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Age-related differences in the number of chronic diseases in association with trajectories of depressive symptoms: a population-based cohort study

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Abstract

Background The number of chronic diseases has been associated with changes in depressive symptoms over time among middle-aged and older adults. This study aimed to explore the association between the number of chronic diseases and trajectories of depressive symptoms and the role of age in this association.

Methods A total of 12,974 middle-aged and older Chinese adults (≥ 45 years) participated in the China Health and Retirement Longitudinal Study (CHARLS) in waves 2011, 2013, 2015, 2018, and 2020. The number of chronic diseases was determined by self-reported hospital diagnosis of hypertension, dyslipidemia, diabetes, cancer, chronic lung diseases, liver disease, heart diseases, stroke, kidney diseases, digestive diseases, emotional, nervous, or psychiatric problems, memory-related disease, arthritis or rheumatism, asthma, and then obtaining the total number of chronic diseases. Depressive symptoms were measured by the 10-item Center for Epidemiologic Studies Depression Scale (CESD-10). Group-based trajectory modeling (GBTM) was adopted to capture the trajectories of depressive symptoms over time. Multinomial logistic regressions were conducted to examine the association between the number of chronic diseases and trajectories of depressive symptoms and the role of age in this association.

Results Four distinct trajectories of depressive symptoms were observed in 34.68% individuals in mild, 40.76% in moderate, 19.41% in increasing, and 5.15% in severe group. Compared to participants without chronic diseases, those with one, two, three or more chronic diseases had a 1.81, 3, and 7.49-fold higher risk of developing severe depressive symptom trajectory, respectively. Moreover, the association between the number of chronic diseases and severe depressive symptoms trajectory differed by age (45–59 and ≥ 60 years) (*P* for interaction < 0.05).

Conclusion Participants with middle age may play a promoting role in the association between the number of chronic disease and severe depressive symptoms. The severe depressive symptoms intervention may be more beneficial for middle-aged adults.

Keywords Number of chronic diseases, Depressive symptoms, Age, Group-based trajectory modeling, CHARLS

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Background

Depression is the leading cause of the global burden of diseases [1]. The prevalence of depressive symptoms in middle-aged and older adults is 26.0%, and the prevalence rises with age [2]. Studies have revealed that depression may significantly predict cognitive decline and the development of chronic physical conditions [3], which may be exaggerated by the increasing age as well [4]. However, it is still unknown whether there is an interaction between chronic disease and age on depression.

A recent meta-analysis has shown a strong positive association between multimorbidity and depressive disorder, but a weak positive association between the number of chronic conditions and depressive symptoms, this indicated that the association between the number of chronic diseases and depressive symptoms is likely to be influenced by other factors, such as age [5]. However, all the studies included in this meta-analysis were cross-sectional in nature and the direction of causality for these relationships cannot be determined. More importantly, the majority of the available studies have focused on one specific disease [6–9] or multimorbidity [5, 10, 11] individually, rather than considering one specific disease and multimorbidity simultaneously that affecting middle-aged and older adults. On the other hand, the traditional methods were used to study changes in population based average levels of depressive symptoms, rather than using the trajectory of depressive symptoms which may better capture the change in depressive symptoms over time [12] and provide scientific evidence to optimize personalized depressive symptom interventions focused on the needs of specific subpopulations [13]. Therefore, the studies on the association between the number of chronic diseases and trajectories of depressive symptoms were limited.

Older age always means that human beings have reached the age of 60 and above in China, a stage of rapid deterioration of physical functions [14]. Meanwhile, older age is a consistent and important risk factor for chronic diseases [11]. However, the causal effect of physical disease effects on depressive symptoms is weakened in older adults [15]. A cross-sectional study from South Korea found that middle-aged adults with chronic diseases had a higher risk of experiencing depressive symptoms than their older peers [16], which was confirmed by the findings from another nationwide longitudinal study in US [17] using a relatively narrow range of chronic disease (including cancer, stroke, heart disease, chronic obstructive pulmonary disease, diabetes, hypertension, and arthritis). A review has further discussed the potential mechanisms behind this phenomenon was that older adults tended to overlap the somatic symptoms of depression and illness. This leads to complicating the diagnosis of depression in late life [18]. Therefore, it is highly plausible that having a higher number of chronic diseases in middle age has a greater impact on depressive symptoms than having a higher number of chronic diseases in older age. However, to our best knowledge, the interaction effect between the number of chronic diseases and age on trajectories of depressive symptoms remains unknown.

This study aimed to identify trajectories of depressive symptoms over nine years among middle-aged and older Chinese adults, to examine whether the number of chronic diseases is associated with trajectories of depressive symptoms, and to assess whether the number of chronic diseases and age have an interaction effect on trajectories of depressive symptoms.

Methods

Study design and participants

Participants of the current study were derived from a national population-based observational survey, the China Health and Retirement Longitudinal Study (CHARLS). In brief, 17,705 participants aged 45 years and older were recruited by multistage stratified probability proportional sampling from 150 counties of 28 provinces in China at baseline (2011) and the information on participants' sociodemographics, living habits, self-reported health status, and other aspects were collected. Subsequent follow-ups were conducted every 2–3 years (2013, 2015, 2018, and 2020). The detailed study design and sampling method have been documented elsewhere [19].

As shown in Fig. 1, participants were excluded due to age<45 (n=368), missing information on the number of chronic diseases (n=862), and depressive symptoms (n=2079) at baseline; and participants with missing information on depressive symptoms from wave 2 to wave 5 (n=1422). Consequently, 12,974 participants remained in the analytical sample.

The number of chronic diseases

At baseline (2011), the number of chronic diseases was measured through a standardized questionnaire by asking whether the participants had ever been diagnosed by a doctor with hypertension, dyslipidemia, diabetes, cancer, chronic lung diseases, liver disease, heart diseases, stroke, kidney diseases, digestive diseases, emotional, nervous, or psychiatric problems, memory-related disease, arthritis or rheumatism, asthma, and then obtaining the total number of chronic diseases(ranging from 0 to 14). It was further divided into four groups: 0 (no chronic disease), 1 (one chronic disease), 2 (two chronic diseases), and ≥3 (greater than or equal to three chronic diseases). A history of these diseases was considered a disease event at baseline (2011) if it had occurred no later

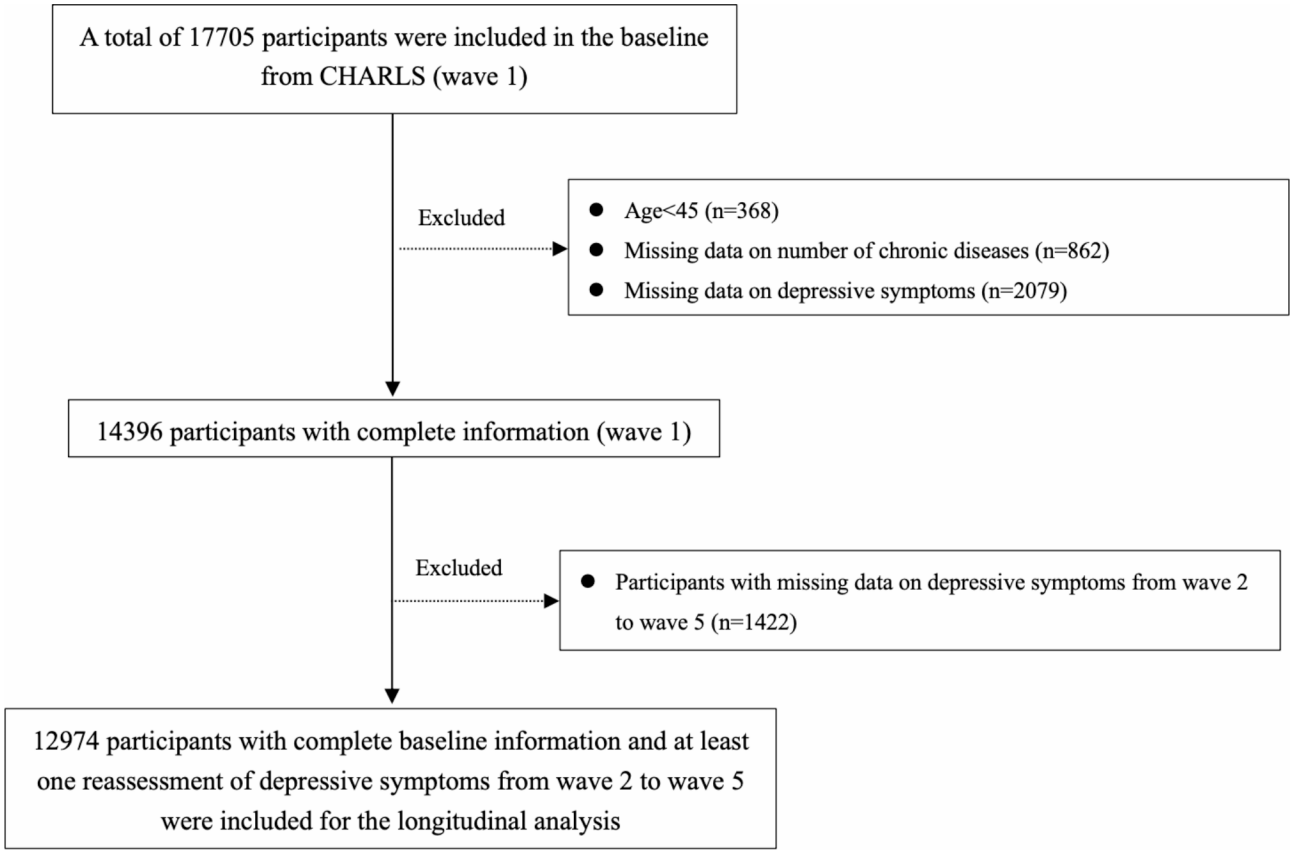

Fig. 1 Flowchart of the study population

than the baseline interview (2011), including any patients who had had it in the past but had recovered from it [19].

Depressive symptoms

Depressive symptoms were measured at baseline (2011) and in subsequent follow-ups (2013, 2015, 2018, and 2020) by the 10-item Center for Epidemiologic Studies Depression Scale (CESD-10), ranging from 0 to 30. The total score is positively associated with the severity of depressive symptoms [20]. Then they were dichotomized as <12 and ≥12 to identify participants with significant depressive symptoms [20].

Covariates

The information on sociodemographic variables (age, sex, education level, marital status, and living residence), health-related behaviors (smoking and drinking status), and health status (body mass index and functional disability) were obtained by the questionnaire or standard protocols. Height and weight were measured by a portable height gauge and digital body weight scale respectively [19]. Age was dichotomized as 45–59 and ≥60 years. Education level was classified as no formal education, primary school, middle or high school, and college or above. Marital status was classified as married/cohabitated and others (including unmarried, divorced, widowed, etc.). Living residence was dichotomized as rural and urban. Smoking status was categorized into current smokers and non-current smokers (including never smokers and ex-smokers). Drinking status was dichotomized as regular drinkers (≥3 times/week) and non-regular drinkers. Body mass index was calculated by dividing weight (kg) by height squared (m^2) [21]. Functional disability was assessed using both the Katz scale for Activities of Daily Living (ADLs) and the Lawton scale for Instrumental Activities of Daily Living (IADLs). The Katz scale includes six ADL items: eating, bathing, dressing, transferring (getting in and out of bed), using the toilet, and controlling urination [22]. The Lawton scale includes five IADL items: shopping for groceries, preparing hot meals, doing household chores, managing money, and taking medications [23]. Each item on these scales was categorized as follows: (1) no difficulty; (2) some difficulty but still possible; (3) some difficulty requiring help; and (4) unable to perform. In accordance with previous studies, each item was dichotomized into 0 (no difficulty) and 1 (some difficulty but still possible, some difficulty requiring help, or unable to perform) [19]. The total score ranges from 0 to 11, with ADLs contributing a score of 0 to 6 and IADLs contributing a score of 0

to 5 [24]. This total score was further divided into three groups: 0 (no limitation), 1–2 (mild limitation), and ≥3 (severe limitation) [25]. This classification is based on thresholds used in previous studies and practical considerations for distinguishing different levels of functional disability and is considered reliable [25, 26].

Statistical analysis

Group-based trajectory modeling (GBTM) is a data-driven approach to estimate the probability of different trajectories of depressive symptoms. The year of data collection was used as the time scale, and depressive symptom scores (continuous) in 2011, 2013, 2015, 2018, and 2020 were used to estimate trajectories of depressive symptoms through a censored normal distribution. We used the Stata commands *traj* and *trajplot* to perform the analysis and present the trajectories graphically. To determine the optimal number of trajectory groups, we initially considered models ranging from one to five groups. The criteria for the optimal number of accumulations and the best-fit shape include: (1) absolute BIC value is close to 0; (2) AvePP≥70%, and (3) reasonable interpretation of the model for data [27, 28]. Multinomial logistic regression models were used to examine the association between the number of chronic diseases and trajectories of depressive symptoms and quantify the interaction effect of the number of chronic diseases and age/sex on trajectories of depressive symptoms. Interaction on the multiplicative scale was assessed by conducting likelihood ratio tests. Sensitivity analysis was conducted by repeating the main analyses: excluding participants with memory-related disease from the baseline (n=178) to reduce recall bias. All data analyses in this study were performed with Stata SE16. Two-tailed $P<0.05$ is statistical significance.

Results

According to the above-mentioned criteria in the method section, a trajectory model with 4 trajectory groups and shapes (2 2 2 2) were used in subsequent analyses (Table S1). Therefore, four distinct trajectories of depressive symptoms were identified and characterized by mild (n=4500, 34.68%), moderate (n=5288, 40.76%), increasing (n=2518, 19.41%), and severe (n=668, 5.15%) (Fig. 2).

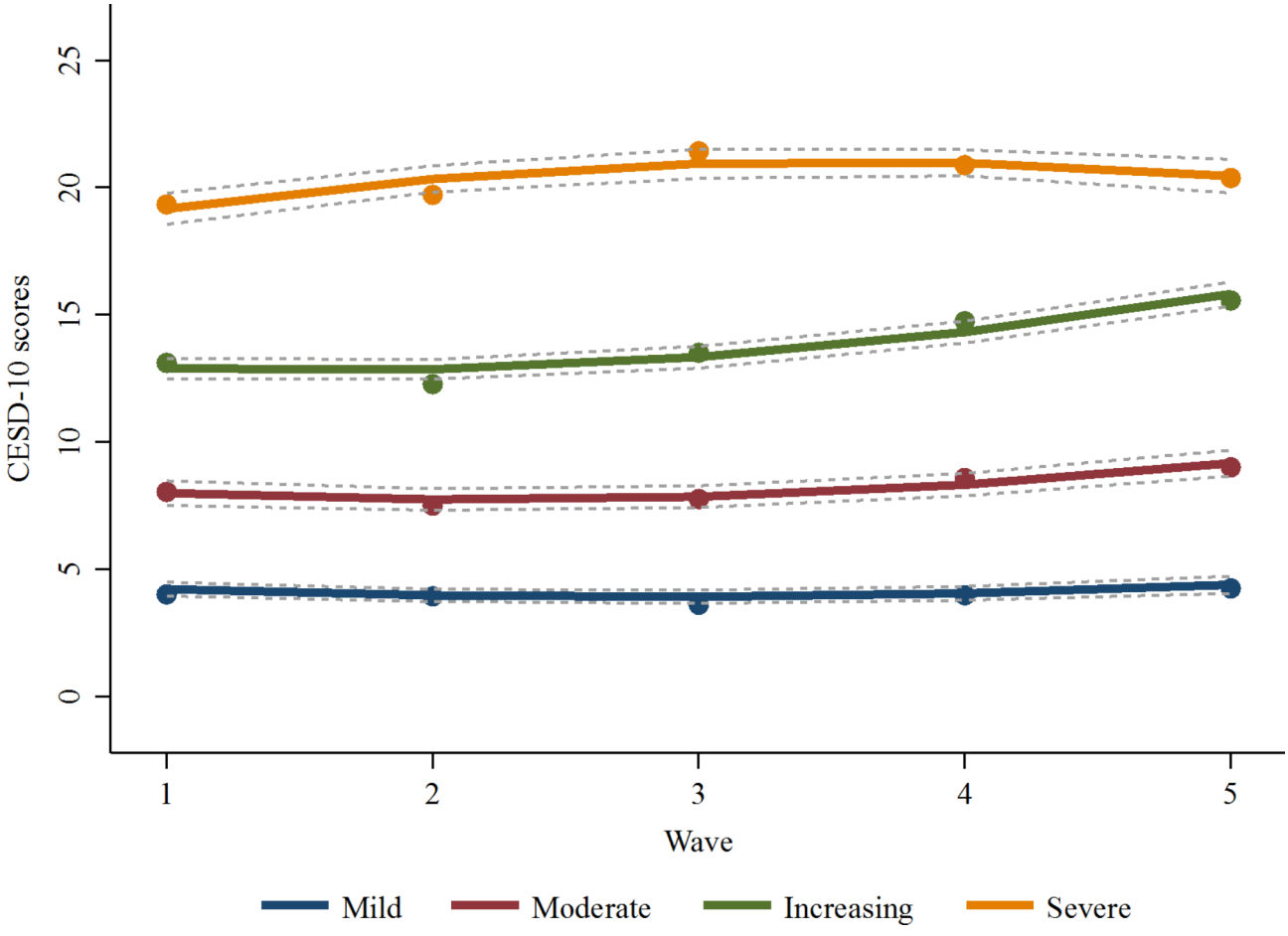

Fig. 2 Trajectories of depressive symptoms from 2011 to 2020

As summarized in Table 1, age, sex, education level, marital status, living residence, smoking status, drinking status, body mass index, and functional disability differed across trajectory groups. Interestingly, as the depressive symptoms trajectory group becomes more severe, a higher tendency towards older age was observed (Table 1).

Compared to participants without chronic diseases, participants with one, two, three or more chronic diseases had a higher risk of experiencing moderate, increasing, and severe depressive symptom trajectories, especially for severe depressive symptoms trajectory: one chronic disease (RR=1.81, 95% CI=1.35–2.43), two chronic diseases (RR=3, 95% CI=2.19–4.09), and three or more chronic diseases (RR=7.49, 95% CI=5.54–10.11) (Fig. 3). A stratified analysis by age and sex showed that having one, two, and three or more chronic diseases in the middle-age group was more related to severe depressive symptom trajectory than in the older-age group (2 vs. 1.60, 4.68 vs. 1.79, 9.30 vs. 5.78). In addition, the association between the number of chronic diseases and severe depressive symptoms trajectory differed by age (45–59 and ≥60 years) (P for interaction<0.05), but did not by sex (male and female) (P for interaction>0.05) (Fig. 4). Similar findings were found in sensitivity analyses (Figure S1, Figure S2).

Table 1 Baseline characteristics of the total sample and the sample by four trajectories of depressive symptoms (n=12,974)

Characteristics	Total sample (N=12,974)	Trajectory Group				*P*-value [b]
		Mild (n=4500)	Moderate (n=5288)	Increasing (n=2518)	Severe (n=668)	
NCDs						<0.001
0	4303 (33.17)	1955 (43.44)	1717 (32.47)	531 (21.09)	100 (14.97)	
1	3891 (29.99)	1388 (30.84)	1607 (30.39)	737 (29.27)	159 (23.80)	
2	2483 (19.14)	695 (15.44)	1058 (20.01)	586 (23.27)	144 (21.56)	
≥3	2297 (17.70)	462 (10.27)	906 (17.13)	664 (26.37)	265 (39.67)	
Age, years						<0.001
45–59	7508 (57.89)	2793 (62.07)	3001 (56.78)	1376 (54.67)	338 (50.60)	
≥60	5462 (42.11)	1707 (37.93)	2284 (43.22)	1141 (45.33)	330 (49.40)	
Sex						<0.001
Male	6238 (48.12)	2664 (59.23)	2494 (47.21)	908 (36.10)	172 (25.75)	
Femal	6726 (51.88)	1834 (40.77)	2789 (52.79)	1607 (63.90)	496 (74.25)	
Education level [a]						<0.001
No formal education	5573 (42.97)	1391 (30.92)	2297 (43.45)	1445 (57.41)	440 (65.87)	
Primary school	2908 (22.42)	964 (21.43)	1271 (24.04)	546 (21.69)	127 (19.01)	
Middle or high school	3855 (29.72)	1753 (38.97)	1523 (28.81)	483 (19.19)	96 (14.37)	
College or above	634 (4.89)	390 (8.67)	196 (3.71)	43 (1.71)	5 (0.75)	
Marital status						<0.001
Married/cohabitated	11,547 (89.00)	4162 (92.49)	4699 (88.86)	2154 (85.54)	532 (79.64)	
Others	1427 (11.00)	338 (7.51)	589 (11.14)	364 (14.46)	136 (20.36)	
Living residence						<0.001
Rural	9776 (76.58)	2996 (67.51)	4067 (78.21)	2134 (86.36)	579 (88.26)	
Urban	2989 (23.42)	1442 (32.49)	1133 (21.79)	337 (13.64)	77 (11.74)	
Smoking status						<0.001
Non-current smokers	8959 (69.06)	2932 (65.17)	3640 (68.85)	1853 (73.59)	534 (79.94)	
Current smokers	4013 (30.94)	1567 (34.83)	1647 (31.15)	665 (26.41)	134 (20.06)	
Drinking status						<0.001
Non-regular drinkers	10,729 (87.19)	3543 (83.60)	4371 (87.45)	2210 (91.32)	605 (93.08)	
Regular drinkers	1577 (12.81)	695 (16.40)	627 (12.55)	210 (8.68)	45 (6.92)	
Body mass index, Mean (SD)	23.35 (3.52)	23.60 (3.35)	23.32 (3.54)	23.08 (3.68)	22.94 (3.60)	<0.001
Functional disability [a]						<0.001
None	9710 (75.63)	3930 (88.41)	4006 (76.57)	1496 (59.89)	278 (41.93)	
Mild	2052 (15.98)	421 (9.47)	862 (16.48)	594 (23.78)	175 (26.40)	
Severe	1076 (8.38)	94 (2.11)	364 (6.96)	408 (16.33)	210 (31.67)	

Abbreviation: NCDs, number of chronic disease; SD, standard deviation

[a] Missing data: 4 for age, 10 for sex, 4 for education level, 209 for living residence, 2 for smoking, 668 for drinking, 1899 for body mass index, 136 for functional disability

[b] Categorical variables were based on χ^2 exact test and continuous variables were analyzed by Kruskal-Wallis H test becase of it did not pass Bartlett's test

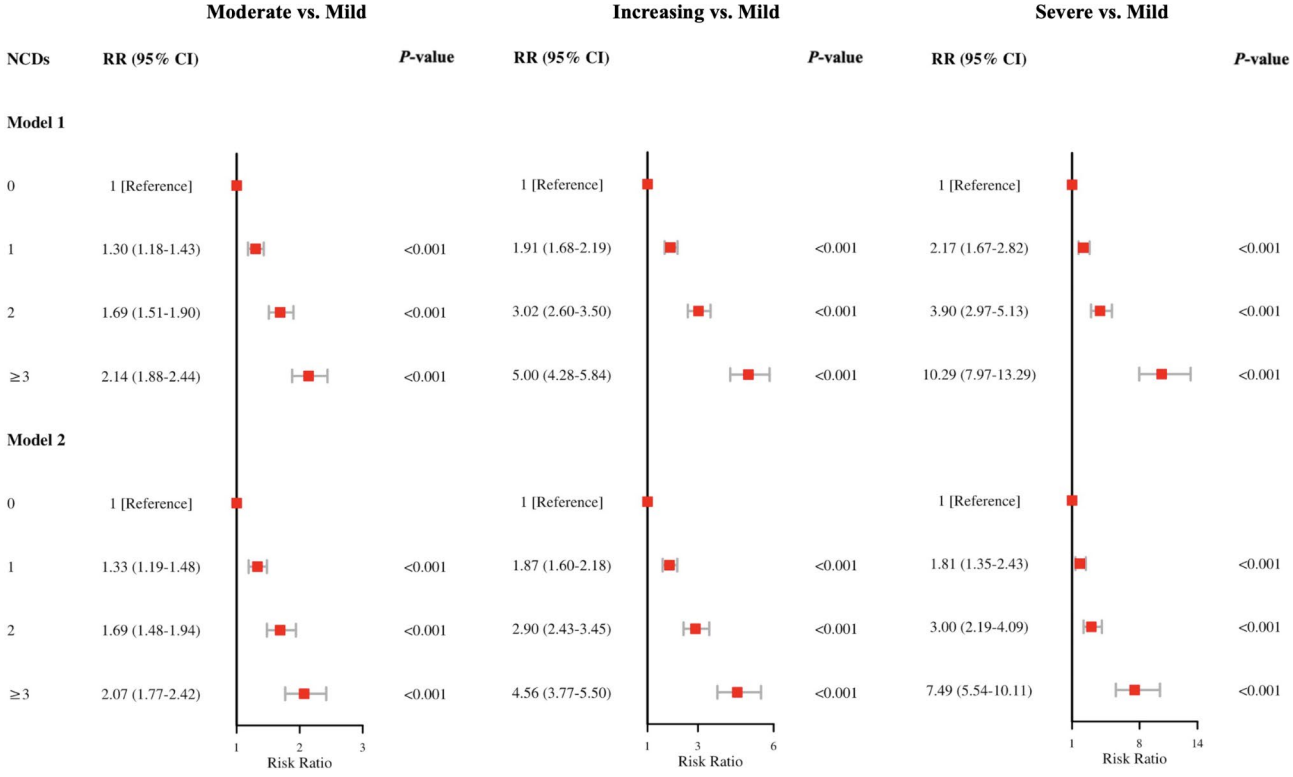

Fig. 3 The trajectories of depressive symptoms over 9 years were associated with the number of chronic diseases. Model 1: age, sex-adjusted. Model 2: multivariable-adjusted, including age, sex, education level, marital status, living residence, smoking status, drinking status, body mass index, and function disability

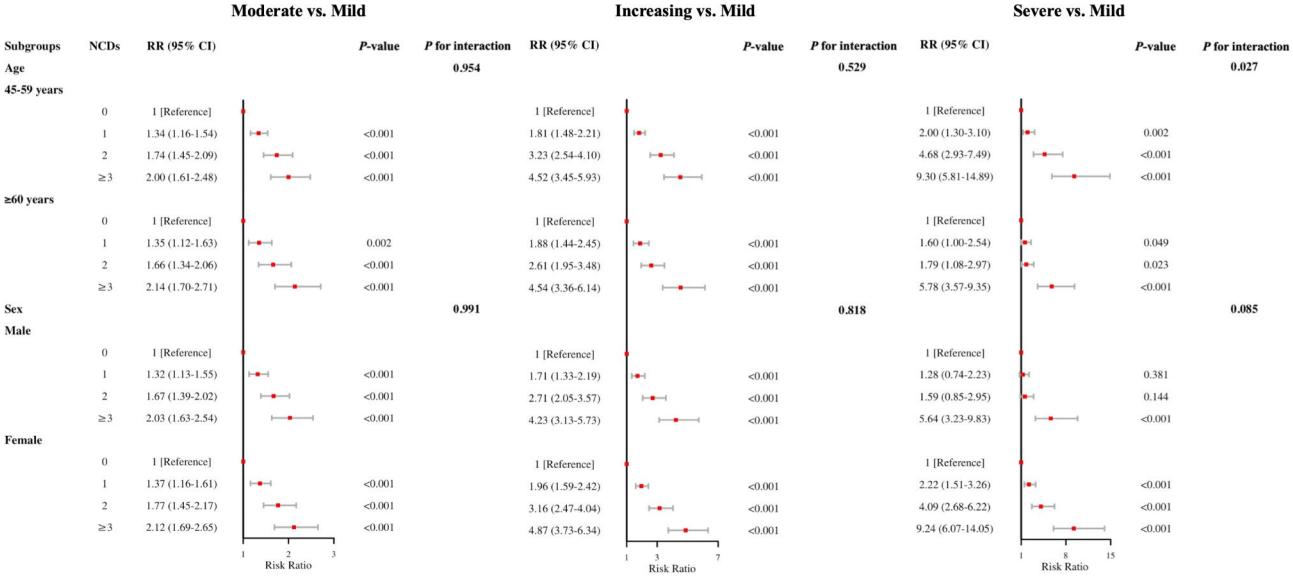

Fig. 4 Stratified analysis by age and sex for the association between the number of chronic diseases and trajectories of depressive symptoms. Adjusted for age, sex, education level, marital status, living residence, smoking status, drinking status, body mass index, and function disability

Discussion

In this population-based cohort study, four trajectories of depressive symptoms were identified, i.e., mild, moderate, increasing, and severe. In comparison to participants without chronic diseases, those with one, two, three or more chronic diseases were all related to accelerated moderate, increasing, and severe depressive symptom trajectories. In addition, the effect of the coexistence of an increasing number of chronic diseases and middle age (45–59 years) was higher than the combination of

the corresponding number of chronic diseases and older age (≥60 years) on the severe depressive symptom trajectory. This suggested that participants with middle age may play a promoting role in the effect of the number of chronic diseases on severe depressive symptoms.

Our findings of four trajectories of depressive symptoms were supported by a Health and Retirement Study cohort study in which similar trajectories of depressive symptoms were identified: no, low, low-moderate, moderate, and elevated and increasing depressive symptoms [29]. A CHARLS cohort study with a slightly different battery of trajectories, i.e., low, moderate, increasing, and high depressive symptoms [26]. This may be attributed to the exclusion of participants with significant depressive symptoms (CESD-10 score≥12) at baseline. This speculation has been confirmed by the additional analysis (Figure S3) that similar trends were observed when we followed the criteria of the previous study [26].

The present study showed that participants with chronic diseases at the baseline were more likely to have moderate, increasing, and severe depressive symptom trajectories during a 9-year follow-up period. This was supported by several longitudinal epidemiological investigations focusing on the association between the number of chronic diseases and depressive symptoms using similar age groups [30–32]. Our study extends their finding by capturing the changes in depressive symptoms over time. Regarding the association between chronic diseases, age, and depressive symptoms, as far as we know, only one US study has been done by using a relatively narrow range of chronic diseases, i.e., cancer, stroke, heart disease, chronic obstructed pulmonary disease, diabetes, hypertension, and arthritis, and found that those with chronic diseases early in life tended to report more depressive symptoms than those who develop chronic diseases later in life [17]. The range of chronic diseases (14 chronic diseases) used in this study was broader and already covered the major chronic diseases that significantly affect the health status of middle-aged and older adults [33, 34].

Several potential mechanistic pathways link the increasing number of chronic diseases and middle age to a higher risk of developing severe depressive symptoms trajectory. First, middle-aged adults have historically been primary breadwinners for their families and the dominant long-term caregivers for older parents and children in China. Once diagnosed with chronic diseases, they were more likely to experience negative emotions and affections since they were afraid of being unable to take care of family and being outliers among their peers and had a higher likelihood of ever stopping work and limiting paid work [35]. Second, well-educated participants have higher health-related knowledge levels and more healthcare access and thus express their feelings correctly [36]. It has been shown that highly-educated participants were more likely to have depressive symptoms since they have higher expectations of matching between education and work, and when mismatched, they tend to experience more psychological tension, disappointment, and frustration, thus increasing the likelihood of depression [37]. Our findings of the proportion of middle-aged adults with higher education levels (middle school or above) were higher than those of older adults (44.76% vs. 20.67%) may support this inference. Third, despite the remarkable progress in the construction of the elderly care service system and essential public health services in China in the last decade, the health and social service system specifically for middle-aged adults is not well developed [38].

Currently, the essential public health services in China are mainly focused on monitoring chronic diseases such as hypertension, diabetes, and severe mental disorders, whereas routine monitoring of mental health is not available. Our findings may help in the understanding of potential mechanisms linking the number of chronic diseases, age, and depressive symptoms in middle-aged and older adults, provide scientific evidence to optimize personalized depressive symptom interventions focused on specific subpopulations who can get higher benefit from interventions, highlight the importance of monitoring mental health from middle life in a national level is warranted.

Strengths and limitations

The strength of this study included using a nationally representative sample and prospective design in terms of the repeated measurements of outcome (i.e., depressive symptom scores) at baseline as well as at each wave of the follow-up since previous research has suggested that older adults appear to experience distinct patterns of depressive symptoms over time [26]. Meanwhile, the repeated measurements of depressive symptoms data were used in GBTM analysis, which is a reliable approach to capturing different patterns of depressive symptoms over time [27]. Several limitations should be considered. First, reporting bias might have occurred because the information on the number of chronic diseases and depressive symptoms was self-reported. This may lead to some degree of exposure and outcome misclassification. However, after excluding participants with memory-related disease from the baseline, the estimation remained similar, showing reporting bias may not be a major concern. Second, residual confounding or unmeasured confounding bias cannot be ruled out due to a lack of information on some potential confounders, such as the history of antidepressants. Third, the measurement of chronic diseases was only determined by the number in this study, leaving the severity of chronic diseases uninvestigated, such as disease stages.

Conclusion

The results of longitudinal association between the increasing number of chronic diseases and a higher risk of developing severe depressive symptom trajectories, especially in middle-aged adults suggest that middle age may play a promoting role in this association. Future interventions for depressive symptoms should pay more attention to the middle-aged (aged 45–59) adults.

Abbreviations

CHARLS	The China Health and Retirement Longitudinal Study
CESD-10	The Center for Epidemiological Studies Depression-10
GBTM	Group-Based Trajectory Modeling
RR	Risk ratio
CI	Confidence interval
ADLs	Activities of daily living
IADLs	Instrumental activities of daily living
AvePP	Average posterior probability
BIC	Bayesian information criterion
NCD_S	Number of chronic diseases

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-024-19975-9.

Additional file 1: **Table S1**. Goodness-of-fit statistics of group-based trajectory analysis. **Figure S1**. The trajectories of depressive symptoms over 9 years were associated with the number of chronic diseases after excluding participants with memory-related diseases ($n = 12836$). **Figure S2.** Stratified analysis by age and sex for the association between the number of chronic diseases and trajectories of depressive symptoms after excluding participants with memory-related diseases ($n = 12836$). **Figure S3.** Trajectories of depressive symptoms from 2011 to 2020 excluded participants with significant depressive symptoms at baseline.

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Author contributions

JH and RT proposed the idea for the study. JH performed the analysis and wrote the original draft of the article. JH, RT, TX, YD, and YL reviewed and edited the article. RT acquired funding. JH and RT are responsible for ensuring the integrity and accuracy of the study. All authors have read and approved the final manuscript.

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Data availability

The data supporting this study's findings are available from the CHARLS website: https://charls.pku.edu.cn/.

Declarations

Ethics approval and consent to participate

CHARLS has been approved by the Biomedical Ethics Review Committee of Peking University (IRB001052-11015), and informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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