Dyslipidemia, Liver disease and Kidney disease	252.95
46	Hypertension, Chronic lung diseases and Stroke	249.13
47	Stroke, Memory-related disease and Arthritis or rheumatism	249.11
48	Dyslipidemia, Chronic lung diseases and Liver disease	248.40
49	Cancer or malignant tumor, Chronic lung diseases and Heart disease	247.14
50	Chronic lung diseases, Heart disease and Emotional, nervous, or psychiatric problems	247.14
51	Hypertension, Dyslipidemia and Asthma	244.47
52	Cancer or malignant tumor, Heart disease and Stomach or other digestive disease	234.50
53	Chronic lung diseases, Memory-related disease and Arthritis or rheumatism	229.69
54	Chronic lung diseases, Stroke and Stomach or other digestive disease	211.98
55	Hypertension, Stroke and Arthritis or rheumatism	210.41
56	Chronic lung diseases, Liver disease and Heart disease	210.03
57	Hypertension, Cancer or malignant tumor and Heart disease	206.71
58	Hypertension, Heart disease and Emotional, nervous, or psychiatric problems	206.71
59	Memory-related disease, Arthritis or rheumatism and Asthma	202.98
60	Emotional, nervous, or psychiatric problems, Memory-related disease and Arthritis or rheumatism	202.98
61	Stroke, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	202.98
62	Stroke, Kidney disease and Arthritis or rheumatism	200.49
63	Dyslipidemia, Diabetes or high blood sugar and Stomach or other digestive disease	194.98
64	Liver disease, Stomach or other digestive disease and Memory-related disease	185.73
65	Dyslipidemia, Stomach or other digestive disease and Asthma	184.90
66	Diabetes or high blood sugar, Stomach or other digestive disease and Memory-related disease	184.37
67	Diabetes or high blood sugar, Heart disease and Arthritis or rheumatism	183.74

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68	Chronic lung diseases, Stroke and Arthritis or rheumatism	164.06
69	Kidney disease, Arthritis or rheumatism and Asthma	163.36
70	Dyslipidemia, Diabetes or high blood sugar and Arthritis or rheumatism	162.98
71	Hypertension, Diabetes or high blood sugar and Memory-related disease	162.52
72	Hypertension, Dyslipidemia and Kidney disease	160.98
73	Hypertension, Heart disease and Kidney disease	158.80
74	Chronic lung diseases, Liver disease and Kidney disease	157.53
75	Dyslipidemia, Liver disease and Stomach or other digestive disease	157.13
76	Heart disease, Kidney disease and Stomach or other digestive disease	154.42
77	Cancer or malignant tumor, Liver disease and Stomach or other digestive disease	151.34
78	Liver disease, Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	151.34
79	Heart disease, Arthritis or rheumatism and Asthma	145.20
80	Stroke, Kidney disease and Stomach or other digestive disease	143.91
81	Liver disease, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	140.56
82	Diabetes or high blood sugar, Arthritis or rheumatism and Asthma	139.53
83	Hypertension, Dyslipidemia and Liver disease	138.50
84	Hypertension, Heart disease and Asthma	137.80
85	Kidney disease, Stomach or other digestive disease and Arthritis or rheumatism	136.43
86	Chronic lung diseases, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	133.68
87	Hypertension, Liver disease and Asthma	133.40
88	Hypertension, Diabetes or high blood sugar and Cancer or malignant tumor	132.42
89	Chronic lung diseases, Stomach or other digestive disease and Arthritis or rheumatism	131.24
90	Hypertension, Diabetes or high blood sugar and Kidney disease	130.80
91	Heart disease, Stomach or other digestive disease and Arthritis or rheumatism	128.06
92	Dyslipidemia, Heart disease and Stomach or other digestive disease	121.74
93	Hypertension, Heart disease and Arthritis or rheumatism	121.06
94	Stomach or other digestive disease, Arthritis or rheumatism and Asthma	118.39
95	Chronic lung diseases, Heart disease and Arthritis or rheumatism	117.36
96	Hypertension, Liver disease and Heart disease	117.11
97	Diabetes or high blood sugar, Kidney disease and Arthritis or rheumatism	114.85
98	Chronic lung diseases, Heart disease and Stomach or other digestive disease	113.73
99	Hypertension, Diabetes or high blood sugar and Liver disease	112.54
100	Diabetes or high blood sugar, Chronic lung diseases and Heart disease	104.24
101	Liver disease, Stomach or other digestive disease and Arthritis or rheumatism	104.21
102	Stroke, Stomach or other digestive disease and Arthritis or rheumatism	103.78

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103	Hypertension, Kidney disease and Emotional, nervous, or psychiatric problems	103.36
104	Chronic lung diseases, Liver disease and Arthritis or rheumatism	102.25
105	Hypertension, Dyslipidemia and Arthritis or rheumatism	100.61
106	Liver disease, Kidney disease and Stomach or other digestive disease	99.65
107	Dyslipidemia, Cancer or malignant tumor and Stomach or other digestive disease	92.45
108	Dyslipidemia, Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	92.45
109	Hypertension, Dyslipidemia and Chronic lung diseases	92.21
110	Hypertension, Chronic lung diseases and Heart disease	89.11
111	Heart disease, Stroke and Arthritis or rheumatism	89.10
112	Hypertension, Heart disease and Stomach or other digestive disease	88.07
113	Chronic lung diseases, Heart disease and Kidney disease	81.37
114	Chronic lung diseases, Kidney disease and Arthritis or rheumatism	79.23
115	Diabetes or high blood sugar, Chronic lung diseases and Arthritis or rheumatism	78.94
116	Chronic lung diseases, Kidney disease and Stomach or other digestive disease	75.82
117	Hypertension, Diabetes or high blood sugar and Arthritis or rheumatism	75.46
118	Hypertension, Dyslipidemia and Stomach or other digestive disease	75.00
119	Chronic lung diseases, Liver disease and Stomach or other digestive disease	73.39
120	Hypertension, Memory-related disease and Arthritis or rheumatism	73.19
121	Stomach or other digestive disease, Memory-related disease and Arthritis or rheumatism	72.65
122	Heart disease, Kidney disease and Arthritis or rheumatism	71.71
123	Liver disease, Arthritis or rheumatism and Asthma	70.28
124	Diabetes or high blood sugar, Cancer or malignant tumor and Arthritis or rheumatism	69.76
125	Kidney disease, Memory-related disease and Arthritis or rheumatism	66.83
126	Dyslipidemia, Heart disease and Arthritis or rheumatism	65.96
127	Diabetes or high blood sugar, Heart disease and Stomach or other digestive disease	65.94
128	Dyslipidemia, Chronic lung diseases and Heart disease	64.15
129	Hypertension, Kidney disease and Arthritis or rheumatism	63.81
130	Dyslipidemia, Stomach or other digestive disease and Arthritis or rheumatism	63.66
131	Hypertension, Chronic lung diseases and Memory-related disease	62.28
132	Dyslipidemia, Kidney disease and Stomach or other digestive disease	60.88
133	Hypertension, Stroke and Stomach or other digestive disease	59.10
134	Cancer or malignant tumor, Chronic lung diseases and Stomach or other digestive disease	57.58

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135	Cancer or malignant tumor, Chronic lung diseases and Arthritis or rheumatism	53.47
136	Hypertension, Stomach or other digestive disease and Arthritis or rheumatism	52.98
137	Dyslipidemia, Memory-related disease and Arthritis or rheumatism	52.69
138	Dyslipidemia, Stroke and Arthritis or rheumatism	52.69
139	Hypertension, Cancer or malignant tumor and Chronic lung diseases	50.75
140	Hypertension, Chronic lung diseases and Kidney disease	50.13
141	Liver disease, Heart disease and Arthritis or rheumatism	46.27
142	Hypertension, Cancer or malignant tumor and Arthritis or rheumatism	44.73
143	Hypertension, Liver disease and Kidney disease	43.92
144	Hypertension, Chronic lung diseases and Liver disease	43.13
145	Dyslipidemia, Cancer or malignant tumor and Arthritis or rheumatism	42.93
146	Dyslipidemia, Arthritis or rheumatism and Asthma	42.93
147	Hypertension, Diabetes or high blood sugar and Chronic lung diseases	42.81
148	Dyslipidemia, Kidney disease and Arthritis or rheumatism	42.40
149	Stomach or other digestive disease, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	42.28
150	Hypertension, Liver disease and Arthritis or rheumatism	41.18
151	Hypertension, Stomach or other digestive disease and Memory-related disease	39.40
152	Diabetes or high blood sugar, Stomach or other digestive disease and Arthritis or rheumatism	39.24
153	Hypertension, Arthritis or rheumatism and Asthma	37.27
154	Dyslipidemia, Liver disease and Arthritis or rheumatism	36.48
155	Heart disease, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	36.30
156	Hypertension, Chronic lung diseases and Arthritis or rheumatism	34.95
157	Dyslipidemia, Chronic lung diseases and Arthritis or rheumatism	34.70
158	Hypertension, Diabetes or high blood sugar and Stomach or other digestive disease	33.85
159	Cancer or malignant tumor, Stomach or other digestive disease and Arthritis or rheumatism	33.83
160	Liver disease, Heart disease and Stomach or other digestive disease	33.21
161	Dyslipidemia, Chronic lung diseases and Stomach or other digestive disease	29.89
162	Diabetes or high blood sugar, Liver disease and Arthritis or rheumatism	29.64
163	Hypertension, Kidney disease and Stomach or other digestive disease	26.42
164	Diabetes or high blood sugar, Chronic lung diseases and Stomach or other digestive disease	24.29
165	Hypertension, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	22.36
166	Hypertension, Liver disease and Stomach or other digestive disease	20.46

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167	Hypertension, Cancer or malignant tumor and Stomach or other digestive disease	16.05
168	Hypertension, Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	16.05
169	Hypertension, Chronic lung diseases and Stomach or other digestive disease	15.57

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BMJ Open

Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-024268.R3
Article Type:	Research
Date Submitted by the Author:	27-Apr-2019
Complete List of Authors:	zhang, ran; China Pharmaceutical University, School of International Pharmaceutical Business Lu, Yun; China Pharmaceutical University, School of International Pharmaceutical Business Shi, Liuyan; China Pharmaceutical University, School of International Pharmaceutical Business Zhang, SongLin; China Pharmaceutical University, School of International Pharmaceutical Business Chang, Feng; China Pharmaceutical University, School of International Pharmaceutical Business
Primary Subject Heading:	Health informatics
Secondary Subject Heading:	Public health, Qualitative research
Keywords:	multimorbidity, cross-sectional study, Prevalence, Observed-to-expected ratio, China

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Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data

Author

NAME: Ran Zhang

Postal address: 639 Longmian Road, Nanjing, Jiangsu Province, CHINA

E-mail:ranzai7@126.com

Institutions: China Pharmaceutical University

City & Country: Jiangsu Province, CHINA

Telephone: +86-18115161231

Co-Authors

NAME: Yun Lu, Liuyan Shi, Songlin Zhang

Institutions: China Pharmaceutical University

City & Country: Jiangsu Province, CHINA

Corresponding Author

NAME: Feng Chang

Postal address: 639 Longmian Road, Nanjing, Jiangsu Province, CHINA

E-mail: cpucf@163.com

Institutions: China Pharmaceutical University

City & Country: Jiangsu Province, CHINA

Telephone: +86-13805153128

Keywords:

multimorbidity, Cross-sectional study, Prevalence, Observed-to-expected ratio, China

Word count: 4911

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ABSTRACT

Objectives: Examination of the prevalence and patterns of multimorbidity among the elderly in China.

Design: Cross-sectional study.

Setting: More than 10,000 households in 28 of the 34 provinces of mainland China.

Participants: 11,707 Chinese adults aged 60 and over.

Primary outcome measures: Prevalence and patterns of multimorbidity among the participants. Relative risks were calculated to estimate the probability of up to 14 chronic conditions coexisting with each other. Observed-to-expected (O/E) ratios were used to analyze the patterns of multimorbidity.

Results: Multimorbidity was present in 43.6% of respondents from the sample population, with women having the greater prevalence compared to men. There were 804 different comorbidity combinations identified, including 76 dyad combinations and 169 triad combinations. The top 10 morbidity dyads and triads accounted for 69.01% and 47.05% of the total dyad and triad combinations observed, respectively. Among the 14 chronic conditions included in the study, asthma, stroke, heart attack and six other chronic conditions were the main components of multimorbidity due to their high relative risk ratios. The most frequently occurring clusters with higher O/E ratios were stroke along with emotional, nervous, or psychiatric problems; memory-related diseases together emotional, nervous, or psychiatric problems; and memory-related diseases and asthma accompanied by chronic lung diseases and asthma.

Conclusions: The results of this study highlight the high prevalence of multimorbidity in the elderly population in China. Further studies are required to understand the etiology of multimorbidity, and future primary healthcare policies should be made while taking multimorbidity into consideration.

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Strengths and limitations of this study

Strengths

- This is the first study to estimate the prevalence and patterns of multimorbidity among the elderly population in China.
- Data for this study were collected from a nationally representative longitudinal survey of 17,708 Chinese residents.

Limitations

- Only 14 predefined chronic diseases were included in the study, and these may not be comprehensive of the conditions of the population.
- The data analyzed from the CHARLS were originally collected by population self-reporting, not clinician evaluation, and could partially reflect some associated biases or confounds.
- This study only included older patients aged 60 years and above with complete data, and there was no selection bias between the inclusion cases and exclusion cases, but further research would be needed in other populations.

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INTRODUCTION

Multimorbidity, or the simultaneous occurrence of two or more chronic conditions in an individual, is becoming increasingly common, and this has been reported to increase progressively with age. [1, 2] At present, with China's aging population having an increasing prevalence of chronic conditions, multimorbidity among the elderly poses an enormous societal cost due to increased mortality rates and healthcare utilization. [3] However, to date, research on chronic conditions in China has focused on single disease states, and the coexistence of multiple chronic conditions has not been investigated systematically and thoroughly.

There is a significant difference in the etiological analysis between patients with single chronic conditions and those with multimorbidity. [4] The coexistence of chronic conditions in a patient is more than a random event, it is more typically due to the causal relationship between some diseases and shared pathogenic factors. [5, 6] Moreover, the interactions between diseases or between a disease and host result in differences in the severity of multimorbidity and functional status and prognosis of patients with multimorbidity. [7] Consequently, it is imperative to begin research on multimorbidity in China for the cost-effective treatments that the results may help to suggest. [8] The purpose of this study was therefore to determine the prevalence of multimorbidity among the elderly in China and to reveal morbidity combinations, which may benefit the design and implementation of a modified healthcare system with consideration for patients with multimorbidity.

METHODS

Data source

Data for this study were collected from the third response of the China Health and Retirement Longitudinal Survey (CHARLS), which is the most current data available. The CHARLS is a nationally representative longitudinal survey of Chinese residents aged 45 and older that was conducted by the Chinese Center for Disease Control and Prevention, along with Peking University, to help China to adjust to the rapid aging of its population through the evaluation of social, economic, and health circumstances on

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the community level using data collected by interviews, physical measurements and blood sample collection. [9] The national baseline survey began in 2011 and involved 17,708 respondents from 150 county-level units, 450 village-level units, and approximately 10,000 households. Afterwards, CHARLS respondents were followed every second year, with their informed consent, and the study was approved by the Peking University Biomedical Ethics Committee (IRB00001052-14013-exemption).

Variables

The core CHARLS questionnaires included sections requesting information on demographic factors, family structure and changes, health status and functioning, healthcare and insurance, work, retirement and pension, income and consumption, and assets (individual and household). Information was collected by interview by trained staff. For the current study, the eligible and included participants were determined by being aged 60 and over, and data on gender, age and health status was used from the general health status and disease history section of senior citizens in the 2015 CHARLS data. This information included the following 14 common chronic health problems: hypertension, dyslipidemia (high blood lipids or low cholesterol), diabetes or elevated blood glucose (including impaired glucose tolerance and fasting blood glucose), cancer (excluding mild skin cancers), chronic lung disease such as chronic bronchitis or emphysema, pulmonary heart disease (excluding tumors or cancer), liver disease (other than fatty liver, tumors, or cancer), heart disease (such as myocardial infarction, coronary heart disease, angina pectoris, congestive heart failure and other heart diseases), stroke, kidney disease (excluding tumors or cancer), stomach or other digestive diseases (excluding tumors or cancer), emotional and mental problems, memory-related diseases (such as Alzheimer's disease, brain atrophy, Parkinson's disease), arthritis or rheumatism, and asthma. All these data were based on self-reports. Accordingly, multimorbidity was defined as the coexistence of more than one of the 14 chronic conditions, with acute or subacute forms of certain conditions being excluded in this study due to the CHARLS data collection protocol.

Statistical analysis

To detect the demographic characteristics of patients with multimorbidity, respondents were divided into two groups: those with multiple chronic conditions (MCC group) and those without multiple chronic conditions (Non-MCC group).

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Descriptive statistics were calculated and expressed as means (SD) and frequencies (percentage). We applied the T^2 and χ^2 texts to test the differences in age, gender and the mean number of chronic conditions across different subgroups. Respective prevalence in the MCC group and the non-MCC group were calculated separately. Given the exclusion of participants with incomplete data, a sensitivity analysis was conducted to compare the characteristics of the complete cases aged 60 years and above and the counterpart in the incomplete cases, which is presented in Annex 1.

To determine the most common combination of chronic diseases, the prevalence of morbidity and multimorbidity dyads and triads were estimated, respectively. Next, the expected number of patients with a chronic disease were calculated, and the observed-to-expected (O/E) ratios were determined by dividing the number of patients in those groups by the expected number of patients. Observed-to-expected ratios were used to estimate the conditional probability of coexistence of two or three chronic conditions. [10] As an important indicator for assessing the correlation between diseases, the O/E ratio has been used in many areas of comorbidity. [10， 11] The relative risk of comorbidity for individual chronic conditions was also calculated. Relative risk of comorbidity (RR) is the ratio of the number of people with a certain chronic condition who suffer from multimorbidity to the number of patients with the same disease who do not suffer from multimorbidity. [11, 12] In other words, a higher RR value means a higher probability that the disease coexists with other diseases. However, it should be noted that there is no direct relationship between the relative risk of comorbidity and the overall prevalence of the diseases. [13, 14]

All analyses in this study were completed using Stata softwareV.14.0 for Windows (Stata Corp). P Values <0.05 were considered to be statistically significant.

Patient and public involvement

Patients and the public were not 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 results to study participants.

RESULTS

Characteristics of participants

The data were gathered from the third response set of CHARLS. After exclusion

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of participants with incomplete data (1,002) or aged under 60 (9,259), there were 11,707 respondents with available information on related chronic diseases that were included in this study. The selection process of study sample is shown in Figure 1. The demographic characteristics of sample respondents and statistical significance test results are presented in Table 1.

Overall, the mean age for the sample population was 70.5 (ranging from 60 to 107). The sample population consisted of 5,705 (48.7%) males and 6002 (51.2%) females, and 43.6% of them suffered from multimorbidity. The median of chronic conditions in the MCC group was 3.01, compared to 0.45 in the Non-MCC group. Samples in the MCC group were 0.66 year older than those belonged to the non-MCC group. Gender differences with regard to the age of samples between the MCC group and the non-MCC group (70.57 for MCC group and 69.51 for non-MCC group) were small but statistically significant ($p < 0.001$). The prevalence of multimorbidity in the female population was higher than that for the males (54.41% vs 45.59%). Figure 2 shows the number and proportion of respondents over 60 according to morbidity numbers. It can be seen that among all the participants aged over 60, only 30.9% of them did not have the 14 chronic diseases and 43.6% suffer from multimorbidity.

Table 1. Demographic characteristics of all respondents, the MCC group and non-MCC group

	All respondents	**MCC group**	**Non-MCC group**	**P***
Number of people	11707	5107	6600	
Proportion (%)	100%	43.62%	56.38%	
Mean age				
All respondents (SD)	70.20(7.907)	70.57(7.701)	69.91(8.051)	<0.001
Male (SD)	69.97(7.575)	70.50(7.348)	69.60(7.707)	<0.001
Female (SD)	70.39(8.189)	70.62(7.892)	70.19(8.359)	<0.001
Gender（% females）	51.28%	54.41%	48.83%	<0.001
Mean number of chronic conditions				
All respondents（SD）	1.57(1.560)	3.01(1.259)	0.45(0.498)	<0.001
Male（SD）	1.47(1.534)	2.98(1.265)	0.44(0.496)	<0.001
Female（SD）	1.65(1.581)	3.03(7.982)	0.47(0.499)	<0.001

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SD = standard deviation;

p* = statistical significance of the difference between the MCC and the non-MCC sample (t-tests were performed for comparison of means, and chi-square-tests for differences between percentages)

Prevalence of chronic conditions

The prevalence of chronic conditions in the entire sample, the MCC group and the non-MCC group are shown in Figure 3. The prevalence of all fourteen chronic conditions in the MCC group was significantly higher than that in the entire sample. For instance， the prevalence of arthritis or rheumatism, hypertension, stomach or other digestive disease, heart disease and chronic lung disease were 65.97%, 48.82%, 45.86%, 29.00% and 24.97% in the MCC group, compared to 38.49%, 26.41%, 24.52%, 12.32% and 12.32% in the entire sample, respectively.

Table 2 shows the relative risks of comorbidity determined for the 14 chronic diseases reported in this study. It can be seen that the overall relative risks for asthma, stroke, heart disease and six other conditions were all above 10, which meant these diseases were >10 times easier to coexist with other chronic conditions and result in multimorbidity. In addition, the relative risks for certain diseases were positively associated with gender. For example, men had significantly higher relative risks for asthma, but lower relative risks for diabetes or high blood sugar, compared to women.

Table 2 Relative risks of multimorbidity for different chronic conditions according to gender

Chronic conditions	All respondents	95% Confidence Interval		Female	95% Confidence Interval		Male	95% Confidence Interval	
		Lower Bound	Upper Bound		Lower Bound	Upper Bound		Lower Bound	Upper Bound
High relative risk of multimorbidity									
Asthma	26.18	17.82	38.46	20.67	11.85	36.06	32.68	19.18	55.67
Stroke	18.62	12.11	28.64	21.57	10.61	43.86	17.43	10.13	29.99
Heart disease	15.56	12.99	18.63	16.48	12.80	21.21	14.26	11.02	18.46
Diabetes or high blood sugar	14.40	11.18	18.55	15.68	10.86	22.63	13.11	9.24	18.62

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Dyslipidemia	14.05	11.54	17.12	15.13	11.37	20.14	12.97	9.86	17.05
Memory-related disease	13.69	8.85	21.16	34.17	12.63	92.44	9.28	5.66	15.21
Kidney disease	11.57	9.24	14.49	15.01	10.17	22.43	10.24	7.78	13.48
Liver disease	11.10	8.37	14.71	16.07	9.70	26.63	9.15	6.49	12.89
Chronic lung diseases	9.87	8.43	11.55	10.71	8.26	13.88	9.74	8.00	11.86
Low relative risk of multimorbidity									
Emotional, nervous, or psychiatric problems	7.42	4.94	11.15	6.24	3.78	10.30	9.36	4.65	18.85
Stomach or other digestive disease	5.73	5.25	6.25	6.20	5.48	7.02	5.23	4.62	5.91
Hypertension	5.38	4.96	5.84	4.90	4.40	5.47	5.92	5.24	6.69
Cancer or malignant tumor	4.88	3.20	7.45	5.33	3.06	9.29	3.99	2.07	7.72
Arthritis or rheumatism	3.83	3.61	4.05	3.70	3.43	3.99	3.91	3.59	4.26

Common multimorbidity combinations

There were 804 possible comorbidity combinations that were identified in the MCC group after statistical analysis, including 72 dyads and 169 triads. The 10 most frequently occurring morbidity dyads and triads are presented respectively in Table 3 and Table 4.

Table3 Prevalence of the 10 most common morbidity dyads

Rank	Morbidity dyads	Prevalence			Mean
		All respondents	female	male	Age
1	Arthritis or rheumatism and Stomach or other digestive disease	4.73%	3.56%	5.96%	69.20
2	Arthritis or rheumatism and Hypertension	2.85%	2.20%	3.53%	71.25
3	Arthritis or rheumatism and Chronic lung diseases	1.13%	1.22%	1.04%	71.55
4	Hypertension and heart problems	1.03%	1.00%	1.06%	71.80
5	Hypertension and Stomach or other digestive disease	0.89%	0.83%	0.95%	69.07
6	Hypertension	0.86%	0.81%	0.91%	68.58

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	and Dyslipidemia				
7	Arthritis or rheumatism and heart problems	0.76%	0.53%	1.00%	70.72
8	Arthritis or rheumatism and Kidney disease	0.64%	0.73%	0.54%	68.24
9	Hypertension and Diabetes or high blood sugar	0.58%	0.50%	0.67%	70.97
10	Chronic lung diseases and Asthma	0.53%	0.65%	0.40%	71.15

Table 4 Prevalence of the 10 most common morbidity triads

Rank	Morbidity triads	Prevalence			Mean Age
		All respondents	female	male	
1	Arthritis or rheumatism, Stomach or other digestive disease and Hypertension	1.19%	0.80%	1.60%	70.96
2	Arthritis or rheumatism, Stomach or other digestive disease and Chronic lung diseases	0.82%	0.97%	0.67%	70.82
3	Arthritis or rheumatism, Heart disease and Hypertension	0.63%	0.37%	0.91%	69.93
4	Arthritis or rheumatism, Heart disease and Stomach or other digestive disease	0.59%	0.25%	0.95%	71.51
5	Hypertension, Dyslipidemia and Arthritis or rheumatism	0.44%	0.31%	0.57%	70.13
6	Hypertension, Dyslipidemia and Heart problems	0.42%	0.35%	0.49%	71.17
7	Arthritis or rheumatism, Kidney disease and Stomach or other digestive disease	0.42%	0.40%	0.44%	70.14
8	Arthritis or rheumatism, Asthma and Chronic lung diseases	0.40%	0.46%	0.33%	69.18
9	Hypertension, Dyslipidemia and Diabetes or high blood sugar	0.35%	0.35%	0.35%	71.51
10	Arthritis or rheumatism, Stomach or other digestive disease	0.53%	0.57%	0.49%	70.29

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and Liver disease

Theoretically, there are 91 dyad combinations and 364 triad combinations possible given the 14 different chronic conditions considered in this study. However, only 72 types (79.12%) of dyads and 169 types (46.43%) of triads emerged in the sample. The 10 most frequently occurring morbidity dyads accounted for 69.01% of the 72 dyad combinations, and the proportion of the 10 most common triad combinations in the 169 triad combinations was 47.05%. Arthritis or rheumatism, which appeared in five of the top 10 dyad combinations and eight of the top 10 triad combinations of chronic conditions, was the main component of the leading morbidity dyads and triads.

There were significant gender differences observed in the occurrences of these multimorbidity combinations. The numbers of women with triad combinations of chronic diseases were generally higher than for men with the same morbidity triads. For example, women had significantly higher prevalence of arthritis and hypertension and hyperlipidemia than men (78.26% vs 21.74%). Among morbidity dyads, the prevalence of heart disease and arthritis or rheumatism in women was nearly two times higher than that in men, while the cluster of arthritis or rheumatism and kidney disease occurred more frequently in men than in women. No age difference was detected in the probability of these particular multimorbidity combinations occurring.

The O/E ratio was also used to analyze the multimorbidity pattern. [15] The higher the O/E value, the higher the probability of coexistence of chronic conditions. [16] Table 5 shows O/E ratios determined for the 10 most prevalent morbidity dyads and triads. The prevalence of each conditions and the dyad and triad prevalence are presented in Annex 2. In the midst of those triad combinations of chronic conditions, the two clusters with significantly higher O/E ratios were emotional, nervous, or psychiatric problems and stroke and memory-related disease (O/E ratio = 10287.72), emotional, nervous, or psychiatric problems and memory-related disorders and asthma (O/E ratio = 8498.56). These four conditions also dominated the three leading dyads

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with the highest O/E ratios: 97.73 for the combination of emotional and mental disorders and memory- related diseases, 23.66 for the combination of stroke and memory related disease and 19.55 for the combination of memory-related disease and asthma.

Table 5 O/E ratios for the 10 most prevalent morbidity dyads and triads

Number of chronic conditions	Rank	Chronic conditions	O/E ratio
2	1	Chronic lung diseases and Asthma	162.15
	2	Emotional, nervous, or psychiatric problems and Memory-related disease	97.73
	3	Dyslipidemia and Diabetes or high blood sugar	38.39
	4	Heart disease and Memory-related disease	25.69
	5	Stroke and Memory-related disease	23.66
	6	Hypertension and Stroke	22.85
	7	Hypertension and Diabetes or high blood sugar	20.64
	8	Cancer or malignant tumor and Stroke	19.55
	9	Memory-related disease and Asthma	19.55
	10	Stroke and Asthma	19.55
3	1	Stroke, Emotional, nervous, or psychiatric problems and Memory-related disease	10287.72
	2	Emotional, nervous, or psychiatric problems, Memory-related disease and Asthma	8498.56
	3	Emotional, nervous, or psychiatric problems, Chronic lung diseases and Asthma	2274.26
	4	Heart disease, Stroke and Memory-related disease	2253.50
	5	Chronic lung diseases, Heart disease and Asthma	1992.69
	6	Dyslipidemia, Heart disease and Memory-related disease	1443.25
	7	Hypertension, Dyslipidemia and Diabetes or high blood sugar	1398.31

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8	Hypertension, Stroke and Memory-related disease	1387.35
9	Chronic lung diseases, Memory-related disease and Asthma	1376.53
10	Chronic lung diseases, Arthritis or rheumatism and Asthma	1265.95

DISCUSSION

This is the first study to estimate the prevalence and patterns of multimorbidity among the elderly in China based on the nationally representative data from CHARLS, which covered 11,707 Chinese senior citizens of age 60 and over. The results of the study indicated that 69.1% of the elderly population in China had at least one of the 14 diseases and 43.6% of them suffered from multimorbidity. The average age of the MCC group was 0.66 years higher than that of the non-MCC group and in the MCC group, the mean age of women was 0.12 years higher than that of men, which was comparable to the results of previous studies. [17-21]

The prevalence of multimorbidity estimated in this study was much lower than that from previous studies in other developed countries. For example, a study of 543 patients over age 65 in Ghent, Belgium showed that the multimorbidity rate was as high as 82.6%, [22]. Another study in Australia showed that 83.2% of the respondents suffered from multimorbidity. [23] However, it is difficult to compare the prevalence generated from different studies due to differences in the selected definitions of multimorbidity, demographic characteristics of the samples, and different study methodologies. [24-28]

In agreement with previous reports, arthritis or rheumatism, hypertension, stomach or other digestive disease were the most common diseases in the MCC group. [11] The prevalence of these three conditions was each above 20% in the entire sample, and above 45% in the MCC group. The most prevalent chronic combinations in the sample could also be found in other studies. [22] The results of this study showed that the prevalence of arthritis or rheumatism was high and easy to coexist with other conditions.

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In addition to the chronic conditions mentioned above, previous studies demonstrated that women with rheumatoid arthritis might have a predisposition to gallstones which could manifest in middle or older age compared with women in the general population. This phenomenon could be related to chronic inflammation and HDL metabolism. [29]

Although arthritis or rheumatism, a component of all the leading three morbidity dyads and triads, was also the most commonly occurring disease in multimorbidity, the relative risk of this disease was only 4.65, the lowest in the 14 chronic diseases. Moreover, arthritis or rheumatism is less common in morbidity clusters with large O/E ratios. Therefore, the frequent occurrence of arthritis or rheumatism in multimorbidity might be simply due to the high prevalence of the disease. Doctor-diagnosed arthritis is a common and disabling chronic condition in the world. During 2013 to 2015, an average of more than one in five (54.4 million) adults in the United States were diagnosed with arthritis [30]. The unadjusted prevalences of arthritis among adults with obesity, heart disease, or diabetes were 30.6%, 49.3%, and 47.1%, respectively. In adults with obesity, heart disease, or diabetes, the age-adjusted prevalences of arthritis were respectively 1.5, 1.7 and 1.9 times higher than those without these diseases. Improving the health of adults with arthritis and related comorbid conditions calls for wider dissemination and implementation of evidence-based interventions, such as self-management education and physical activity promotion [31].

The relative risks for asthma, stroke, heart disease, and six other conditions were all above 10, which means that patients with these diseases were 10 times more likely to be afflicted by multimorbidity. These diseases also occurred at a high frequency in multimorbidity with high O/E ratios, such as the clusters of pulmonary disease and asthma, emotional and mental illness and memory-related disease, dyslipidemia and diabetes, and stroke and emotional or mental illness and memory-related disease. Patients with these diseases were more likely to express comorbidity compared to those without these diseases, and thus should be the focus of future research studies.

This study featured a nationally representative sample of the Chinese elderly

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population, which was crucial to get an overall understanding of multimorbidity among the elderly in China. However, there were also limitations with the data sample and study. For example, this study used data from the third wave report of CHARLS, a survey which was conducted in 2015, and there is accordingly a time lag to now that exists. Additionally, the chronic diseases included in the study were not comprehensive, since only 14 chronic conditions were included in the survey. Finally, the data obtained from the survey was based on self-reporting, which may have introduced some misclassification bias or other confounds. Later research on the prevalence and patterns of multimorbidity should be carried out in-depth with a more extensive survey of chronic disease.

CONCLUSIONS

Multimorbidity remains an underexplored area of research in China. [32]. Despite the increasing prevalence of multimorbidity, there are no specific proposals for its diagnosis and treatment. [33] This study contributes to the understanding of the prevalence and patterns of comorbidity among the elderly in China. Considering China's aging population and the high prevalence of comorbidity in senior citizens, the elderly should be prioritized in the fields of disease prevention and health promotion.

Acknowledgements The authors would like to thank the Chinese Center for Disease Control and Prevention and Peking University for access to China Health and Retirement Longitudinal Survey data.

Contributors RZ analyzed and interpreted data, drafted the manuscript, approved the final manuscript as submitted. YL revised the manuscript for important intellectual content. YLS analyzed and interpreted data and revised the manuscript for important intellectual content. SLZ analyzed and checked the data of the full text. FC helped on the study design and revised the manuscript.

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Funding This work was funded by the National Natural Science Foundation of China (7167030838).

Competing interests None declared.

Patient consent Obtained.

Ethics approval The original CHARLS was approved by the ethics review committee of Peking University, and all participants gave written informed consent at the time of participation

Data sharing statement No additional data are available

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Figure legends

Figure 1 Flowchart for selecting the study sample from the original sample population. CHARLS, China Health and Retirement Longitudinal Survey

Figure 2 Frequency and percentage of people aged over 60 suffering from different diseases based on CHARLS data

Figure 3 Prevalence Rates of chronic condition in elderly people over 60 years old based on CHARLS data

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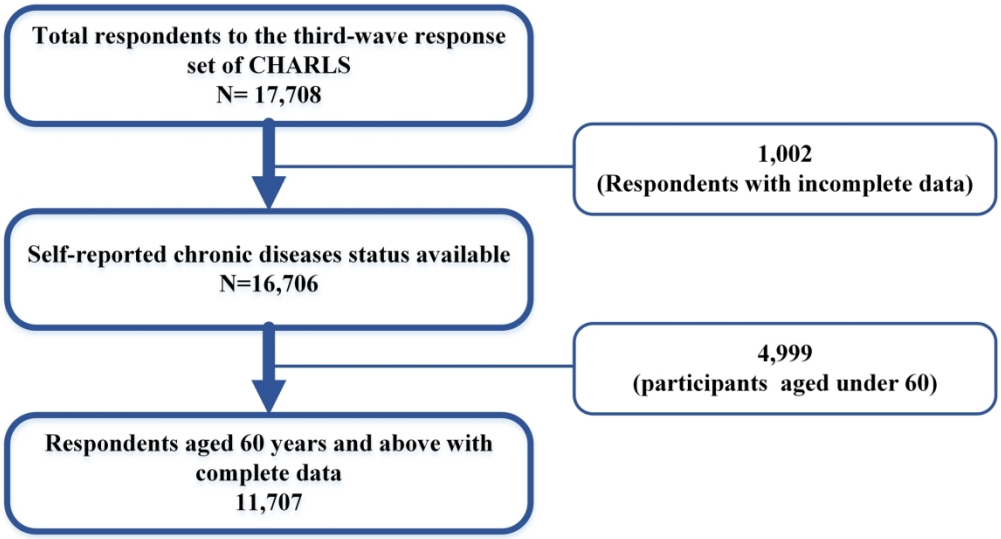

Figure 1 Flowchart for selecting the study sample from the original sample population. CHARLS, China Health and Retirement Longitudinal Survey

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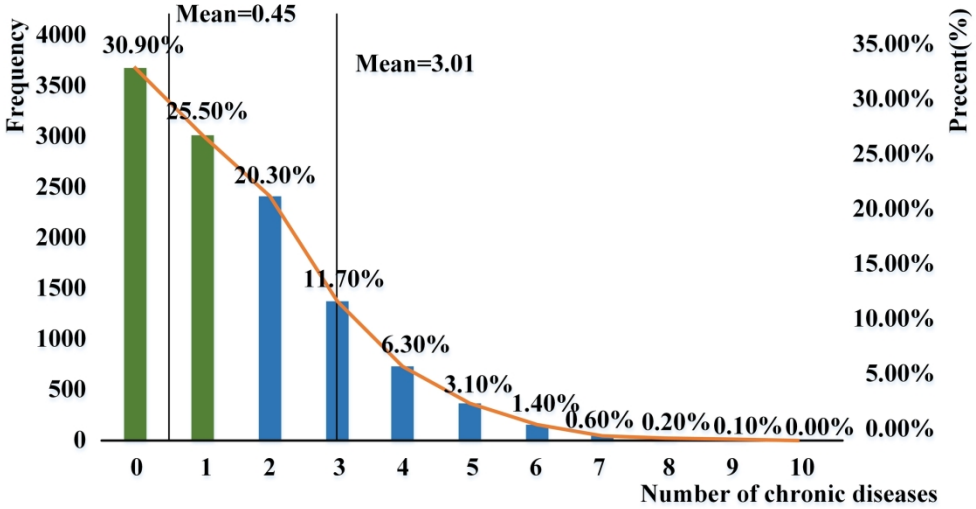

Figure 2 Frequency and percentage of people aged over 60 suffering from different diseases based on CHARLS data

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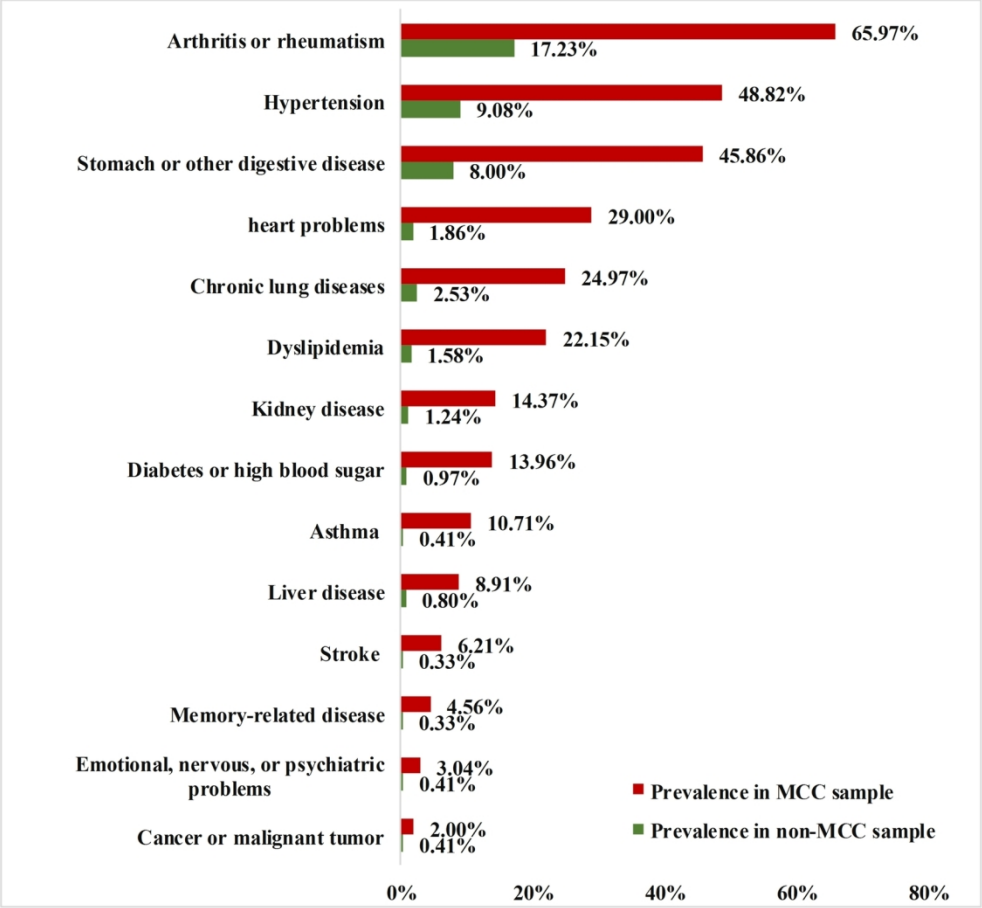

Figure 3 Prevalence Rates of chronic condition in elderly people over 60 years old based on CHARLS data

151x140mm (300 x 300 DPI)

Annex 1 Sensitivity analysis, Comparison of the characteristics of complete cases and incomplete cases

	Complete cases	**Incomplete cases**	**P***
Number of people	11707	876	
Proportion (%)	93.04%	6.96%	
Mean age All respondents (SD)	70.20(7.907)	69.60（7.824）	<0.001
Male (SD)	69.97(7.575)	69.58（7.721）	<0.001
Female (SD)	70.39(8.189)	69.62（7.973）	<0.001
Gender（% females）	51.28%	49.27%	0.193

p* = statistical significance of the difference between the complete cases and the incomplete cases (t-tests were performed for comparison of means, and chi-square-tests for differences between percentages)

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Annex 2 O/E ratio of all binary and triads comorbidities pattern present in participants

Rank	binary comorbidities pattern	O/E ratio
1	Chronic lung diseases and Asthma	161.00
2	Emotional, nervous, or psychiatric problems and Memory-related disease	98.57
3	Dyslipidemia and Diabetes or high blood sugar	38.69
4	Heart disease and Memory-related disease	25.96
5	Stroke and Memory-related disease	24.19
6	Hypertension and Stroke	23.10
7	Hypertension and Diabetes or high blood sugar	20.77
8	Cancer or malignant tumor and Stroke	19.71
9	Memory-related disease and Asthma	19.71
10	Stroke and Asthma	19.71
11	Hypertension and Heart disease	19.07
12	Hypertension and Dyslipidemia	18.98
13	Dyslipidemia and Heart disease	17.39
14	Diabetes or high blood sugar and Heart disease	14.87
15	Diabetes or high blood sugar and Liver disease	14.40
16	Cancer or malignant tumor and Liver disease	13.65
17	Diabetes or high blood sugar and Kidney disease	13.38
18	Hypertension and Memory-related disease	13.33
19	Dyslipidemia and Cancer or malignant tumor	12.51
20	Stomach or other digestive disease and Arthritis or rheumatism	10.80
21	Liver disease and Heart disease	10.49
22	Dyslipidemia and Stroke	10.23
23	Dyslipidemia and Stomach or other digestive disease	9.81
24	Dyslipidemia and Kidney disease	9.61
25	Chronic lung diseases and Memory-related disease	9.56
26	Chronic lung diseases and Stroke	9.56
27	Kidney disease and Arthritis or rheumatism	9.42
28	Heart disease and Kidney disease	9.29
29	Chronic lung diseases and Heart disease	9.12
30	Stomach or other digestive disease and Asthma	9.03
31	Liver disease and Kidney disease	8.99
32	Kidney disease and Stomach or other digestive disease	8.92
33	Memory-related disease and Arthritis or rheumatism	8.89
34	Stroke and Arthritis or rheumatism	8.89
35	Arthritis or rheumatism and Asthma	8.77
36	Liver disease and Memory-related disease	8.38
37	Diabetes or high blood sugar and Memory-related disease	8.32
38	Diabetes or high blood sugar and Stroke	8.32
39	Chronic lung diseases and Arthritis or rheumatism	8.14
40	Heart disease and Stomach or other digestive disease	8.11

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41	Heart disease and Arthritis or rheumatism	7.45
42	Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	7.39
43	Liver disease and Stomach or other digestive disease	7.33
44	Diabetes or high blood sugar and Cancer or malignant tumor	6.78
45	Diabetes or high blood sugar and Asthma	6.78
46	Diabetes or high blood sugar and Arthritis or rheumatism	6.44
47	Liver disease and Arthritis or rheumatism	6.16
48	Chronic lung diseases and Kidney disease	5.98
49	Chronic lung diseases and Stomach or other digestive disease	5.97
50	Hypertension and Arthritis or rheumatism	5.74
51	Chronic lung diseases and Liver disease	5.52
52	Kidney disease and Emotional, nervous, or psychiatric problems	5.29
53	Kidney disease and Asthma	5.29
54	Chronic lung diseases and Emotional, nervous, or psychiatric problems	5.19
55	Dyslipidemia and Memory-related disease	5.12
56	Hypertension and Emotional, nervous, or psychiatric problems	5.07
57	Hypertension and Chronic lung diseases	5.03
58	Hypertension and Kidney disease	5.01
59	Cancer or malignant tumor and Arthritis or rheumatism	4.96
60	Cancer or malignant tumor and Stomach or other digestive disease	4.93
61	Dyslipidemia and Arthritis or rheumatism	4.75
62	Hypertension and Liver disease	4.61
63	Diabetes or high blood sugar and Chronic lung diseases	4.38
64	Heart disease and Stroke	4.33
65	Dyslipidemia and Asthma	4.17
66	Hypertension and Stomach or other digestive disease	3.85
67	Cancer or malignant tumor and Heart disease	3.53
68	Heart disease and Asthma	3.53
69	Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	3.43
70	Diabetes or high blood sugar and Stomach or other digestive disease	3.12
71	Hypertension and Cancer or malignant tumor	2.17
72	Hypertension and Asthma	2.17
73	Stomach or other digestive disease and Memory-related disease	2.02
74	Stroke and Stomach or other digestive disease	2.02
75	Dyslipidemia and Liver disease	1.77
76	Dyslipidemia and Chronic lung diseases	1.35

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Rank	triads comorbidities pattern	O/E ratio
1	Stroke, Emotional, nervous, or psychiatric problems and Memory-related disease	10491.60
2	Emotional, nervous, or psychiatric problems, Memory-related disease, Asthma,	8548.88
3	Heart disease, Stroke and Memory-related disease	2302.62
4	Chronic lung diseases, Emotional, nervous, or psychiatric problems and Asthma	2252.13
5	Chronic lung diseases, Heart disease, Asthma,	1977.13
6	Dyslipidemia, Heart disease and Memory-related disease	1461.04
7	Hypertension, Stroke and Memory-related disease	1418.54
8	Hypertension, Dyslipidemia and Diabetes or high blood sugar	1409.29
9	Chronic lung diseases, Memory-related disease and Asthma	1381.96
10	Chronic lung diseases, Arthritis or rheumatism and Asthma	1256.63
11	Dyslipidemia, Diabetes or high blood sugar and Kidney disease	1255.51
12	Cancer or malignant tumor, Chronic lung diseases and Asthma	1126.07
13	Chronic lung diseases, Kidney disease and Asthma	1112.24
14	Liver disease, Kidney disease and Asthma	974.52
15	Dyslipidemia, Diabetes or high blood sugar and Liver disease	972.21
16	Chronic lung diseases, Liver disease and Asthma	956.96
17	Dyslipidemia, Diabetes or high blood sugar and Stroke	935.99
18	Chronic lung diseases, Stomach or other digestive disease and Asthma	921.21
19	Hypertension, Dyslipidemia and Heart disease	876.36
20	Diabetes or high blood sugar, Liver disease and Kidney disease	822.11
21	Hypertension, Diabetes or high blood sugar and Stroke	812.58
22	Hypertension, Chronic lung diseases and Asthma	812.01
23	Hypertension, Dyslipidemia and Stroke	800.07
24	Dyslipidemia, Heart disease and Asthma	793.67
25	Diabetes or high blood sugar, Heart disease and Stroke	791.41
26	Hypertension, Emotional, nervous, or psychiatric problems and Memory-related disease	770.58
27	Dyslipidemia, Diabetes or high blood sugar and Cancer or malignant tumor	762.67
28	Dyslipidemia, Diabetes or high blood sugar and Emotional, nervous, or psychiatric problems	762.67
29	Dyslipidemia, Diabetes or high blood sugar and Heart disease	669.54
30	Liver disease, Heart disease and Emotional, nervous, or psychiatric problems	649.62
31	Heart disease, Kidney disease and Memory-related disease	617.74
32	Heart disease, Stroke and Kidney disease	617.74
33	Dyslipidemia, Chronic lung diseases and Asthma	584.58
34	Diabetes or high blood sugar, Liver disease and Heart disease	548.02

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35	Hypertension, Diabetes or high blood sugar and Heart disease	523.14
36	Hypertension, Heart disease and Stroke	507.36
37	Diabetes or high blood sugar, Chronic lung diseases and Asthma	474.98
38	Liver disease, Stomach or other digestive disease and Asthma	454.02
39	Stomach or other digestive disease, Emotional, nervous, or psychiatric problems and Memory-related disease	437.10
40	Hypertension, Memory-related disease, Asthma,	385.29
41	Diabetes or high blood sugar, Stomach or other digestive disease and Asthma	300.46
42	Hypertension, Dyslipidemia and Memory-related disease	300.03
43	Liver disease, Kidney disease and Arthritis or rheumatism	277.66
44	Hypertension, Heart disease and Memory-related disease	253.68
45	Dyslipidemia, Liver disease and Kidney disease	252.95
46	Hypertension, Chronic lung diseases and Stroke	249.13
47	Stroke, Memory-related disease and Arthritis or rheumatism	249.11
48	Dyslipidemia, Chronic lung diseases and Liver disease	248.40
49	Cancer or malignant tumor, Chronic lung diseases and Heart disease	247.14
50	Chronic lung diseases, Heart disease and Emotional, nervous, or psychiatric problems	247.14
51	Hypertension, Dyslipidemia and Asthma	244.47
52	Cancer or malignant tumor, Heart disease and Stomach or other digestive disease	234.50
53	Chronic lung diseases, Memory-related disease and Arthritis or rheumatism	229.69
54	Chronic lung diseases, Stroke and Stomach or other digestive disease	211.98
55	Hypertension, Stroke and Arthritis or rheumatism	210.41
56	Chronic lung diseases, Liver disease and Heart disease	210.03
57	Hypertension, Cancer or malignant tumor and Heart disease	206.71
58	Hypertension, Heart disease and Emotional, nervous, or psychiatric problems	206.71
59	Memory-related disease, Arthritis or rheumatism and Asthma	202.98
60	Emotional, nervous, or psychiatric problems, Memory-related disease and Arthritis or rheumatism	202.98
61	Stroke, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	202.98
62	Stroke, Kidney disease and Arthritis or rheumatism	200.49
63	Dyslipidemia, Diabetes or high blood sugar and Stomach or other digestive disease	194.98
64	Liver disease, Stomach or other digestive disease and Memory-related disease	185.73
65	Dyslipidemia, Stomach or other digestive disease and Asthma	184.90
66	Diabetes or high blood sugar, Stomach or other digestive disease and Memory-related disease	184.37
67	Diabetes or high blood sugar, Heart disease and Arthritis or rheumatism	183.74

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68	Chronic lung diseases, Stroke and Arthritis or rheumatism	164.06
69	Kidney disease, Arthritis or rheumatism and Asthma	163.36
70	Dyslipidemia, Diabetes or high blood sugar and Arthritis or rheumatism	162.98
71	Hypertension, Diabetes or high blood sugar and Memory-related disease	162.52
72	Hypertension, Dyslipidemia and Kidney disease	160.98
73	Hypertension, Heart disease and Kidney disease	158.80
74	Chronic lung diseases, Liver disease and Kidney disease	157.53
75	Dyslipidemia, Liver disease and Stomach or other digestive disease	157.13
76	Heart disease, Kidney disease and Stomach or other digestive disease	154.42
77	Cancer or malignant tumor, Liver disease and Stomach or other digestive disease	151.34
78	Liver disease, Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	151.34
79	Heart disease, Arthritis or rheumatism and Asthma	145.20
80	Stroke, Kidney disease and Stomach or other digestive disease	143.91
81	Liver disease, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	140.56
82	Diabetes or high blood sugar, Arthritis or rheumatism and Asthma	139.53
83	Hypertension, Dyslipidemia and Liver disease	138.50
84	Hypertension, Heart disease and Asthma	137.80
85	Kidney disease, Stomach or other digestive disease and Arthritis or rheumatism	136.43
86	Chronic lung diseases, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	133.68
87	Hypertension, Liver disease and Asthma	133.40
88	Hypertension, Diabetes or high blood sugar and Cancer or malignant tumor	132.42
89	Chronic lung diseases, Stomach or other digestive disease and Arthritis or rheumatism	131.24
90	Hypertension, Diabetes or high blood sugar and Kidney disease	130.80
91	Heart disease, Stomach or other digestive disease and Arthritis or rheumatism	128.06
92	Dyslipidemia, Heart disease and Stomach or other digestive disease	121.74
93	Hypertension, Heart disease and Arthritis or rheumatism	121.06
94	Stomach or other digestive disease, Arthritis or rheumatism and Asthma	118.39
95	Chronic lung diseases, Heart disease and Arthritis or rheumatism	117.36
96	Hypertension, Liver disease and Heart disease	117.11
97	Diabetes or high blood sugar, Kidney disease and Arthritis or rheumatism	114.85
98	Chronic lung diseases, Heart disease and Stomach or other digestive disease	113.73
99	Hypertension, Diabetes or high blood sugar and Liver disease	112.54
100	Diabetes or high blood sugar, Chronic lung diseases and Heart disease	104.24
101	Liver disease, Stomach or other digestive disease and Arthritis or rheumatism	104.21
102	Stroke, Stomach or other digestive disease and Arthritis or rheumatism	103.78

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103	Hypertension, Kidney disease and Emotional, nervous, or psychiatric problems	103.36
104	Chronic lung diseases, Liver disease and Arthritis or rheumatism	102.25
105	Hypertension, Dyslipidemia and Arthritis or rheumatism	100.61
106	Liver disease, Kidney disease and Stomach or other digestive disease	99.65
107	Dyslipidemia, Cancer or malignant tumor and Stomach or other digestive disease	92.45
108	Dyslipidemia, Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	92.45
109	Hypertension, Dyslipidemia and Chronic lung diseases	92.21
110	Hypertension, Chronic lung diseases and Heart disease	89.11
111	Heart disease, Stroke and Arthritis or rheumatism	89.10
112	Hypertension, Heart disease and Stomach or other digestive disease	88.07
113	Chronic lung diseases, Heart disease and Kidney disease	81.37
114	Chronic lung diseases, Kidney disease and Arthritis or rheumatism	79.23
115	Diabetes or high blood sugar, Chronic lung diseases and Arthritis or rheumatism	78.94
116	Chronic lung diseases, Kidney disease and Stomach or other digestive disease	75.82
117	Hypertension, Diabetes or high blood sugar and Arthritis or rheumatism	75.46
118	Hypertension, Dyslipidemia and Stomach or other digestive disease	75.00
119	Chronic lung diseases, Liver disease and Stomach or other digestive disease	73.39
120	Hypertension, Memory-related disease and Arthritis or rheumatism	73.19
121	Stomach or other digestive disease, Memory-related disease and Arthritis or rheumatism	72.65
122	Heart disease, Kidney disease and Arthritis or rheumatism	71.71
123	Liver disease, Arthritis or rheumatism and Asthma	70.28
124	Diabetes or high blood sugar, Cancer or malignant tumor and Arthritis or rheumatism	69.76
125	Kidney disease, Memory-related disease and Arthritis or rheumatism	66.83
126	Dyslipidemia, Heart disease and Arthritis or rheumatism	65.96
127	Diabetes or high blood sugar, Heart disease and Stomach or other digestive disease	65.94
128	Dyslipidemia, Chronic lung diseases and Heart disease	64.15
129	Hypertension, Kidney disease and Arthritis or rheumatism	63.81
130	Dyslipidemia, Stomach or other digestive disease and Arthritis or rheumatism	63.66
131	Hypertension, Chronic lung diseases and Memory-related disease	62.28
132	Dyslipidemia, Kidney disease and Stomach or other digestive disease	60.88
133	Hypertension, Stroke and Stomach or other digestive disease	59.10
134	Cancer or malignant tumor, Chronic lung diseases and Stomach or other digestive disease	57.58

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135	Cancer or malignant tumor, Chronic lung diseases and Arthritis or rheumatism	53.47
136	Hypertension, Stomach or other digestive disease and Arthritis or rheumatism	52.98
137	Dyslipidemia, Memory-related disease and Arthritis or rheumatism	52.69
138	Dyslipidemia, Stroke and Arthritis or rheumatism	52.69
139	Hypertension, Cancer or malignant tumor and Chronic lung diseases	50.75
140	Hypertension, Chronic lung diseases and Kidney disease	50.13
141	Liver disease, Heart disease and Arthritis or rheumatism	46.27
142	Hypertension, Cancer or malignant tumor and Arthritis or rheumatism	44.73
143	Hypertension, Liver disease and Kidney disease	43.92
144	Hypertension, Chronic lung diseases and Liver disease	43.13
145	Dyslipidemia, Cancer or malignant tumor and Arthritis or rheumatism	42.93
146	Dyslipidemia, Arthritis or rheumatism and Asthma	42.93
147	Hypertension, Diabetes or high blood sugar and Chronic lung diseases	42.81
148	Dyslipidemia, Kidney disease and Arthritis or rheumatism	42.40
149	Stomach or other digestive disease, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	42.28
150	Hypertension, Liver disease and Arthritis or rheumatism	41.18
151	Hypertension, Stomach or other digestive disease and Memory-related disease	39.40
152	Diabetes or high blood sugar, Stomach or other digestive disease and Arthritis or rheumatism	39.24
153	Hypertension, Arthritis or rheumatism and Asthma	37.27
154	Dyslipidemia, Liver disease and Arthritis or rheumatism	36.48
155	Heart disease, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	36.30
156	Hypertension, Chronic lung diseases and Arthritis or rheumatism	34.95
157	Dyslipidemia, Chronic lung diseases and Arthritis or rheumatism	34.70
158	Hypertension, Diabetes or high blood sugar and Stomach or other digestive disease	33.85
159	Cancer or malignant tumor, Stomach or other digestive disease and Arthritis or rheumatism	33.83
160	Liver disease, Heart disease and Stomach or other digestive disease	33.21
161	Dyslipidemia, Chronic lung diseases and Stomach or other digestive disease	29.89
162	Diabetes or high blood sugar, Liver disease and Arthritis or rheumatism	29.64
163	Hypertension, Kidney disease and Stomach or other digestive disease	26.42
164	Diabetes or high blood sugar, Chronic lung diseases and Stomach or other digestive disease	24.29
165	Hypertension, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	22.36
166	Hypertension, Liver disease and Stomach or other digestive disease	20.46

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167	Hypertension, Cancer or malignant tumor and Stomach or other digestive disease	16.05
168	Hypertension, Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	16.05
169	Hypertension, Chronic lung diseases and Stomach or other digestive disease	15.57

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BMJ Open

Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-024268.R4
Article Type:	Research
Date Submitted by the Author:	30-May-2019
Complete List of Authors:	zhang, ran; China Pharmaceutical University, School of International Pharmaceutical Business Lu, Yun; China Pharmaceutical University, School of International Pharmaceutical Business Shi, Liuyan; China Pharmaceutical University, School of International Pharmaceutical Business Zhang, SongLin; China Pharmaceutical University, School of International Pharmaceutical Business Chang, Feng; China Pharmaceutical University, School of International Pharmaceutical Business
Primary Subject Heading:	Health informatics
Secondary Subject Heading:	Public health, Qualitative research
Keywords:	multimorbidity, cross-sectional study, Prevalence, Observed-to-expected ratio, China

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Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data

Author

NAME: Ran Zhang

Postal address: 639 Longmian Road, Nanjing, Jiangsu Province, CHINA

E-mail:ranzai7@126.com

Institutions: China Pharmaceutical University

City & Country: Jiangsu Province, CHINA

Telephone: +86-18115161231

Co-Authors

NAME: Yun Lu, Liuyan Shi, Songlin Zhang

Institutions: China Pharmaceutical University

City & Country: Jiangsu Province, CHINA

Corresponding Author

NAME: Feng Chang

Postal address: 639 Longmian Road, Nanjing, Jiangsu Province, CHINA

E-mail: cpucf@163.com

Institutions: China Pharmaceutical University

City & Country: Jiangsu Province, CHINA

Telephone: +86-13805153128

Keywords:

multimorbidity, Cross-sectional study, Prevalence, Observed-to-expected ratio, China

Word count: 4911

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ABSTRACT

Objectives: Examination of the prevalence and patterns of multimorbidity among the elderly in China.

Design: Cross-sectional study.

Setting: More than 10,000 households in 28 of the 34 provinces of mainland China.

Participants: 11,707 Chinese adults aged 60 and over.

Primary outcome measures: Prevalence and patterns of multimorbidity among the participants. Relative risks were calculated to estimate the probability of up to 14 chronic conditions coexisting with each other. Observed-to-expected (O/E) ratios were used to analyze the patterns of multimorbidity.

Results: Multimorbidity was present in 43.6% of respondents from the sample population, with women having the greater prevalence compared to men. There were 804 different comorbidity combinations identified, including 76 dyad combinations and 169 triad combinations. The top 10 morbidity dyads and triads accounted for 69.01% and 47.05% of the total dyad and triad combinations observed, respectively. Among the 14 chronic conditions included in the study, asthma, stroke, heart attack and six other chronic conditions were the main components of multimorbidity due to their high relative risk ratios. The most frequently occurring clusters with higher O/E ratios were stroke along with emotional, nervous, or psychiatric problems; memory-related diseases together emotional, nervous, or psychiatric problems; and memory-related diseases and asthma accompanied by chronic lung diseases and asthma.

Conclusions: The results of this study highlight the high prevalence of multimorbidity in the elderly population in China. Further studies are required to understand the etiology of multimorbidity, and future primary healthcare policies should be made while taking multimorbidity into consideration.

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Strengths and limitations of this study

Strengths

- This is the first study to estimate the prevalence and patterns of multimorbidity among the elderly population in China.
- Data for this study were collected from a nationally representative longitudinal survey of 17,708 Chinese residents.

Limitations

- Only 14 predefined chronic diseases were included in the study, and these may not be comprehensive of the conditions of the population.
- The data analyzed from the CHARLS were originally collected by population self-reporting, not clinician evaluation, and could partially reflect some associated biases or confounds.
- This study only included older patients aged 60 years and above with complete data. Although exclusion of incomplete data may cause a selection bias, significant differences between included and excluded cases were not observed.

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INTRODUCTION

Multimorbidity, or the simultaneous occurrence of two or more chronic conditions in an individual, is becoming increasingly common, and this has been reported to increase progressively with age. [1, 2] At present, with China's aging population having an increasing prevalence of chronic conditions, multimorbidity among the elderly poses an enormous societal cost due to increased mortality rates and healthcare utilization. [3] However, to date, research on chronic conditions in China has focused on single disease states, and the coexistence of multiple chronic conditions has not been investigated systematically and thoroughly.

There is a significant difference in the etiological analysis between patients with single chronic conditions and those with multimorbidity. [4] The coexistence of chronic conditions in a patient is more than a random event, it is more typically due to the causal relationship between some diseases and shared pathogenic factors. [5, 6] Moreover, the interactions between diseases or between a disease and host result in differences in the severity of multimorbidity and functional status and prognosis of patients with multimorbidity. [7] Consequently, it is imperative to begin research on multimorbidity in China for the cost-effective treatments that the results may help to suggest. [8] The purpose of this study was therefore to determine the prevalence of multimorbidity among the elderly in China and to reveal morbidity combinations, which may benefit the design and implementation of a modified healthcare system with consideration for patients with multimorbidity.

METHODS

Data source

Data for this study were collected from the third response of the China Health and Retirement Longitudinal Survey (CHARLS), which is the most current data available. The CHARLS is a nationally representative longitudinal survey of Chinese residents aged 45 and older that was conducted by the Chinese Center for Disease Control and Prevention, along with Peking University, to help China to adjust to the rapid aging of its population through the evaluation of social, economic, and health circumstances on

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the community level using data collected by interviews, physical measurements and blood sample collection. [9] The national baseline survey began in 2011 and involved 17,708 respondents from 150 county-level units, 450 village-level units, and approximately 10,000 households. Afterwards, CHARLS respondents were followed every second year, with their informed consent, and the study was approved by the Peking University Biomedical Ethics Committee (IRB00001052-14013-exemption).

Variables

The core CHARLS questionnaires included sections requesting information on demographic factors, family structure and changes, health status and functioning, healthcare and insurance, work, retirement and pension, income and consumption, and assets (individual and household). Information was collected by interview by trained staff. For the current study, the eligible and included participants were determined by being aged 60 and over, and data on gender, age and health status was used from the general health status and disease history section of senior citizens in the 2015 CHARLS data. This information included the following 14 common chronic health problems: hypertension, dyslipidemia (high blood lipids or low cholesterol), diabetes or elevated blood glucose (including impaired glucose tolerance and fasting blood glucose), cancer (excluding mild skin cancers), chronic lung disease such as chronic bronchitis or emphysema, pulmonary heart disease (excluding tumors or cancer), liver disease (other than fatty liver, tumors, or cancer), heart disease (such as myocardial infarction, coronary heart disease, angina pectoris, congestive heart failure and other heart diseases), stroke, kidney disease (excluding tumors or cancer), stomach or other digestive diseases (excluding tumors or cancer), emotional and mental problems, memory-related diseases (such as Alzheimer's disease, brain atrophy, Parkinson's disease), arthritis or rheumatism, and asthma. All these data were based on self-reports. Accordingly, multimorbidity was defined as the coexistence of more than one of the 14 chronic conditions, with acute or subacute forms of certain conditions being excluded in this study due to the CHARLS data collection protocol.

Statistical analysis

To detect the demographic characteristics of patients with multimorbidity, respondents were divided into two groups: those with multiple chronic conditions (MCC group) and those without multiple chronic conditions (Non-MCC group).

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Descriptive statistics were calculated and expressed as means (SD) and frequencies (percentage). We applied the T^2 and χ^2 texts to test the differences in age, gender and the mean number of chronic conditions across different subgroups. Respective prevalence in the MCC group and the non-MCC group were calculated separately. Given the exclusion of participants with incomplete data, a sensitivity analysis was conducted to compare the characteristics of the complete cases aged 60 years and above and the counterpart in the incomplete cases, which is presented in Annex 1.

To determine the most common combination of chronic diseases, the prevalence of morbidity and multimorbidity dyads and triads were estimated, respectively. Next, the expected number of patients with a chronic disease were calculated, and the observed-to-expected (O/E) ratios were determined by dividing the number of patients in those groups by the expected number of patients. Observed-to-expected ratios were used to estimate the conditional probability of coexistence of two or three chronic conditions. [10] As an important indicator for assessing the correlation between diseases, the O/E ratio has been used in many areas of comorbidity. [10， 11] The relative risk of comorbidity for individual chronic conditions was also calculated. Relative risk of comorbidity (RR) is the ratio of the number of people with a certain chronic condition who suffer from multimorbidity to the number of patients with the same disease who do not suffer from multimorbidity. [11, 12] In other words, a higher RR value means a higher probability that the disease coexists with other diseases. However, it should be noted that there is no direct relationship between the relative risk of comorbidity and the overall prevalence of the diseases. [13, 14]

All analyses in this study were completed using Stata softwareV.14.0 for Windows (Stata Corp). P Values <0.05 were considered to be statistically significant.

Patient and public involvement

Patients and the public were not 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 results to study participants.

RESULTS

Characteristics of participants

The data were gathered from the third response set of CHARLS. After exclusion

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of participants with incomplete data (1,002) or aged under 60 (9,259), there were 11,707 respondents with available information on related chronic diseases that were included in this study. The selection process of study sample is shown in Figure 1. The demographic characteristics of sample respondents and statistical significance test results are presented in Table 1.

Overall, the mean age for the sample population was 70.5 (ranging from 60 to 107). The sample population consisted of 5,705 (48.7%) males and 6002 (51.2%) females, and 43.6% of them suffered from multimorbidity. The median of chronic conditions in the MCC group was 3.01, compared to 0.45 in the Non-MCC group. Samples in the MCC group were 0.66 year older than those belonged to the non-MCC group. Gender differences with regard to the age of samples between the MCC group and the non-MCC group (70.57 for MCC group and 69.51 for non-MCC group) were small but statistically significant ($p < 0.001$). The prevalence of multimorbidity in the female population was higher than that for the males (54.41% vs 45.59%). Figure 2 shows the number and proportion of respondents over 60 according to morbidity numbers. It can be seen that among all the participants aged over 60, only 30.9% of them did not have the 14 chronic diseases and 43.6% suffer from multimorbidity.

Table 1. Demographic characteristics of all respondents, the MCC group and non-MCC group

	All respondents	**MCC group**	**Non-MCC group**	**P***
Number of people	11707	5107	6600	
Proportion (%)	100%	43.62%	56.38%	
Mean age				
All respondents (SD)	70.20(7.907)	70.57(7.701)	69.91(8.051)	<0.001
Male (SD)	69.97(7.575)	70.50(7.348)	69.60(7.707)	<0.001
Female (SD)	70.39(8.189)	70.62(7.892)	70.19(8.359)	<0.001
Gender（% females）	51.28%	54.41%	48.83%	<0.001
Mean number of chronic conditions				
All respondents（SD）	1.57(1.560)	3.01(1.259)	0.45(0.498)	<0.001
Male（SD）	1.47(1.534)	2.98(1.265)	0.44(0.496)	<0.001
Female（SD）	1.65(1.581)	3.03(7.982)	0.47(0.499)	<0.001

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SD = standard deviation;

p* = statistical significance of the difference between the MCC and the non-MCC sample (t-tests were performed for comparison of means, and chi-square-tests for differences between percentages)

Prevalence of chronic conditions

The prevalence of chronic conditions in the entire sample, the MCC group and the non-MCC group are shown in Figure 3. The prevalence of all fourteen chronic conditions in the MCC group was significantly higher than that in the entire sample. For instance， the prevalence of arthritis or rheumatism, hypertension, stomach or other digestive disease, heart disease and chronic lung disease were 65.97%, 48.82%, 45.86%, 29.00% and 24.97% in the MCC group, compared to 38.49%, 26.41%, 24.52%, 12.32% and 12.32% in the entire sample, respectively.

Table 2 shows the relative risks of comorbidity determined for the 14 chronic diseases reported in this study. It can be seen that the overall relative risks for asthma, stroke, heart disease and six other conditions were all above 10, which meant these diseases were >10 times easier to coexist with other chronic conditions and result in multimorbidity. In addition, the relative risks for certain diseases were positively associated with gender. For example, men had significantly higher relative risks for asthma, but lower relative risks for diabetes or high blood sugar, compared to women.

Table 2 Relative risks of multimorbidity for different chronic conditions according to gender

Chronic conditions	All respondents	95% Confidence Interval		Female	95% Confidence Interval		Male	95% Confidence Interval	
		Lower Bound	Upper Bound		Lower Bound	Upper Bound		Lower Bound	Upper Bound
High relative risk of multimorbidity									
Asthma	26.18	17.82	38.46	20.67	11.85	36.06	32.68	19.18	55.67
Stroke	18.62	12.11	28.64	21.57	10.61	43.86	17.43	10.13	29.99
Heart disease	15.56	12.99	18.63	16.48	12.80	21.21	14.26	11.02	18.46
Diabetes or high blood sugar	14.40	11.18	18.55	15.68	10.86	22.63	13.11	9.24	18.62

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Dyslipidemia	14.05	11.54	17.12	15.13	11.37	20.14	12.97	9.86	17.05
Memory-related disease	13.69	8.85	21.16	34.17	12.63	92.44	9.28	5.66	15.21
Kidney disease	11.57	9.24	14.49	15.01	10.17	22.43	10.24	7.78	13.48
Liver disease	11.10	8.37	14.71	16.07	9.70	26.63	9.15	6.49	12.89
Chronic lung diseases	9.87	8.43	11.55	10.71	8.26	13.88	9.74	8.00	11.86
Low relative risk of multimorbidity									
Emotional, nervous, or psychiatric problems	7.42	4.94	11.15	6.24	3.78	10.30	9.36	4.65	18.85
Stomach or other digestive disease	5.73	5.25	6.25	6.20	5.48	7.02	5.23	4.62	5.91
Hypertension	5.38	4.96	5.84	4.90	4.40	5.47	5.92	5.24	6.69
Cancer or malignant tumor	4.88	3.20	7.45	5.33	3.06	9.29	3.99	2.07	7.72
Arthritis or rheumatism	3.83	3.61	4.05	3.70	3.43	3.99	3.91	3.59	4.26

Common multimorbidity combinations

There were 804 possible comorbidity combinations that were identified in the MCC group after statistical analysis, including 72 dyads and 169 triads. The 10 most frequently occurring morbidity dyads and triads are presented respectively in Table 3 and Table 4.

Table3 Prevalence of the 10 most common morbidity dyads

Rank	Morbidity dyads	Prevalence			Mean
		All respondents	female	male	Age
1	Arthritis or rheumatism and Stomach or other digestive disease	4.73%	3.56%	5.96%	69.20
2	Arthritis or rheumatism and Hypertension	2.85%	2.20%	3.53%	71.25
3	Arthritis or rheumatism and Chronic lung diseases	1.13%	1.22%	1.04%	71.55
4	Hypertension and heart problems	1.03%	1.00%	1.06%	71.80
5	Hypertension and Stomach or other digestive disease	0.89%	0.83%	0.95%	69.07
6	Hypertension	0.86%	0.81%	0.91%	68.58

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	and Dyslipidemia				
7	Arthritis or rheumatism and heart problems	0.76%	0.53%	1.00%	70.72
8	Arthritis or rheumatism and Kidney disease	0.64%	0.73%	0.54%	68.24
9	Hypertension and Diabetes or high blood sugar	0.58%	0.50%	0.67%	70.97
10	Chronic lung diseases and Asthma	0.53%	0.65%	0.40%	71.15

Table 4 Prevalence of the 10 most common morbidity triads

Rank	Morbidity triads	Prevalence			Mean Age
		All respondents	female	male	
1	Arthritis or rheumatism, Stomach or other digestive disease and Hypertension	1.19%	0.80%	1.60%	70.96
2	Arthritis or rheumatism, Stomach or other digestive disease and Chronic lung diseases	0.82%	0.97%	0.67%	70.82
3	Arthritis or rheumatism, Heart disease and Hypertension	0.63%	0.37%	0.91%	69.93
4	Arthritis or rheumatism, Heart disease and Stomach or other digestive disease	0.59%	0.25%	0.95%	71.51
5	Hypertension, Dyslipidemia and Arthritis or rheumatism	0.44%	0.31%	0.57%	70.13
6	Hypertension, Dyslipidemia and Heart problems	0.42%	0.35%	0.49%	71.17
7	Arthritis or rheumatism, Kidney disease and Stomach or other digestive disease	0.42%	0.40%	0.44%	70.14
8	Arthritis or rheumatism, Asthma and Chronic lung diseases	0.40%	0.46%	0.33%	69.18
9	Hypertension, Dyslipidemia and Diabetes or high blood sugar	0.35%	0.35%	0.35%	71.51
10	Arthritis or rheumatism, Stomach or other digestive disease	0.53%	0.57%	0.49%	70.29

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and Liver disease

Theoretically, there are 91 dyad combinations and 364 triad combinations possible given the 14 different chronic conditions considered in this study. However, only 72 types (79.12%) of dyads and 169 types (46.43%) of triads emerged in the sample. The 10 most frequently occurring morbidity dyads accounted for 69.01% of the 72 dyad combinations, and the proportion of the 10 most common triad combinations in the 169 triad combinations was 47.05%. Arthritis or rheumatism, which appeared in five of the top 10 dyad combinations and eight of the top 10 triad combinations of chronic conditions, was the main component of the leading morbidity dyads and triads.

There were significant gender differences observed in the occurrences of these multimorbidity combinations. The numbers of women with triad combinations of chronic diseases were generally higher than for men with the same morbidity triads. For example, women had significantly higher prevalence of arthritis and hypertension and hyperlipidemia than men (78.26% vs 21.74%). Among morbidity dyads, the prevalence of heart disease and arthritis or rheumatism in women was nearly two times higher than that in men, while the cluster of arthritis or rheumatism and kidney disease occurred more frequently in men than in women. No age difference was detected in the probability of these particular multimorbidity combinations occurring.

The O/E ratio was also used to analyze the multimorbidity pattern. [15] The higher the O/E value, the higher the probability of coexistence of chronic conditions. [16] Table 5 shows O/E ratios determined for the 10 most prevalent morbidity dyads and triads. The prevalence of each conditions and the dyad and triad prevalence are presented in Annex 2. In the midst of those triad combinations of chronic conditions, the two clusters with significantly higher O/E ratios were emotional, nervous, or psychiatric problems and stroke and memory-related disease (O/E ratio = 10287.72), emotional, nervous, or psychiatric problems and memory-related disorders and asthma (O/E ratio = 8498.56). These four conditions also dominated the three leading dyads

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with the highest O/E ratios: 97.73 for the combination of emotional and mental disorders and memory- related diseases, 23.66 for the combination of stroke and memory related disease and 19.55 for the combination of memory-related disease and asthma.

Table 5 O/E ratios for the 10 most prevalent morbidity dyads and triads

Number of chronic conditions	Rank	Chronic conditions	O/E ratio
2	1	Chronic lung diseases and Asthma	162.15
	2	Emotional, nervous, or psychiatric problems and Memory-related disease	97.73
	3	Dyslipidemia and Diabetes or high blood sugar	38.39
	4	Heart disease and Memory-related disease	25.69
	5	Stroke and Memory-related disease	23.66
	6	Hypertension and Stroke	22.85
	7	Hypertension and Diabetes or high blood sugar	20.64
	8	Cancer or malignant tumor and Stroke	19.55
	9	Memory-related disease and Asthma	19.55
	10	Stroke and Asthma	19.55
3	1	Stroke, Emotional, nervous, or psychiatric problems and Memory-related disease	10287.72
	2	Emotional, nervous, or psychiatric problems, Memory-related disease and Asthma	8498.56
	3	Emotional, nervous, or psychiatric problems, Chronic lung diseases and Asthma	2274.26
	4	Heart disease, Stroke and Memory-related disease	2253.50
	5	Chronic lung diseases, Heart disease and Asthma	1992.69
	6	Dyslipidemia, Heart disease and Memory-related disease	1443.25
	7	Hypertension, Dyslipidemia and Diabetes or high blood sugar	1398.31

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8	Hypertension, Stroke and Memory-related disease	1387.35
9	Chronic lung diseases, Memory-related disease and Asthma	1376.53
10	Chronic lung diseases, Arthritis or rheumatism and Asthma	1265.95

DISCUSSION

This is the first study to estimate the prevalence and patterns of multimorbidity among the elderly in China based on the nationally representative data from CHARLS, which included 11,707 older patients aged 60 years and above with complete data. Although exclusion of incomplete data may cause a selection bias, significant differences between included and excluded cases were not observed. The results of the study indicated that 69.1% of the elderly population in China had at least one of the 14 diseases and 43.6% of them suffered from multimorbidity. The average age of the MCC group was 0.66 years higher than that of the non-MCC group and in the MCC group, the mean age of women was 0.12 years higher than that of men, which was comparable to the results of previous studies. [17-21]

The prevalence of multimorbidity estimated in this study was much lower than that from previous studies in other developed countries. For example, a study of 543 patients over age 65 in Ghent, Belgium showed that the multimorbidity rate was as high as 82.6%, [22]. Another study in Australia showed that 83.2% of the respondents suffered from multimorbidity. [23] However, it is difficult to compare the prevalence generated from different studies due to differences in the selected definitions of multimorbidity, demographic characteristics of the samples, and different study methodologies. [24-28]

In agreement with previous reports, arthritis or rheumatism, hypertension, stomach or other digestive disease were the most common diseases in the MCC group. [11] The prevalence of these three conditions was each above 20% in the entire sample, and above 45% in the MCC group. The most prevalent chronic combinations in the sample

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could also be found in other studies. [22] The results of this study showed that the prevalence of arthritis or rheumatism was high and easy to coexist with other conditions. In addition to the chronic conditions mentioned above, previous studies demonstrated that women with rheumatoid arthritis might have a predisposition to gallstones which could manifest in middle or older age compared with women in the general population. This phenomenon could be related to chronic inflammation and HDL metabolism. [29]

Although arthritis or rheumatism, a component of all the leading three morbidity dyads and triads, was also the most commonly occurring disease in multimorbidity, the relative risk of this disease was only 4.65, the lowest in the 14 chronic diseases. Moreover, arthritis or rheumatism is less common in morbidity clusters with large O/E ratios. Therefore, the frequent occurrence of arthritis or rheumatism in multimorbidity might be simply due to the high prevalence of the disease. Doctor-diagnosed arthritis is a common and disabling chronic condition in the world. During 2013 to 2015, an average of more than one in five (54.4 million) adults in the United States were diagnosed with arthritis [30]. The unadjusted prevalences of arthritis among adults with obesity, heart disease, or diabetes were 30.6%, 49.3%, and 47.1%, respectively. In adults with obesity, heart disease, or diabetes, the age-adjusted prevalences of arthritis were respectively 1.5, 1.7 and 1.9 times higher than those without these diseases. Improving the health of adults with arthritis and related comorbid conditions calls for wider dissemination and implementation of evidence-based interventions, such as self-management education and physical activity promotion [31].

The relative risks for asthma, stroke, heart disease, and six other conditions were all above 10, which means that patients with these diseases were 10 times more likely to be afflicted by multimorbidity. These diseases also occurred at a high frequency in multimorbidity with high O/E ratios, such as the clusters of pulmonary disease and asthma, emotional and mental illness and memory-related disease, dyslipidemia and diabetes, and stroke and emotional or mental illness and memory-related disease. Patients with these diseases were more likely to express comorbidity compared to those

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without these diseases, and thus should be the focus of future research studies.

This study featured a nationally representative sample of the Chinese elderly population, which was crucial to get an overall understanding of multimorbidity among the elderly in China. However, there were also limitations with the data sample and study. For example, this study used data from the third wave report of CHARLS, a survey which was conducted in 2015, and there is accordingly a time lag to now that exists. Additionally, the chronic diseases included in the study were not comprehensive, since only 14 chronic conditions were included in the survey. Finally, the data obtained from the survey was based on self-reporting, which may have introduced some misclassification bias or other confounds. Later research on the prevalence and patterns of multimorbidity should be carried out in-depth with a more extensive survey of chronic disease.

CONCLUSIONS

Multimorbidity remains an underexplored area of research in China. [32]. Despite the increasing prevalence of multimorbidity, there are no specific proposals for its diagnosis and treatment. [33] This study contributes to the understanding of the prevalence and patterns of comorbidity among the elderly in China. Considering China's aging population and the high prevalence of comorbidity in senior citizens, the elderly should be prioritized in the fields of disease prevention and health promotion.

Acknowledgements The authors would like to thank the Chinese Center for Disease Control and Prevention and Peking University for access to China Health and Retirement Longitudinal Survey data.

Contributors RZ analyzed and interpreted data, drafted the manuscript, approved the final manuscript as submitted. YL revised the manuscript for important intellectual content. YLS analyzed and interpreted data and revised the manuscript for important

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intellectual content. SLZ analyzed and checked the data of the full text. FC helped on the study design and revised the manuscript.

Funding This work was funded by the National Natural Science Foundation of China (7167030838).

Competing interests None declared.

Patient consent Obtained.

Ethics approval The original CHARLS was approved by the ethics review committee of Peking University, and all participants gave written informed consent at the time of participation

Data sharing statement No additional data are available

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Figure legends

Figure 1 Flowchart for selecting the study sample from the original sample population. CHARLS, China Health and Retirement Longitudinal Survey

Figure 2 Frequency and percentage of people aged over 60 suffering from different diseases based on CHARLS data

Figure 3 Prevalence Rates of chronic condition in elderly people over 60 years old based on CHARLS data

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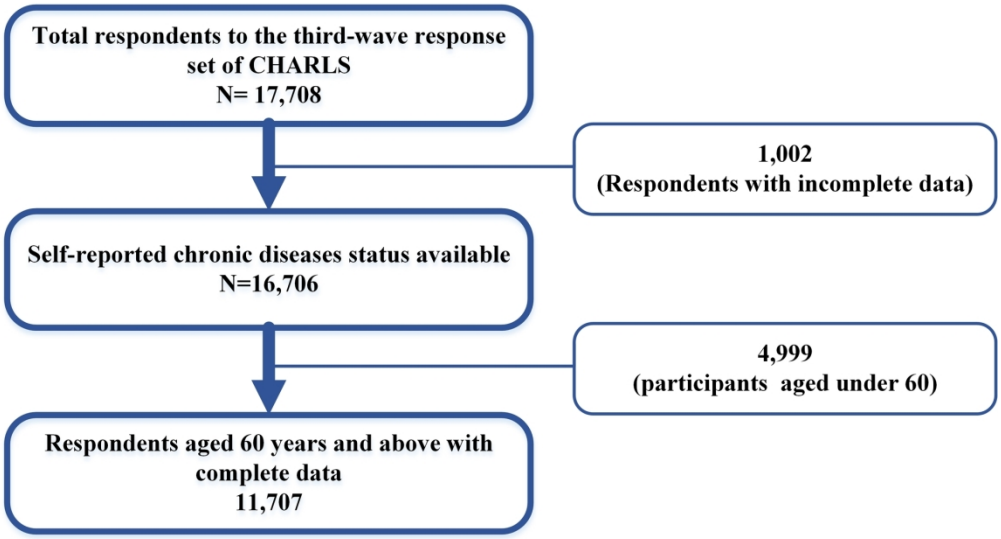

Figure 1 Flowchart for selecting the study sample from the original sample population. CHARLS, China Health and Retirement Longitudinal Survey

171x93mm (300 x 300 DPI)

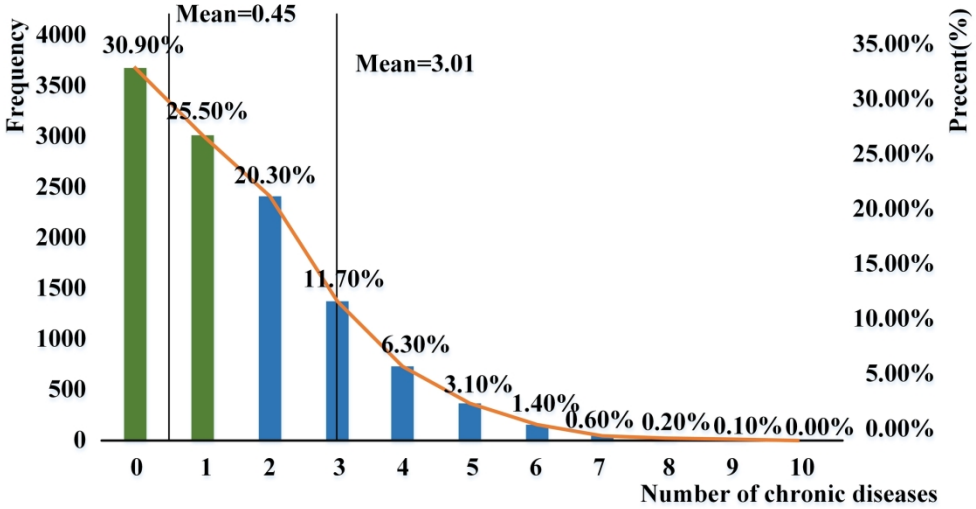

Figure 2 Frequency and percentage of people aged over 60 suffering from different diseases based on CHARLS data

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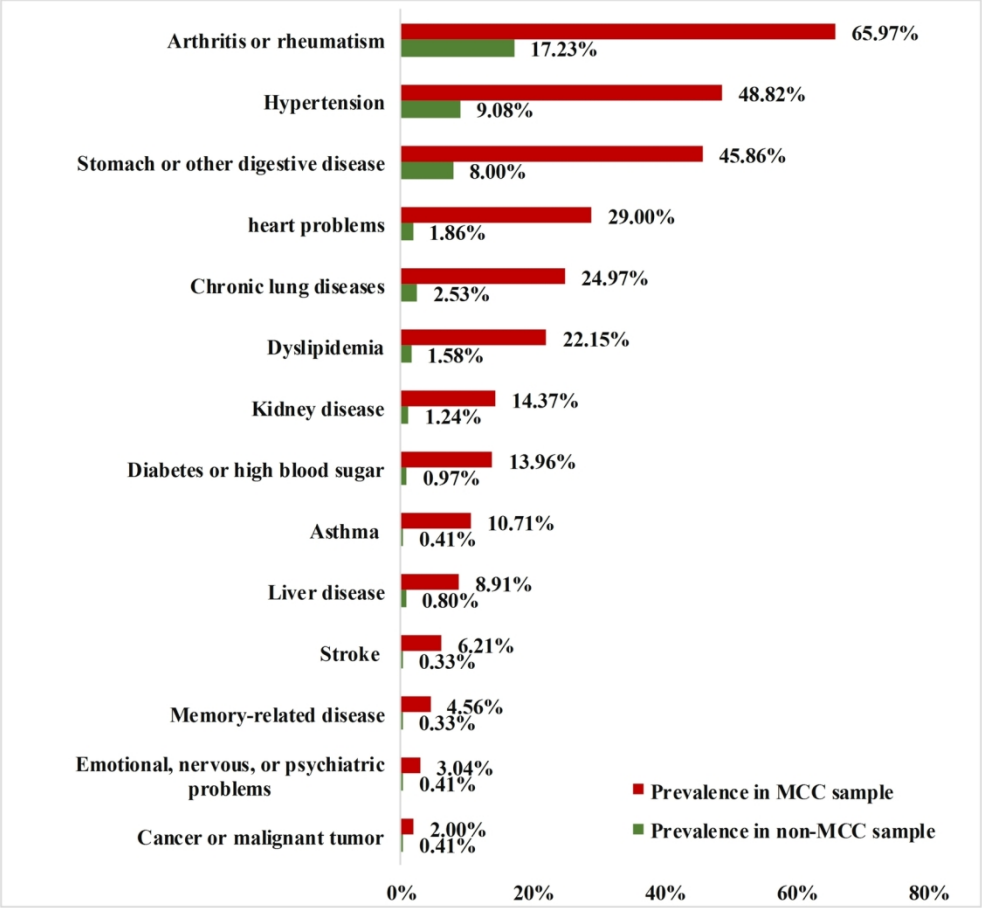

Figure 3 Prevalence Rates of chronic condition in elderly people over 60 years old based on CHARLS data

151x140mm (300 x 300 DPI)

Annex 1 Sensitivity analysis, Comparison of the characteristics of complete cases and incomplete cases

	Complete cases	**Incomplete cases**	**P***
Number of people	11707	876	
Proportion (%)	93.04%	6.96%	
Mean age All respondents (SD)	70.20(7.907)	69.60（7.824）	<0.001
Male (SD)	69.97(7.575)	69.58（7.721）	<0.001
Female (SD)	70.39(8.189)	69.62（7.973）	<0.001
Gender（% females）	51.28%	49.27%	0.193

p* = statistical significance of the difference between the complete cases and the incomplete cases (t-tests were performed for comparison of means, and chi-square-tests for differences between percentages)

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Annex 2 O/E ratio of all binary and triads comorbidities pattern present in participants

Rank	binary comorbidities pattern	O/E ratio
1	Chronic lung diseases and Asthma	161.00
2	Emotional, nervous, or psychiatric problems and Memory-related disease	98.57
3	Dyslipidemia and Diabetes or high blood sugar	38.69
4	Heart disease and Memory-related disease	25.96
5	Stroke and Memory-related disease	24.19
6	Hypertension and Stroke	23.10
7	Hypertension and Diabetes or high blood sugar	20.77
8	Cancer or malignant tumor and Stroke	19.71
9	Memory-related disease and Asthma	19.71
10	Stroke and Asthma	19.71
11	Hypertension and Heart disease	19.07
12	Hypertension and Dyslipidemia	18.98
13	Dyslipidemia and Heart disease	17.39
14	Diabetes or high blood sugar and Heart disease	14.87
15	Diabetes or high blood sugar and Liver disease	14.40
16	Cancer or malignant tumor and Liver disease	13.65
17	Diabetes or high blood sugar and Kidney disease	13.38
18	Hypertension and Memory-related disease	13.33
19	Dyslipidemia and Cancer or malignant tumor	12.51
20	Stomach or other digestive disease and Arthritis or rheumatism	10.80
21	Liver disease and Heart disease	10.49
22	Dyslipidemia and Stroke	10.23
23	Dyslipidemia and Stomach or other digestive disease	9.81
24	Dyslipidemia and Kidney disease	9.61
25	Chronic lung diseases and Memory-related disease	9.56
26	Chronic lung diseases and Stroke	9.56
27	Kidney disease and Arthritis or rheumatism	9.42
28	Heart disease and Kidney disease	9.29
29	Chronic lung diseases and Heart disease	9.12
30	Stomach or other digestive disease and Asthma	9.03
31	Liver disease and Kidney disease	8.99
32	Kidney disease and Stomach or other digestive disease	8.92
33	Memory-related disease and Arthritis or rheumatism	8.89
34	Stroke and Arthritis or rheumatism	8.89
35	Arthritis or rheumatism and Asthma	8.77
36	Liver disease and Memory-related disease	8.38
37	Diabetes or high blood sugar and Memory-related disease	8.32
38	Diabetes or high blood sugar and Stroke	8.32
39	Chronic lung diseases and Arthritis or rheumatism	8.14
40	Heart disease and Stomach or other digestive disease	8.11

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41	Heart disease and Arthritis or rheumatism	7.45
42	Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	7.39
43	Liver disease and Stomach or other digestive disease	7.33
44	Diabetes or high blood sugar and Cancer or malignant tumor	6.78
45	Diabetes or high blood sugar and Asthma	6.78
46	Diabetes or high blood sugar and Arthritis or rheumatism	6.44
47	Liver disease and Arthritis or rheumatism	6.16
48	Chronic lung diseases and Kidney disease	5.98
49	Chronic lung diseases and Stomach or other digestive disease	5.97
50	Hypertension and Arthritis or rheumatism	5.74
51	Chronic lung diseases and Liver disease	5.52
52	Kidney disease and Emotional, nervous, or psychiatric problems	5.29
53	Kidney disease and Asthma	5.29
54	Chronic lung diseases and Emotional, nervous, or psychiatric problems	5.19
55	Dyslipidemia and Memory-related disease	5.12
56	Hypertension and Emotional, nervous, or psychiatric problems	5.07
57	Hypertension and Chronic lung diseases	5.03
58	Hypertension and Kidney disease	5.01
59	Cancer or malignant tumor and Arthritis or rheumatism	4.96
60	Cancer or malignant tumor and Stomach or other digestive disease	4.93
61	Dyslipidemia and Arthritis or rheumatism	4.75
62	Hypertension and Liver disease	4.61
63	Diabetes or high blood sugar and Chronic lung diseases	4.38
64	Heart disease and Stroke	4.33
65	Dyslipidemia and Asthma	4.17
66	Hypertension and Stomach or other digestive disease	3.85
67	Cancer or malignant tumor and Heart disease	3.53
68	Heart disease and Asthma	3.53
69	Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	3.43
70	Diabetes or high blood sugar and Stomach or other digestive disease	3.12
71	Hypertension and Cancer or malignant tumor	2.17
72	Hypertension and Asthma	2.17
73	Stomach or other digestive disease and Memory-related disease	2.02
74	Stroke and Stomach or other digestive disease	2.02
75	Dyslipidemia and Liver disease	1.77
76	Dyslipidemia and Chronic lung diseases	1.35

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Rank	triads comorbidities pattern	O/E ratio
1	Stroke, Emotional, nervous, or psychiatric problems and Memory-related disease	10491.60
2	Emotional, nervous, or psychiatric problems, Memory-related disease, Asthma,	8548.88
3	Heart disease, Stroke and Memory-related disease	2302.62
4	Chronic lung diseases, Emotional, nervous, or psychiatric problems and Asthma	2252.13
5	Chronic lung diseases, Heart disease, Asthma,	1977.13
6	Dyslipidemia, Heart disease and Memory-related disease	1461.04
7	Hypertension, Stroke and Memory-related disease	1418.54
8	Hypertension, Dyslipidemia and Diabetes or high blood sugar	1409.29
9	Chronic lung diseases, Memory-related disease and Asthma	1381.96
10	Chronic lung diseases, Arthritis or rheumatism and Asthma	1256.63
11	Dyslipidemia, Diabetes or high blood sugar and Kidney disease	1255.51
12	Cancer or malignant tumor, Chronic lung diseases and Asthma	1126.07
13	Chronic lung diseases, Kidney disease and Asthma	1112.24
14	Liver disease, Kidney disease and Asthma	974.52
15	Dyslipidemia, Diabetes or high blood sugar and Liver disease	972.21
16	Chronic lung diseases, Liver disease and Asthma	956.96
17	Dyslipidemia, Diabetes or high blood sugar and Stroke	935.99
18	Chronic lung diseases, Stomach or other digestive disease and Asthma	921.21
19	Hypertension, Dyslipidemia and Heart disease	876.36
20	Diabetes or high blood sugar, Liver disease and Kidney disease	822.11
21	Hypertension, Diabetes or high blood sugar and Stroke	812.58
22	Hypertension, Chronic lung diseases and Asthma	812.01
23	Hypertension, Dyslipidemia and Stroke	800.07
24	Dyslipidemia, Heart disease and Asthma	793.67
25	Diabetes or high blood sugar, Heart disease and Stroke	791.41
26	Hypertension, Emotional, nervous, or psychiatric problems and Memory-related disease	770.58
27	Dyslipidemia, Diabetes or high blood sugar and Cancer or malignant tumor	762.67
28	Dyslipidemia, Diabetes or high blood sugar and Emotional, nervous, or psychiatric problems	762.67
29	Dyslipidemia, Diabetes or high blood sugar and Heart disease	669.54
30	Liver disease, Heart disease and Emotional, nervous, or psychiatric problems	649.62
31	Heart disease, Kidney disease and Memory-related disease	617.74
32	Heart disease, Stroke and Kidney disease	617.74
33	Dyslipidemia, Chronic lung diseases and Asthma	584.58
34	Diabetes or high blood sugar, Liver disease and Heart disease	548.02

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35	Hypertension, Diabetes or high blood sugar and Heart disease	523.14
36	Hypertension, Heart disease and Stroke	507.36
37	Diabetes or high blood sugar, Chronic lung diseases and Asthma	474.98
38	Liver disease, Stomach or other digestive disease and Asthma	454.02
39	Stomach or other digestive disease, Emotional, nervous, or psychiatric problems and Memory-related disease	437.10
40	Hypertension, Memory-related disease, Asthma,	385.29
41	Diabetes or high blood sugar, Stomach or other digestive disease and Asthma	300.46
42	Hypertension, Dyslipidemia and Memory-related disease	300.03
43	Liver disease, Kidney disease and Arthritis or rheumatism	277.66
44	Hypertension, Heart disease and Memory-related disease	253.68
45	Dyslipidemia, Liver disease and Kidney disease	252.95
46	Hypertension, Chronic lung diseases and Stroke	249.13
47	Stroke, Memory-related disease and Arthritis or rheumatism	249.11
48	Dyslipidemia, Chronic lung diseases and Liver disease	248.40
49	Cancer or malignant tumor, Chronic lung diseases and Heart disease	247.14
50	Chronic lung diseases, Heart disease and Emotional, nervous, or psychiatric problems	247.14
51	Hypertension, Dyslipidemia and Asthma	244.47
52	Cancer or malignant tumor, Heart disease and Stomach or other digestive disease	234.50
53	Chronic lung diseases, Memory-related disease and Arthritis or rheumatism	229.69
54	Chronic lung diseases, Stroke and Stomach or other digestive disease	211.98
55	Hypertension, Stroke and Arthritis or rheumatism	210.41
56	Chronic lung diseases, Liver disease and Heart disease	210.03
57	Hypertension, Cancer or malignant tumor and Heart disease	206.71
58	Hypertension, Heart disease and Emotional, nervous, or psychiatric problems	206.71
59	Memory-related disease, Arthritis or rheumatism and Asthma	202.98
60	Emotional, nervous, or psychiatric problems, Memory-related disease and Arthritis or rheumatism	202.98
61	Stroke, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	202.98
62	Stroke, Kidney disease and Arthritis or rheumatism	200.49
63	Dyslipidemia, Diabetes or high blood sugar and Stomach or other digestive disease	194.98
64	Liver disease, Stomach or other digestive disease and Memory-related disease	185.73
65	Dyslipidemia, Stomach or other digestive disease and Asthma	184.90
66	Diabetes or high blood sugar, Stomach or other digestive disease and Memory-related disease	184.37
67	Diabetes or high blood sugar, Heart disease and Arthritis or rheumatism	183.74

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68	Chronic lung diseases, Stroke and Arthritis or rheumatism	164.06
69	Kidney disease, Arthritis or rheumatism and Asthma	163.36
70	Dyslipidemia, Diabetes or high blood sugar and Arthritis or rheumatism	162.98
71	Hypertension, Diabetes or high blood sugar and Memory-related disease	162.52
72	Hypertension, Dyslipidemia and Kidney disease	160.98
73	Hypertension, Heart disease and Kidney disease	158.80
74	Chronic lung diseases, Liver disease and Kidney disease	157.53
75	Dyslipidemia, Liver disease and Stomach or other digestive disease	157.13
76	Heart disease, Kidney disease and Stomach or other digestive disease	154.42
77	Cancer or malignant tumor, Liver disease and Stomach or other digestive disease	151.34
78	Liver disease, Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	151.34
79	Heart disease, Arthritis or rheumatism and Asthma	145.20
80	Stroke, Kidney disease and Stomach or other digestive disease	143.91
81	Liver disease, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	140.56
82	Diabetes or high blood sugar, Arthritis or rheumatism and Asthma	139.53
83	Hypertension, Dyslipidemia and Liver disease	138.50
84	Hypertension, Heart disease and Asthma	137.80
85	Kidney disease, Stomach or other digestive disease and Arthritis or rheumatism	136.43
86	Chronic lung diseases, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	133.68
87	Hypertension, Liver disease and Asthma	133.40
88	Hypertension, Diabetes or high blood sugar and Cancer or malignant tumor	132.42
89	Chronic lung diseases, Stomach or other digestive disease and Arthritis or rheumatism	131.24
90	Hypertension, Diabetes or high blood sugar and Kidney disease	130.80
91	Heart disease, Stomach or other digestive disease and Arthritis or rheumatism	128.06
92	Dyslipidemia, Heart disease and Stomach or other digestive disease	121.74
93	Hypertension, Heart disease and Arthritis or rheumatism	121.06
94	Stomach or other digestive disease, Arthritis or rheumatism and Asthma	118.39
95	Chronic lung diseases, Heart disease and Arthritis or rheumatism	117.36
96	Hypertension, Liver disease and Heart disease	117.11
97	Diabetes or high blood sugar, Kidney disease and Arthritis or rheumatism	114.85
98	Chronic lung diseases, Heart disease and Stomach or other digestive disease	113.73
99	Hypertension, Diabetes or high blood sugar and Liver disease	112.54
100	Diabetes or high blood sugar, Chronic lung diseases and Heart disease	104.24
101	Liver disease, Stomach or other digestive disease and Arthritis or rheumatism	104.21
102	Stroke, Stomach or other digestive disease and Arthritis or rheumatism	103.78

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103	Hypertension, Kidney disease and Emotional, nervous, or psychiatric problems	103.36
104	Chronic lung diseases, Liver disease and Arthritis or rheumatism	102.25
105	Hypertension, Dyslipidemia and Arthritis or rheumatism	100.61
106	Liver disease, Kidney disease and Stomach or other digestive disease	99.65
107	Dyslipidemia, Cancer or malignant tumor and Stomach or other digestive disease	92.45
108	Dyslipidemia, Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	92.45
109	Hypertension, Dyslipidemia and Chronic lung diseases	92.21
110	Hypertension, Chronic lung diseases and Heart disease	89.11
111	Heart disease, Stroke and Arthritis or rheumatism	89.10
112	Hypertension, Heart disease and Stomach or other digestive disease	88.07
113	Chronic lung diseases, Heart disease and Kidney disease	81.37
114	Chronic lung diseases, Kidney disease and Arthritis or rheumatism	79.23
115	Diabetes or high blood sugar, Chronic lung diseases and Arthritis or rheumatism	78.94
116	Chronic lung diseases, Kidney disease and Stomach or other digestive disease	75.82
117	Hypertension, Diabetes or high blood sugar and Arthritis or rheumatism	75.46
118	Hypertension, Dyslipidemia and Stomach or other digestive disease	75.00
119	Chronic lung diseases, Liver disease and Stomach or other digestive disease	73.39
120	Hypertension, Memory-related disease and Arthritis or rheumatism	73.19
121	Stomach or other digestive disease, Memory-related disease and Arthritis or rheumatism	72.65
122	Heart disease, Kidney disease and Arthritis or rheumatism	71.71
123	Liver disease, Arthritis or rheumatism and Asthma	70.28
124	Diabetes or high blood sugar, Cancer or malignant tumor and Arthritis or rheumatism	69.76
125	Kidney disease, Memory-related disease and Arthritis or rheumatism	66.83
126	Dyslipidemia, Heart disease and Arthritis or rheumatism	65.96
127	Diabetes or high blood sugar, Heart disease and Stomach or other digestive disease	65.94
128	Dyslipidemia, Chronic lung diseases and Heart disease	64.15
129	Hypertension, Kidney disease and Arthritis or rheumatism	63.81
130	Dyslipidemia, Stomach or other digestive disease and Arthritis or rheumatism	63.66
131	Hypertension, Chronic lung diseases and Memory-related disease	62.28
132	Dyslipidemia, Kidney disease and Stomach or other digestive disease	60.88
133	Hypertension, Stroke and Stomach or other digestive disease	59.10
134	Cancer or malignant tumor, Chronic lung diseases and Stomach or other digestive disease	57.58

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135	Cancer or malignant tumor, Chronic lung diseases and Arthritis or rheumatism	53.47
136	Hypertension, Stomach or other digestive disease and Arthritis or rheumatism	52.98
137	Dyslipidemia, Memory-related disease and Arthritis or rheumatism	52.69
138	Dyslipidemia, Stroke and Arthritis or rheumatism	52.69
139	Hypertension, Cancer or malignant tumor and Chronic lung diseases	50.75
140	Hypertension, Chronic lung diseases and Kidney disease	50.13
141	Liver disease, Heart disease and Arthritis or rheumatism	46.27
142	Hypertension, Cancer or malignant tumor and Arthritis or rheumatism	44.73
143	Hypertension, Liver disease and Kidney disease	43.92
144	Hypertension, Chronic lung diseases and Liver disease	43.13
145	Dyslipidemia, Cancer or malignant tumor and Arthritis or rheumatism	42.93
146	Dyslipidemia, Arthritis or rheumatism and Asthma	42.93
147	Hypertension, Diabetes or high blood sugar and Chronic lung diseases	42.81
148	Dyslipidemia, Kidney disease and Arthritis or rheumatism	42.40
149	Stomach or other digestive disease, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	42.28
150	Hypertension, Liver disease and Arthritis or rheumatism	41.18
151	Hypertension, Stomach or other digestive disease and Memory-related disease	39.40
152	Diabetes or high blood sugar, Stomach or other digestive disease and Arthritis or rheumatism	39.24
153	Hypertension, Arthritis or rheumatism and Asthma	37.27
154	Dyslipidemia, Liver disease and Arthritis or rheumatism	36.48
155	Heart disease, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	36.30
156	Hypertension, Chronic lung diseases and Arthritis or rheumatism	34.95
157	Dyslipidemia, Chronic lung diseases and Arthritis or rheumatism	34.70
158	Hypertension, Diabetes or high blood sugar and Stomach or other digestive disease	33.85
159	Cancer or malignant tumor, Stomach or other digestive disease and Arthritis or rheumatism	33.83
160	Liver disease, Heart disease and Stomach or other digestive disease	33.21
161	Dyslipidemia, Chronic lung diseases and Stomach or other digestive disease	29.89
162	Diabetes or high blood sugar, Liver disease and Arthritis or rheumatism	29.64
163	Hypertension, Kidney disease and Stomach or other digestive disease	26.42
164	Diabetes or high blood sugar, Chronic lung diseases and Stomach or other digestive disease	24.29
165	Hypertension, Emotional, nervous, or psychiatric problems and Arthritis or rheumatism	22.36
166	Hypertension, Liver disease and Stomach or other digestive disease	20.46

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167	Hypertension, Cancer or malignant tumor and Stomach or other digestive disease	16.05
168	Hypertension, Stomach or other digestive disease and Emotional, nervous, or psychiatric problems	16.05
169	Hypertension, Chronic lung diseases and Stomach or other digestive disease	15.57

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STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*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 pre-specified 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	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	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
Bias	9	Describe any efforts to address potential sources of bias	Not applicable
Study size	10	Explain how the study size was arrived at	4
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	5
		(*c*) Explain how missing data were addressed	Not applicable
		(*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	5

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		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	Not applicable
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	4
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	5
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Not applicable
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Not applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	5
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
		(*b*) Report category boundaries when continuous variables were categorized	8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	10
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-12
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
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	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
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	14

*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.

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