BMJ Global Health

# Medical costs and out-of-pocket expenditures associated with multimorbidity in China: quantile regression analysis

Yang Zhao ,[1,2] Rifat Atun ,[3,4] Kanya Anindya ,[5] Barbara McPake,[5] Tiara Marthias,[5,6] Tianxin Pan,[7] Alexander van Heusden,[5] Puhong Zhang,[1,8] Nadila Duolikun,[1] John Tayu Lee[5,9]

**To cite:** Zhao Y, Atun R, Anindya K, *et al*. Medical costs and out-of-pocket expenditures associated with multimorbidity in China: quantile regression analysis. *BMJ Global Health* 2021;**6**:e004042. doi:10.1136/bmjgh-2020-004042

**Handling editor** Lei Si

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/bmjgh-2020-004042).

Received 24 September 2020
Revised 7 January 2021
Accepted 11 January 2021



For numbered affiliations see end of article.

**Correspondence to**
Dr Yang Zhao;
Wzhao@georgeinstitute.org.cn

## ABSTRACT

**Objective** Multimorbidity is a growing challenge in low-income and middle-income countries. This study investigates the effects of multimorbidity on annual medical costs and the out-of-pocket expenditures (OOPEs) along the cost distribution.

**Methods** Data from the nationally representative China Health and Retirement Longitudinal Study (CHARLS 2015), including 10 592 participants aged ≥45 years and 15 physical and mental chronic diseases, were used for this nationally representative cross-sectional study. Quantile multivariable regressions were employed to understand variations in the association of chronic disease multimorbidity with medical cost and OOPE.

**Results** Overall, 69.5% of middle-aged and elderly Chinese had multimorbidity in 2015. Increased number of chronic diseases was significantly associated with greater health expenditures across every cost quantile groups. The effect of chronic diseases on total medical cost was found to be larger among the upper tail than those in the lower tail of the cost distributions (coefficients 12, 95% CI 6 to 17 for 10th percentile; coefficients 296, 95% CI 71 to 522 for 90th percentile). Annual OOPE also increased with chronic diseases from the 10th percentile to the 90th percentile. Multimorbidity had larger effects on OOPE and was more pronounced at the upper tail of the health expenditure distribution (regression coefficients of 8 and 84 at the 10th percentile and 75th percentile, respectively).

**Conclusion** Multimorbidity is associated with escalating healthcare costs in China. Further research is required to understand the impact of multimorbidity across different population groups.

### Key questions

**What is already known?**

- The prevalence of chronic disease multimorbidity is common in both developed and developing countries.
- People with multimorbidity have higher health service use compared with persons with a single disease.
- Chronic disease multimorbidity has potential impacts on individuals and households.

**What are the new findings?**

- The prevalence of chronic disease multimorbidity is high among Chinese adults.
- Increased number of chronic diseases is significantly associated with greater medical expenditures.
- Multimorbidity has larger effects on out-of-pocket expenditures and is more pronounced at the upper tail of the health expenditure distribution.

**What do the new findings imply?**

- More focus is needed for primary and secondary prevention of multimorbidity.
- There is a need to identify cost-effective strategies and payment systems for management of multimorbidity.
- Development of specific guidelines for multimorbidity and its risk factors is essential.

## INTRODUCTION

Non-communicable diseases (NCDs) have been a leading cause of morbidity and mortality.[1] The burden of multimorbidity, defined as two or more coexisting NCDs in one person, is rising rapidly in the low-income and middle-income countries (LMICs), primarily due to increased longevity and increased exposure to risk factors.[2–4] A study in Scotland found a profound difference in the proportion of multimorbidity in the study population, where 59% of those aged 65–74 years had multimorbidity, compared with 8.1% of those aged between 25 and 34 years.[5] Similarly, a recent study in China, based on 11 physical NCDs, found that the prevalence of multimorbidity increased from 51% for those aged 50–54 years to 71% for those aged 75 years and above.[6] Patients with multimorbidity are costly to healthcare systems due

to the complex needs and greater health service utilisation.[7 8] Evidence from high-income countries (HICs) suggest that the economic consequences of a health condition may differ significantly among the highest users of health services, compared with those at the bottom or middle of treatment cost distributions.[8] However, there is no current systematic review of the association between total medical costs and multimorbidity. It has public health and policy implications to identify significant gaps in the existing evidence about healthcare delivery strategies for multimorbidity, economic burdens and financing systems in both HICs and LMICs.

By 2011, China reached near-universal health insurance coverage by establishing a social health insurance system. However, levels of insurance coverage and service benefit vary significantly across social health insurance schemes and locations, and patients were required to pay a substantial amount of user fees for their medical treatment costs. Recent statistics by the WHO suggests that private expenditures constitute approximately 40% of the total health expenditure in China, a level considerably higher than those of HICs with levels around 25%.[8] The heavy reliance of out-of-pocket expenditure (OOPE) to fund healthcare systems for chronic conditions is concerning as evidence suggests that user fees can have negative effects on health outcomes among patients with multimorbidity. User fees in the presence of rising levels of multimorbidity can be especially harmful for the poorest population in China as they likely have higher underlying risks for several NCDs,[2 6] while also having fewer financial resources to pay for their healthcare expenses.

Similar to many LMICs and neighbouring countries in Asia, China's healthcare delivery remains fragmented and hospital centred, with limited coordination between the different levels of healthcare providers within the health system.[9] Strong primary care consisting of multidisciplinary teams and lead by a general practitioner is pertinent to improve multimorbidity prevention and treatment.[10 11] Evidence from HICs suggested that people-centred integrated care for multimorbidity patients can sometimes be cost-effective. It is also worth noting that many LMICs may face the double burden of NCDs and infectious diseases. Therefore, the health service delivery model for multimorbidity care in LMICs also needs to pay attention to the management of NCDs with infectious disease. Rigorous evaluation of these new healthcare delivery models is warranted to ensure effectiveness, efficiency and quality of care.

Despite the increasing burden of multimorbidity in China, there has been minimal research investigating the effect of multimorbidity on economic outcomes of individuals, households and whole health systems.[12 13] Of these studies, multimorbidity was found to be associated with higher healthcare utilisation and OOPE.[12 13] Previous studies that estimate the average effect of the multimorbidity ignore the fact that the effect of multimorbidity might be very different in those with high medical costs than those have low medical costs.[12–15] Unlike traditional regression methods, such as the ordinary least squares (OLS) regression or the generalised linear model that focus on population average/mean effects, quantile regression models look at the effect of multimorbidity on healthcare costs across the outcome distribution. The quantile regression analyses provide more detail information and a deep understanding of the financial burden of multimorbidity.[16] Alternative estimation strategies using quantile regression analysis has been increasingly adopted in health systems research to investigate the associations between outcomes of interest and the explanatory variables across the distribution of a given dependent variable.[16] Based on a nationally representative survey data, we present the first study that investigates the impact of multimorbidity on annual medical costs and OOPE across cost distributions.

## METHODS

### Data sources

We used the 2015 China Health and Retirement Longitudinal Study (CHARLS) dataset, which is a nationally representative survey that collects high-quality data from respondents aged 45 years and older. The CHARLS was conducted using multistage stratified probability-proportionate-to-size sampling with ongoing follow-up surveys conducted every 2 years. The baseline sample size was 17 708 individuals. The details of the objectives, design and methods of the CHARLS are available elsewhere.[17] For this study, we identified 13 354 respondents with blood test and biomarker information. After removing respondents with missing values for the dependent or independent variables, the final sample consists of 10 592 respondents. (The flow chart of subjects' selection can be found in appendix online supplemental figure S1).

### Measures

For this study, NCD multimorbidity was defined as the presence of two or more chronic NCDs.[18–20] A total of 15 chronic diseases were included in the survey and were used to calculate the number of NCDs for each respondent. The chronic diseases included were hypertension, diabetes and dyslipidaemia, which was measured based on biomarkers or blood test and 10 self-reported chronic diseases (heart disease, stroke, chronic lung disease, kidney disease, digestive diseases, liver disease, cancer, memory-related illness, asthma and arthritis).

For mental illness, measured depression and self-reported diagnosed psychological disease were included in the study. Symptoms of depression were assessed using the 10-item Centre for Epidemiologic Studies Depression Scale (CESD-10),[21] which has been validated and is a reliable tool for mental health assessment among China older population.[20] The details of CESD-19 have been described elsewhere.[22] There were four possible responses for the CESD-10: (1) rarely; (2) some days (1–2 days per week); (3) occasionally (3–4 days per week); and (4) most

of the time (5–7 days per week). Respondents' answers were coded using a range between 0 (rarely) to 3 (most of the time) for the negative question. For two positive questions included in this study, we reversed the coding as 3 (rarely) to 0 (most of the time).[23] CESD-10 scoring ranged from 0 to 30. In this study, respondents with a CESD-10 score of at least 10 was defined as having depression symptoms. We also constructed a binary variable for depression.

In the CHARLS, respondents' systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured three times by a trained nurse using the HEM-7112 electronic monitor. Hypertension diagnosis was defined as SBP ≥140 mm Hg and/or DBP ≥90 mm Hg and/or receiving medication for hypertension.[24 25] Diabetes diagnosis was defined as having one or combination of the following: (1) fasting blood plasma glucose level of ≥126 mg/dL; (2) Glycated hemoglobin (HbA1c) concentration of ≥6.5%; and (3) receiving insulin treatment and/or medication for high blood sugar level.[26 27] Dyslipidaemia was defined based on: (1) total cholesterol ≥240 mg/dL; and/or (2) low-density lipoprotein cholesterol ≥160 mg/dL; and/or (3) high-density lipoprotein cholesterol <40 mg/dL; and/or (4) triglyceride ≥200 mg/dL; and/or (5) receiving antidyslipidaemia medication.[28 29]

Our primary outcome variables include the total treatment costs (defined as total annual health expenditure) and the annual OOPE, defined as the total direct payments for outpatient and inpatient visits occurring 1 year prior to the survey, after reimbursement from health insurance. As the total expenditure and OOPE for outpatient care was measured for 1 month at a time, we multiplied the costs by 12 months to obtain the annual outpatient care costs.[2 30]

This study also included the following covariates in the regression analyses: age, gender, marital status (married and partnered, unmarried and others), education attainment (illiterate, primary school, secondary school, college and above), place of residency (rural and urban), region of residency (east, central and west), household economic status quartiles (annual per capita household consumption expenditure) and social health insurance coverage (yes or no).

### Statistical analysis

We summarised the mean of total treatment cost and annual OOPE by the number of chronic diseases. The number of NCDs was considered as the independent variable in the regression models. For individuals with positive total health expenditure and OOPE (expenditures >0 US$), we applied linear regression models to assess the overall effects of NCDs and quantile regression analysis to estimate the effect of multimorbidity on health expenditures at the 10th, 25th, 50th, 75th and 90th percentiles. The quantile regression is similar to OLS regression, that is, estimating the median or other quantiles for the outcome variable associated with a set of independent variables and covariates without assuming normality or homoscedasticity of the underlying distribution.[31–33] The quantile regression is robust to outliers as it allows for assessing the full distribution of the outcome variable and is suitable for modelling outcomes that are not normally distributed or are highly skewed.[16 34]

We performed the Shapiro-Wilk W test for total medical cost and OOPE in our sample, and the results illustrated the skewed nature of both OOPE and total medical spending ($p<0.05$). It is becoming more important to understand the potential differential effect of multimorbidity across population group; therefore, this method has recently been widely used in health service research and policy evaluation, including the following studies that assessed costs outcomes (including OOPE or total medical costs).[20 21]

The coefficients at lower percentiles (10th and 25th percentiles) present the association of multimorbidity with total treatment cost and OOPE in those individuals with low health expenditures, while upper percentiles (75th and 90th percentiles) reflect the association on those with higher health expenditures. The statistical analyses in this study were conducted using Stata software V.16.0. P values <0.05 were considered statistically significant.

## RESULTS

We analysed data from 10 592 respondents. The median age of participants was 61.0 years (IQR 53.5–67.0) in 2015. There was a slightly higher percentage of female (53.1%) than male respondents. Most of the respondents were married (86.7%) and resided in rural areas (64.1%). Only 32.3% of the respondents had attained a level of education higher than primary school, and 91.5% of the respondents were enrolled in social health insurance in China. The overall prevalence of multimorbidity was 69.5%, with a high proportion in the older populations and unmarried individuals (table 1).

Table 2 shows the proportion and total treatment cost and OOPE across the number of chronic diseases. Of the total participants, 28.5% and 27.4% of total participants experienced an occurrence of total treatment cost and OOPE during the last year. Overall, the mean total treatment cost and annual OOPE was US$740 and US$474 in our sample, respectively. Having multimorbidity was associated with a higher frequency of OOPE (two chronic diseases: 23.9%; three conditions: 27.7%; four or more conditions 40.6%) compared with having no NCDs or only one chronic disease (17.7% and 18.0%, respectively). Having four chronic diseases or above was associated with a substantially greater OOPE of US$717 compared with US$236 for those without any chronic diseases. Similarly, for annual medical cost, individuals with more chronic diseases had greater healthcare costs than those with a single disease.

Table 1 Characteristics of participants and prevalence of chronic disease*

| | Overall | | No condition | | One condition | | | |
|---|---|---|---|---|---|---|---|---|
| | (n=10 592) | | (n=947) | | (n=2276) | | Multimorbidity (n=7369) | |
| Characteristic | N | % | % | 95% CI | % | 95% CI | % | 95% CI |
| Total | 10 592 | 100 | 9 | 8.4 to 9.7 | 21.5 | 20.5 to 22.5 | 69.5 | 68.3 to 70.6 |
| Age (year) | | | | | | | | |
| 45–54 | 2869 | 27.1 | 11.7 | 10.4 to 13.2 | 30.1 | 27.9 to 32.5 | 58.2 | 55.7 to 60.6 |
| 55–64 | 4036 | 38.1 | 9.8 | | 19.2 | 17.7 to 20.7 | 71 | 69.3 to 72.8 |
| 65–74 | 2727 | 25.8 | 6.1 | 5.1 to 7.2 | 17.4 | 15.9 to 19.1 | 76.5 | 74.6 to 78.3 |
| 75 and above | 960 | 9.1 | 6.5 | | 16.9 | 14.2 to 19.8 | 76.6 | 73.2 to 79.7 |
| Gender | | | | | | | | |
| Male | 4963 | 46.9 | 9 | 8.2 to 10 | 22.6 | 21.1 to 24.2 | 68.4 | 66.6 to 70 |
| Female | 5629 | 53.1 | 9.1 | 8.2 to 10 | 20.5 | 19.3 to 21.8 | 70.4 | 69 to 71.9 |
| Marital status | | | | | | | | |
| Married and partnered | 9188 | 86.7 | 9.5 | 8.8 to 10.3 | 21.9 | 20.8 to 23 | 68.6 | 67.4 to 69.8 |
| Unmarried and other | 1404 | 13.3 | 6 | 4.7 to 7.7 | 19 | 16.7 to 21.5 | 75 | 72.2 to 77.5 |
| Education status | | | | | | | | |
| Illiterate | 4766 | 45 | 7.5 | 6.6 to 8.4 | 19.2 | 18 to 20.5 | 73.3 | 71.8 to 74.7 |
| Primary school | 2404 | 22.7 | 7.7 | 6.5 to 9.2 | 21.1 | 19.3 to 23.1 | 71.2 | 68.9 to 73.3 |
| Secondary school | 2299 | 21.7 | 11.6 | 10.1 to 13.3 | 23.7 | 21.6 to 26 | 64.7 | 62.1 to 67.2 |
| College and above | 1123 | 10.6 | 12 | 10 to 14.5 | 25.7 | 21.9 to 29.9 | 62.3 | 57.9 to 66.5 |
| Residence place | | | | | | | | |
| Urban | 3799 | 35.9 | 9.9 | 8.7 to 11.2 | 21.6 | 19.8 to 23.5 | 68.5 | 66.4 to 70.6 |
| Rural | 6793 | 64.1 | 8.4 | 7.7 to 9.2 | 21.4 | 20.4 to 22.5 | 70.2 | 69 to 71.3 |
| Region | | | | | | | | |
| East | 4013 | 37.9 | 10.5 | 9.4 to 11.8 | 23.2 | 21.4 to 25.1 | 66.3 | 64.2 to 68.4 |
| Central | 4029 | 38 | 8.5 | 7.5 to 9.6 | 20.1 | 18.7 to 21.5 | 71.4 | 69.8 to 73 |
| West | 2550 | 24.1 | 7.4 | 6.3 to 8.5 | 20.8 | 19 to 22.6 | 71.9 | 69.9 to 73.8 |
| PCE, quartile | | | | | | | | |
| Q1, the lowest | 2648 | 25 | 8.1 | 6.9 to 9.4 | 19.5 | 17.8 to 21.3 | 72.4 | 70.3 to 74.4 |
| Q2 | 2648 | 25 | 9.3 | 8 to 10.6 | 23.6 | 21.4 to 25.9 | 67.2 | 64.8 to 69.4 |
| Q3 | 2649 | 25 | 9.6 | 8.4 to 11 | 21.2 | 19.5 to 23 | 69.2 | 67.1 to 71.2 |
| Q4 (the highest) | 2647 | 25 | 9.2 | 7.9 to 10.7 | 21.6 | 19.6 to 23.7 | 69.3 | 66.8 to 71.6 |
| Social health insurance | | | | | | | | |
| No | 902 | 8.5 | 8.9 | 6.9 to 11.4 | 24.5 | 20.9 to 28.5 | 66.6 | 62.5 to 70.4 |
| Yes | 9690 | 91.5 | 9.1 | 8.4 to 9.8 | 21.2 | 20.2 to 22.2 | 69.7 | 68.6 to 70.9 |

The values are weighted percentages unless otherwise indicated.
PCE, per capita household consumption expenditure.

### Results of quantile regression analysis

Table 3 presents the effects of the number of chronic diseases on total treatment cost by the treatment cost quantile. An increase in the number of chronic diseases was significantly associated with greater health expenditure across every quantile group. The effect of chronic diseases on total treatment cost was found to be larger among the upper tail than those in the lower tail of cost distributions (coefficients 12, 95% CI 6 to 17 for 10th percentile; coefficients 296, 95% CI 71 to 522 for 90th percentile). Table 4 shows that annual OOPE increased with chronic diseases from the 10th percentile to the 90th percentile. Multimorbidity had larger effects on OOPE and more pronounced at the upper tail of the outcome distribution (coefficients of 20 at the 25th percentile and 84 at the 75th percentile, respectively). Regarding socio-demographic covariates, the results only showed that household wealth has significant positive associations with health total medical cost and OOPE.

The result of quantile regression analysis among those incurring any healthcare costs suggests that an increased number of chronic diseases was significantly associated

Table 2 Treatment costs and out-of-pocket health expenditure by the number of chronic conditions

| | Any total treatment cost (%) | | Total annual treatment cost (US$) | | Any OOPE (%) | | Total annual OOPE (US$) | |
|---|---|---|---|---|---|---|---|---|
| Variable | Proportion | 95% CI | Mean | 95% CI | Proportion | 95% CI | Mean | 95% CI |
| Total participants | 28.5 | 27.3 to 29.6 | 740 | 658 to 822 | 27.4 | 26.3 to 28.6 | 474 | 413 to 534 |
| No conditions | 18 | 15.2 to 20.8 | 387 | 158 to 616 | 17.7 | 15 to 20.5 | 236 | 76 to 396 |
| One condition | 19.1 | 17.2 to 21 | 497 | 342 to 652 | 18 | 16.2 to 19.8 | 312 | 220 to 405 |
| Two conditions | 24.8 | 22.1 to 27.6 | 635 | 463 to 807 | 23.9 | 21.1 to 26.6 | 417 | 289 to 545 |
| Three conditions | 28.4 | 25.9 to 30.9 | 735 | 517 to 954 | 27.7 | 25.2 to 30.1 | 482 | 300 to 663 |
| Four conditions and above | 42.1 | 39.8 to 44.4 | 1131 | 974 to 1289 | 40.6 | 38.3 to 42.9 | 717 | 599 to 835 |

The values are weighted percentages and means unless otherwise indicated.
OOPE, out-of-pocket expenditure.

with greater total medical cost and OOPE at higher health expenditure quantiles compared with lower health expenditure quantiles (figure 1A,B). The total medical cost and OOPE attributable to multimorbidity over the distribution of these costs are also depicted in online supplemental figure S2a,b. Using the binary variable of multimorbidity, the total treatment cost and OOPE associated with multimorbidity were significant in almost in all quantiles, except for the 90th quantile of OOPE. Variations in OOPE associated with multimorbidity became more pronounced as expenditure approached the upper percentiles.

## DISCUSSION

### Principal findings

Our results showed that the number of NCD is associated with greater annual medical costs and OOPE. Importantly, our results suggest that the effect of multimorbidity on healthcare spending and OOPE was not constant across the quantiles of health expenditures. The quantile regression method adopted in our study accounts for the important association of number of the NCD with health expenditures that differs along the costs distribution. As a whole, our study identified important heterogeneity among key multimorbidity patient groups at different levels of medical costs and OOPE. Our results reveal a more nuanced measure of the association between NCDs and healthcare costs, and OOPE. These estimates can be used to forecast the future burden of multimorbidity and further evaluate the cost-effectiveness of prevention strategies for multimorbidity across population groups. Our results highlight the need for stronger and clearer analysis on the economic impact of multimorbidity in cost-effectiveness analysis on multimorbidity treatment and prevention strategies.

### Compare with existing literature

In this study, the prevalence of multimorbidity (69.5%) was much higher than previous research in China.[35 36] Using the 2015 CHARLS, a study by Zhang *et al*[35] found that NCD multimorbidity was only present in 43.6% of people aged ≥60 years. The difference in the prevalence could be due to the inclusion of objective biomarker and scale measurements for chronic diseases (hypertension, diabetes, dyslipidaemia and depression) in this study, which may have led to an increased diagnosis of multimorbidity compared with the results from the self-report chronic diseases.

The higher treatment cost and financial burden for individuals with multimorbidity are in line with earlier published studies.[6 13 37] Chen *et al*[13] found that the expenditure on patients with multiple chronic diseases was over three times higher than those with a single disease. This positive relationship between the number of NCDs and OOPE was also consistent with earlier studies.[38 39] Based on an earlier study in China, the mean OOPE for outpatient care was around 1.5 times greater for those with multimorbidity compared with those without any NCDs.[38] Similar results have been documented in earlier studies in both LMICs (eg, India and Mexico) and HICs.[39–42] The presence of mental illness is associated with greater health service use and increased OOPE.[43–45] A study by Hsieh and Qin[44] showed that people with depression were more than 10% more likely to use health services in a year. The economic burden attributable to depressive symptoms and depression accounted for 142 Renminbi (RMB) and 126 RMB per person/year.

Our findings on the higher treatment costs and financial burden may be explained by more prevalent polypharmacy among those with chronic conditions, leading to higher medicine expenditures. The challenges in polypharmacy may be due to the application of single-disease guidelines on patients with multimorbidity, which were designed based on frameworks that exclude multimorbidity conditions.[38 46] Some evidence also suggested that certain combinations of chronic diseases yielded higher medicine expenditure due to certain diseases requiring treatment using more expensive drugs.[7] Multimorbidity patients with higher OOPE on medicines had to allocate fewer resources to other healthcare services, and thus, it is more likely to increase inequality in healthcare and patient outcomes at the health system level when the

**Table 3** Quantile regression on total treatment cost associated with multimorbidity (total treatment cost >0, n=3021)

| | Overall | | 10th percentile | | 25th percentile | | 50th percentile | | 75th percentile | | 90th percentile | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Variable** | **Coeff** | **95% CI** | **Coeff** | **95% CI** | **Coeff** | **95% CI** | **Coeff** | **95% CI** | **Coeff** | **95% CI** | **Coeff** | **95% CI** |
| No. of NCD | 70 | 42 to 97 | 12 | six to 17 | 35 | 23 to 47 | 70 | 41 to 99 | 144 | 70 to 217 | 296 | 71 to 522 |
| Age (years) (45–54) | | | | | | | | | | | | |
| 55–64 | 25 | −88 to 137 | 24 | −1 to 49 | 52 | −4 to 107 | 25 | −98 to 147 | 90 | −247 to 426 | 653 | −529 to 1835 |
| 65–74 | 70 | −66 to 206 | 23 | −4 to 51 | 11 | −49 to 72 | 70 | −64 to 205 | 176 | −257 to 610 | 539 | −741 to 1819 |
| 75 and above | 179 | −23 to 380 | 56 | 13 to 99 | 67 | −23 to 157 | 179 | −30 to 388 | 478 | −143 to 1099 | 1112 | −782 to 3005 |
| Gender (male) | −35 | −146 to 76 | 24 | 3 to 46 | −6 | −52 to 40 | −35 | −138 to 69 | 94 | −201 to 390 | −223 | −1176 to 730 |
| Marital status (married) | −133 | −247 to −19 | −16 | −49 to 17 | −37 | −92 to 18 | −133 | −243 to −23 | −236 | −590 to 118 | −261 | −1594 to 1073 |
| Education status (illiterate) | | | | | | | | | | | | |
| Primary school | −23 | −145 to 100 | 17 | −5 to 40 | 4 | −48 to 56 | −23 | −152 to 106 | 368 | −46 to 783 | 494 | −556 to 1544 |
| Secondary school | 35 | −115 to 185 | −2 | −31 to 27 | 7 | −50 to 63 | 35 | −113 to 182 | 328 | −69 to 725 | 1022 | −534 to 2579 |
| College and above | 121 | −72 to 313 | 22 | −20 to 64 | 91 | −24 to 206 | 121 | −91 to 333 | 428 | −178 to 1035 | 914 | −1021 to 2848 |
| Residence place (urban) | −101 | −215 to 12 | −20 | −43 to 3 | −61 | −104 to −17 | −101 | −206 to 4 | −293 | −674 to 88 | −407 | −1436 to 622 |
| Region (east) | | | | | | | | | | | | |
| Central | −136 | −258 to −14 | 13 | −13 to 40 | −4 | −57 to 48 | −136 | −261 to −11 | −218 | −595 to 158 | −310 | −1592 to 971 |
| West | −247 | −363 to −132 | −3 | −28 to 23 | −51 | −102 to 0 | −247 | −378 to −117 | −466 | −809 to −122 | −953 | −2142 to 237 |
| Social health insurance (no) | −158 | −385 to 70 | 3 | −39 to 45 | −3 | −91 to 84 | −158 | −376 to 61 | −611 | −1511 to 289 | −2016 | −4651 to 618 |
| PCE, quartile (Q1, the lowest) | | | | | | | | | | | | |
| Q2 | −14 | −115 to 88 | 18 | −4 to 39 | 25 | −20 to 70 | −14 | −113 to 85 | 19 | −289 to 327 | −211 | −1161 to 740 |
| Q3 | 185 | 71 to 300 | 46 | 15 to 76 | 89 | 32 to 146 | 185 | 65 to 305 | 572 | 154 to 990 | 967 | −308 to 2242 |
| Q4 (the highest) | 499 | 312 to 687 | 61 | 34 to 88 | 167 | 106 to 227 | 499 | 311 to 687 | 1800 | 1234 to 2366 | 5303 | 3765 to 6841 |

Coefficients estimated after adjusting for study variables, including age, gender, marital status, level of education, residence place, region, household economic level and health insurance status.
NCD, non-communicable disease; PCE, per capita household consumption expenditure.

**Table 4** Quantile regression on OOPE associated with multimorbidity (OOPE >0, n=2926)

| | Overall | | 10th percentile | | 25th percentile | | 50th percentile | | 75th percentile | | 90th percentile | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Variable** | **Coeff** | **95% CI** | **Coeff** | **95% CI** | **Coeff** | **95% CI** | **Coeff** | **95% CI** | **Coeff** | **95% CI** | **Coeff** | **95% CI** |
| **No. of NCD** | 45 | 28 to 62 | 8 | 5 to 11 | 20 | 13 to 28 | 45 | 29 to 61 | 84 | 36 to 133 | 156 | 0 to 312 |
| **Age (years) (45–54)** | | | | | | | | | | | | |
| 55–64 | –31 | –122 to 60 | 8 | –8 to 25 | 18 | –21 to 58 | –31 | –124 to 61 | –149 | –434 to 135 | 173 | –723 to 1070 |
| 65–74 | –72 | –172 to 29 | 2 | –15 to 18 | –36 | –78 to 6 | –72 | –173 to 30 | –74 | –392 to 244 | 193 | –580 to 965 |
| 75 and above | –121 | –235 to –6 | 15 | –7 to 37 | –33 | –88 to 22 | –121 | –246 to 5 | –12 | –381 to 357 | 138 | –1164 to 1440 |
| **Gender (male)** | 8 | –62 to 78 | 7 | –6 to 21 | 8 | –24 to 40 | 8 | –65 to 81 | 113 | –96 to 322 | 520 | –153 to 1193 |
| **Marital status (married)** | –82 | –154 to –9 | –4 | –21 to 13 | –33 | –68 to 1 | –82 | –161 to –3 | –247 | –514 to 20 | –135 | –1463 to 1193 |
| **Education status (illiterate)** | | | | | | | | | | | | |
| Primary school | –13 | –98 to 73 | 11 | –4 to 26 | –1 | –38 to 36 | –13 | –98 to 72 | 124 | –127 to 376 | 330 | –409 to 1069 |
| Secondary school | –20 | –118 to 78 | 5 | –11 to 21 | –27 | –68 to 15 | –20 | –115 to 75 | –6 | –326 to 315 | 473 | –658 to 1604 |
| College and above | –19 | –138 to 101 | 10 | –17 to 37 | –4 | –64 to 56 | –19 | –143 to 106 | 325 | –334 to 984 | 670 | –453 to 1793 |
| **Residence place (urban)** | –6 | –71 to 60 | –13 | –25 to 0 | –21 | –55 to 13 | –6 | –71 to 60 | 70 | –151 to 290 | 126 | –620 to 873 |
| **Region (east)** | | | | | | | | | | | | |
| Central | –15 | –101 to 70 | –2 | –18 to 15 | 8 | –28 to 44 | –15 | –103 to 72 | –84 | –327 to 158 | –433 | –1186 to 321 |
| West | –136 | –214 to –59 | –5 | –19 to 9 | –39 | –79 to 2 | –136 | –216 to –57 | –300 | –549 to –50 | –647 | –1412 to 118 |
| **Social health insurance (no)** | –122 | –274 to 31 | –8 | –38 to 23 | –65 | –135 to 4 | –122 | –288 to 45 | –697 | –1363 to –31 | –2349 | –3985 to –713 |
| **PCE, quartile (Q1, the lowest)** | | | | | | | | | | | | |
| Q2 | –21 | –90 to 48 | 9 | –5 to 23 | 4 | –29 to 37 | –21 | –91 to 49 | 115 | –112 to 342 | 293 | –453 to 1039 |
| Q3 | 166 | 85 to 248 | 11 | –6 to 28 | 57 | 11 to 102 | 166 | 84 to 248 | 431 | 188 to 674 | 672 | –244 to 1588 |
| Q4 (the highest) | 294 | 192 to 396 | 43 | 23 to 64 | 112 | 65 to 159 | 294 | 195 to 394 | 1201 | 812 to 1590 | 3464 | 2106 to 4823 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Q2** | **–21** | **–90 to 48** | **9** | **–5 to 23** | **4** | **–29 to 37** | **–21** | **–91 to 49** | **115** | **–112 to 342** | **293** | **–453 to 1039** |
| Q3 | 166 | 85 to 248 | 11 | –6 to 28 | 57 | 11 to 102 | 166 | 84 to 248 | 431 | 188 to 674 | 672 | –244 to 1588 |
| Q4 (the highest) | 294 | 192 to 396 | 43 | 23 to 64 | 112 | 65 to 159 | 294 | 195 to 394 | 1201 | 812 to 1590 | 3464 | 2106 to 4823 |

Coefficients estimated after adjusting for study variables, including age, gender, marital status, level of education, residence place, region, household economic level and health insurance status.
NCD, non-communicable disease; OOPE, out-of-pocket expenditure; PCE, per capita household consumption expenditure.

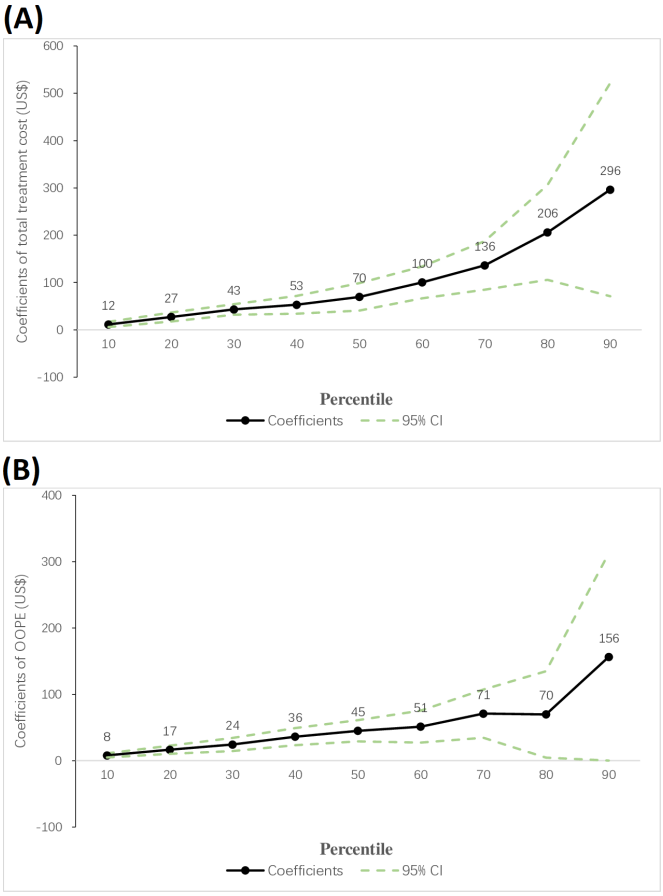


**Figure 1** Distribution of total treatment cost (above) and annual OOPE (below) associated with the number of chronic conditions by medical cost quantiles. OOPE, out-of-pocket expenditure.

social health insurance schemes for people with multimorbidity have not been well established.

## Policy implications

This study presents novel evidence on the increasing financial burden due to multimorbidity among the Chinese population. As multimorbidity is costly to individuals and the health systems, there is a need for concerted efforts and other LMICs with ageing populations to reduce the treatment burden among patients with multimorbidity and its impact on financial risk protection.[6] Prevention strategies for NCDs should adopt approaches that take into account multimorbidity in healthcare management, rather than single-disease approaches, particularly in funds allocation and in designing policies on financial protection.[7] Furthermore, preventing multimorbidity and developing more sustainable models of care is a key priority. Instead of focusing on the prevention and treatment of a single disease, NCD care delivery models should account for patients with multiple comorbid health conditions.[47] Health service delivery models should also adapt to more personalised and structured care, with an emphasis on care cocoordination across multidisciplinary teams alongside with better patient education and self-management. There has been some evidence showing healthcare delivery supported by digital technology and information system can improve effectiveness in managing patient with chronic conditions.[48 49] These insights can be used to guide China' policymaking in NCD prevention and management.

In the context of social health insurance reforms, emphasis should be placed on strengthening the financial risk protection function by reducing OOPE among patients with multimorbidity.[6] Furthermore, policy measures could introduce a special exemption from certain costs for vulnerable populations (eg, the elderly and poor population groups) including lower copayments and vital drugs subsidisation.[9] Prescription drug cost sharing benefit plans and the National Basic Public Health programme should be geared towards providing broader coverage for multimorbidity, particularly for disease combinations that potentially yield higher OOPE and cause catastrophic health expenditure. In terms of clinical implications, to ensure treatment adherence and to avoid patients foregoing treatment due to high OOPE, medical practitioners should consider the risks of financial burden among patients with multimorbidity particularly relating to polypharmacy.[7]

## Strengths and limitations

To our knowledge, this is the first Chinese study that investigated the effect of multimorbidity on treatment cost and OOPE, using nationally representative survey data. Furthermore, the application of quantile regression models allowed us to assess the variations in the impact of multimorbidity across the distribution of healthcare costs and OOPE. This approach provides clearer and more detailed information on the economic consequences of multimorbidity compared with previous studies that used basic regression models such as OLS, which only assess the mean costs under the assumptions that costs are normally distributed and that the impact of multimorbidity on utilisation and OOPE would be similar across the outcome distributions when it is often not. Furthermore, our findings also show that by using quantile regression, we were able to explore further the differences in healthcare cost and OOPE by considering the variations in the level of the multimorbidity. Finally, while quantile regression is still infrequently used in public health studies, this econometric analysis offers broader applicability in studies of healthcare utilisation and associated costs.

Our study has several limitations. First, undiagnosed and untreated chronic diseases might lead to an underestimation of medical costs due to self-reported measures for some of the chronic conditions. Second, there is a limited number of the types of chronic diseases included in the CHARLS questionnaire. Third, we did not account for the different types of combinations of diseases the construction of multimorbidity variable and due to data limitation of diseases' severity. Fourth, because outpatient care expenditures were collected for last month in CHARLS, this study estimated the total annual health

expenditure and annual OOPE by adding up the inpatient care expenditure during last year and the outpatient care expenditure multiplying 12 months. This could underestimate the total spending on outpatient services among patients with chronic diseases because some patients may have no outpatient visit within 4 weeks before the survey.

## CONCLUSION

The effect of multimorbidity on total medical cost and OOPE increases gradually when approaching the higher percentiles of the health expenditure distribution. Policymakers must recognise the need for better equity and reducing economic burdens. To deliver more cost-effective and better care for multimorbidity patients, preventing multimorbidity and developing people-centred integrated care models is a key priority. Social health insurance reforms should emphasise reducing OOPE among patients with multimorbidity by providing more effective methods of financing and service delivery.

**Author affiliations**
[1]The George Institute for Global Health at Peking University Health Science Centre, Beijing, China
[2]Collaborating Centre on Implementation Research for Prevention & Control of NCDs, WHO, Melbourne, Victoria, Australia
[3]Department of Global Health and Population, Harvard T.H. Chan School of Public Health, Harvard University, Boston, MA, USA
[4]Department of Global Health and Social Medicine, Harvard Medical School, Harvard University, Boston, MA, USA
[5]The Nossal Institute for Global Health, The University of Melbourne, Melbourne, Victoria, Australia
[6]Department of Public Health, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia
[7]Melbourne School of Population and Global Health, The University of Melbourne, Melbourne, Victoria, Australia
[8]The George Institute for Global Health, University of New South Wales, Sydney, New South Wales, Australia
[9]Public Health Policy Evaluation Unit, Department of Primary Care and Public Health, School of Public Health, Imperial College London, London, UK

**Twitter** Rifat Atun @RifatAtun

**Acknowledgements** We would like to thank the China Health and Retirement Longitudinal Study (CHARLS) team for providing data. We are grateful for the cooperation of the students who participated in the survey.

**Contributors** YZ and JL conceived and designed the study. YZ, RA and JL did the initial analysis and supervised data analysis. YZ wrote the first draft of the paper, and RA, KA, BM, TM, TP, AvH, PZ, ND and JL critically revised the first draft. All authors reviewed and approved the final version of the paper submitted for publication.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** Not required.

**Ethics approval** The Biomedical Ethics Review Committee of Peking University approved the CHARLS study (approval number: IRB00001052–11015), and all interviewees were required to provide informed consent.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** No additional data are available.



**ORCID iDs**
Yang Zhao http://orcid.org/0000-0002-6011-5948
Rifat Atun http://orcid.org/0000-0002-1531-5983
Kanya Anindya http://orcid.org/0000-0001-6832-0412

## REFERENCES

1 GBD, GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the global burden of disease study 2017. *Lancet* 2018;392:1736–88.
2 Zhao Y, Atun R, Oldenburg B, *et al*. Physical multimorbidity, health service use, and catastrophic health expenditure by socioeconomic groups in China: an analysis of population-based panel data. *Lancet Glob Health* 2020;8:e840–9.
3 Arokiasamy P, Uttamacharya U, Jain K, *et al*. The impact of multimorbidity on adult physical and mental health in low- and middle-income countries: what does the study on global ageing and adult health (SAGE) reveal? *BMC Med* 2015;13:178.
4 Stubbs B, Koyanagi A, Veronese N, *et al*. Physical multimorbidity and psychosis: comprehensive cross sectional analysis including 242,952 people across 48 low- and middle-income countries. *BMC Med* 2016;14:189.
5 McLean G, Gunn J, Wyke S, *et al*. The influence of socioeconomic deprivation on multimorbidity at different ages: a cross-sectional study. *Br J Gen Pract* 2014;64:e440–7.
6 Zhao Y, Zhang P, Oldenburg B, *et al*. The impact of mental and physical multimorbidity on healthcare utilization and health spending in China: a nationwide longitudinal population-based study. *Int J Geriatr Psychiatry* 2020;5. doi:10.1002/gps.5445. [Epub ahead of print: 10 Oct 2020].
7 Sum G, Hone T, Atun R, *et al*. Multimorbidity and out-of-pocket expenditure on medicines: a systematic review. *BMJ Glob Health* 2018;3:e000505.
8 Wang L, Si L, Cocker F, *et al*. A systematic review of cost-of-illness studies of multimorbidity. *Appl Health Econ Health Policy* 2018;16:15–29.
9 Wang X, Sun X, Birch S, *et al*. People-centred integrated care in urban China. *Bull World Health Organ* 2018;96:843–52.
10 Sturmberg JP, Bennett JM, Martin CM, *et al*. 'Multimorbidity' as the manifestation of network disturbances. *J Eval Clin Pract* 2017;23:199–208.
11 Barnett K, Mercer SW, Norbury M, *et al*. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012;380:37–43.
12 Kumar K, Singh A, Kumar S, *et al*. Socio-Economic differentials in Impoverishment effects of out-of-pocket health expenditure in China and India: evidence from who SAGE. *PLoS One* 2015;10:e0135051.
13 Chen H, Chen Y, Cui B. The association of multimorbidity with healthcare expenditure among the elderly patients in Beijing, China. *Arch Gerontol Geriatr* 2018;79:32–8.
14 Wang HHX, Wang JJ, Wong SYS, *et al*. Epidemiology of multimorbidity in China and implications for the healthcare system: cross-sectional survey among 162,464 community household residents in southern China. *BMC Med* 2014;12:188.
15 Bähler C, Huber CA, Brüngger B, *et al*. Multimorbidity, health care utilization and costs in an elderly community-dwelling population: a claims data based observational study. *BMC Health Serv Res* 2015;15:23.
16 Koenker R, Regression Q. *Econometric Society Monographs*. Cambridge: Cambridge University Press, 2005.
17 Zhao Y, Hu Y, Smith JP, *et al*. Cohort profile: the China health and retirement longitudinal study (CHARLS). *Int J Epidemiol* 2014;43:61–8.

18 Fortin M, Stewart M, Poitras M-E, *et al*. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. *Ann Fam Med* 2012;10:142–51.
19 Lehnert T, Heider D, Leicht H, *et al*. Review: health care utilization and costs of elderly persons with multiple chronic conditions. *Med Care Res Rev* 2011;68:387–420.
20 van Oostrom SH, Picavet HSJ, de Bruin SR, *et al*. Multimorbidity of chronic diseases and health care utilization in general practice. *BMC Fam Pract* 2014;15:61.
21 Andresen EM, Malmgren JA, Carter WB, *et al*. Screening for depression in well older adults: evaluation of a short form of the CES-D. *Am J Prev Med* 1994;10:77–84.
22 Boey KW. Cross-Validation of a short form of the CES-D in Chinese elderly. *Int J Geriatr Psychiatry* 1999;14:608–17.
23 Qian J, Li N, Ren X. Obesity and depressive symptoms among Chinese people aged 45 and over. *Sci Rep* 2017;7:45637.
24 Mancia G, Fagard R, Narkiewicz K, *et al*. 2013 ESH/ESC guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European Society of hypertension (ESH) and of the European Society of cardiology (ESC). *J Hypertens* 2013;31:1281–357.
25 Chobanian AV, Bakris GL, Black HR, *et al*. The seventh report of the joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *JAMA* 2003;289:2560–72.
26 American Diabetes Association. 2. Classification and Diagnosis of Diabetes: *Standards of Medical Care in Diabetes-2019*. *Diabetes Care* 2019;42:S13–28.
27 Xu Y, Wang L, He J, *et al*. Prevalence and control of diabetes in Chinese adults. *JAMA* 2013;310:948–59.
28 Zhu J, Gao R, Zhao S, *et al*. 2016 Chinese guidelines for the management of dyslipidemia in adults. *J Geriatr Cardiol* 2018;15:1–29.
29 Zhang M, Deng Q, Wang L, *et al*. Prevalence of dyslipidemia and achievement of low-density lipoprotein cholesterol targets in Chinese adults: a nationally representative survey of 163,641 adults. *Int J Cardiol* 2018;260:196–203.
30 Li C, Young B-R, Jian W. Association of socioeconomic status with financial burden of disease among elderly patients with cardiovascular disease: evidence from the China health and retirement longitudinal survey. *BMJ Open* 2018;8:e018703.
31 Firpo S, Fortin NM, Lemieux T. Unconditional quantile regressions. *Econometrica* 2009;77:953–73.
32 Koenker R, Hallock KF. Quantile regression. *J Econ Perspect* 2001;15:143–56.
33 Gebregziabher M, Lynch CP, Mueller M, *et al*. Using quantile regression to investigate racial disparities in medication non-adherence. *BMC Med Res Methodol* 2011;11:88.
34 Korn FL, Graubard BI. Basic survey methodology. In: Korn FL, Graubard BI, eds. *Analysis of health surveys*. New York: John Wiley & Sons, 1999: 32–3.
35 Zhang R, Lu Y, Shi L, *et al*. Prevalence and patterns of multimorbidity among the elderly in China: a cross-sectional study using national survey data. *BMJ Open* 2019;9:e024268.
36 Chen H, Cheng M, Zhuang Y, *et al*. Multimorbidity among middle-aged and older persons in urban China: prevalence, characteristics and health service utilization. *Geriatr Gerontol Int* 2018;18:1447–52.
37 Blakely T, Kvizhinadze G, Atkinson J, *et al*. Health system costs for individual and comorbid noncommunicable diseases: an analysis of publicly funded health events from New Zealand. *PLoS Med* 2019;16:e1002716.
38 Lee JT, Hamid F, Pati S, *et al*. Impact of noncommunicable disease multimorbidity on healthcare utilisation and out-of-pocket expenditures in middle-income countries: cross sectional analysis. *PLoS One* 2015;10:e0127199.
39 Pati S, Agrawal S, Swain S, *et al*. Non communicable disease multimorbidity and associated health care utilization and expenditures in India: cross-sectional study. *BMC Health Serv Res* 2014;14:451.
40 Rivera-Almaraz A, Manrique-Espinoza B, Chatterji S, *et al*. Longitudinal associations of multimorbidity, disability and out-of-pocket health expenditures in households with older adults in Mexico: the study on global ageing and adult health (SAGE). *Disabil Health J* 2019;12:665–72.
41 McRae I, Yen L, Jeon Y-H, *et al*. Multimorbidity is associated with higher out-of-pocket spending: a study of older Australians with multiple chronic conditions. *Aust J Prim Health* 2013;19:144–9.
42 Schoenberg NE, Kim H, Edwards W, *et al*. Burden of common multiple-morbidity constellations on out-of-pocket medical expenditures among older adults. *Gerontologist* 2007;47:423–37.
43 Fong JH. Out-Of-Pocket health spending among Medicare beneficiaries: which chronic diseases are most costly? *PLoS One* 2019;14:e0222539.
44 Hsieh C-R, Qin X, hurts D. Depression hurts, depression costs: the medical spending attributable to depression and depressive symptoms in China. *Health Econ* 2018;27:525–44.
45 Xu J, Wang J, Wimo A, *et al*. The economic burden of mental disorders in China, 2005–2013: implications for health policy. *BMC Psychiatry* 2016;16.
46 Wallace E, Salisbury C, Guthrie B, *et al*. Managing patients with multimorbidity in primary care. *BMJ* 2015;350:h176.
47 Uhlig K, Leff B, Kent D, *et al*. A framework for crafting clinical practice guidelines that are relevant to the care and management of people with multimorbidity. *J Gen Intern Med* 2014;29:670–9.
48 Ali SH, Luo R, Li Y, *et al*. Application of mobile health technologies aimed at salt reduction: systematic review. *JMIR Mhealth Uhealth* 2019;7:e13250.
49 Peiris D, Sun L, Patel A, *et al*. Systematic medical assessment, referral and treatment for diabetes care in China using lay family health promoters: protocol for the SMARTDiabetes cluster randomised controlled trial. *Implementation Sci* 2015;11:116.