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TITLE PAGE

Early-Life Adversity Predicts Distinct Trajectories of Multimorbidity with Ageing from 50 to 85 years: A Nationwide Longitudinal Study

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ABSTRACT

Background: This study aimed to identify long-term distinct trajectories of multimorbidity with ageing from 50 to 85 years among Chinese older adults and examine the relationship between exposure to early life adversity (including specific types of adversity and accumulation of different adversities) with these long-term multimorbidity trajectories.

Methods: We used data from 9,112 respondents (aged 60 and above) of the 2018 wave of the China Health and Retirement Longitudinal Survey (CHARLS). Each respondent's history of chronic conditions and experiences of early-life adversity (ELA) were collected from the 2011-2018 waves of CHARLS and the 2014 Life History Survey. Group-based trajectory models identified long-term multimorbidity trajectories. Multinomial logistic regression models were used to examine the relationship between ELA and the identified multimorbidity trajectories.

Results: Four heterogeneous long-term trajectories of multimorbidity development were identified: "maintaining-low" (19.1%), "low onset-rapidly increasing" (23.3%), "middle onset-moderately increasing" (41.5%), and "chronically-high" (16.2%). Our findings indicated that the heterogeneity can be explained by ELA experiences. Across various types of different ELA experiences, exposure to food insufficiency and parental quarrel/divorce had the most prominent health-deteriorating impact. The

accumulation of more different ELA experiences was associated with a higher relative risk of developing more severe multimorbidity trajectories.

Conclusions: There are heterogeneous long-term trajectories of multimorbidity in Chinese older adults, and the risk of multimorbidity associated with ELA accumulates over the lifespan. Our findings highlight the role of a supportive early-life family environment in promoting health development across the lifespan, advocating for the integration of life-course approaches to implementing health disparity interventions.

Keywords: chronic disease development; childhood adversity; Chinese older adults; longitudinal trajectory

Strengths and limitations of this study

Strengths

- Taking advantage of time-varying data on the history of chronic conditions, we captured the entire course of individuals' development of multimorbidity from the first chronic disease onset to old age, with the longest time spanning 35 years.
- Our study is among the first to empirically establish the longitudinal association between ELA and long-term differential multimorbidity trajectories.
- Our study linked two important aspects of ELA experiences (specific types and accumulation of ELA) with multimorbidity trajectories, offering a more nuanced picture for testing the life-course models concerning the pathways through which ELA influences health development.

Limitations

- First, our measures of ELA and multimorbidity were retrospective and based on self-reports, which may introduce recall bias into the data.
- Second, we did not consider the frequency and intensity of ELA, which was limited by data unavailability. Additionally, there may be other protective factors (e.g., resilience) related to multimorbidity could not be included in our study.

Key Points

- Using population-based longitudinal data, we identified four distinct long-term trajectories of multimorbidity among Chinese older adults.
- Early life adversity was a strong predictor of long-term trajectories of multimorbidity.
- The most prominent health-deteriorating impact of ELA has been found among individuals who reported exposure to food insufficiency and parental quarrel/divorce.
- Individuals who accumulated more types of ELA experiences reported a higher relative risk of developing more severe multimorbidity trajectories.

INTRODUCTION

Chronic diseases are one of the leading causes of death, placing a huge burden on healthcare systems worldwide [1]. Multimorbidity, defined as the coexistence of two or more chronic conditions, has been observed at an extremely high prevalence in old age[2]. It is estimated that over half of Chinese older adults are living with two or more chronic conditions[3], and this number is expected to increase with continuing population aging and improvements in the survival of people with chronic diseases. Extensive studies have documented a range of adverse outcomes resulting from multimorbidity, including a higher risk of mortality, disability and increased healthcare use [4].

Despite the growing interest in studying multimorbidity and its associated factors, previous research has mostly focused on a list of arbitrarily chosen conditions at a single point or period in time and thus does not cover the complete time-varying picture of multimorbidity [5][6]. Recent research has indicated that older individuals not only show variations in the timing of disease onset but also develop multimorbidity at different rates over time [7][8]. In particular, several studies have successfully identified distinct subgroups of multimorbidity within study populations [9][10][11]. Similar groups emerged across these studies, including a group of older individuals maintaining few conditions, a group characterized by a consistently high number of conditions, and a group of individuals reporting a rapidly increasing number of conditions [12][13]. To our knowledge, however, no study has examined

heterogeneous multimorbidity trajectories by longitudinally capturing the accumulation of chronic conditions throughout the whole period starting from an individual's first-onset condition to his or her very old age. Identifying such long-term trajectories will not only enhance the understanding of the development of multimorbidity but also help prognostic studies better target people at risk of more severe multimorbidity progression and associated adverse outcomes.

Early-life adversity (ELA) has been documented as a potential risk factor for worse health outcomes, including an increased risk of multimorbidity in old age [14][15][16]. ELA is commonly defined as exposure to traumatic events such as parental death, parental divorce, or abuse during childhood [17][18]. According to the life-course perspective, early-life adversity has long-lasting influences on individuals' developmental trajectories of health through different pathways [19]. Among various life-course models, the critical period model asserts that ELA experiences can get "under the skin" by exerting a powerful influence on individuals' brain architecture and behavioral development, ultimately leading to systematic differences in health outcomes later in life [20][21]. A considerable number of studies have demonstrated that exposure to specific types of ELA (e.g., domestic violence and food deprivation) is a distal cause of higher risks of multimorbidity across various older populations [22][23][24][25][26]. The accumulation of risk model is another widely used life-course model for understanding the mechanisms underlying the association between ELA and health development. This model suggests that early-life

disadvantages increase one's exposure to later health risks, forming what is known as the "chain of risk" of health in adulthood [19][20]. Risk factors at different life stages may also accumulate over time because of the "chain of risk" where one adverse experience tends to lead to another. Empirical evidence supporting this model has revealed that individuals who experienced four or more accumulated ELA reported increased risks of multimorbidity and developing specific chronic conditions (e.g., dyslipidemia and psychiatric disease) compared with those who did not experience ELA [27]. To our knowledge, however, no existing studies have simultaneously examined the critical period model and the accumulation of risk model by linking the two aspects of ELA experiences (types and accumulation) with long-term distinct trajectories of multimorbidity.

Using population-based longitudinal data, the present study aimed to identify long-term heterogeneous trajectories of multimorbidity among Chinese older adults starting in late adulthood and followed up to 35 years and to examine the relationship between exposure to ELA (including specific types of adversity and accumulation of different adversities) and these long-term multimorbidity trajectories. Drawing from the life-course perspective and the existing literature, we expected that exposure to certain types of ELA and the accumulation of more different ELA types would be associated with a higher likelihood of more severe multimorbidity trajectories.

METHODS

Data and Sampling

Data used in the present study were derived from the four waves (2011-2018) of the China Health and Retirement Longitudinal Study (CHARLS) and the 2014 Life History Survey. The 2011 baseline survey collected data from 17,706 respondents aged 45 and above on their demographic, socioeconomic and health characteristics. The 2014 Life History Survey interviewed respondents who participated in the 2011 and 2013 surveys and collected information on their early-life experiences, including living environment, family socioeconomic status, and health history. For the purpose of the present study, we restricted our analytical sample to respondents who met the following inclusion criteria: (1) participated in the 2018 wave and the 2014 Life History survey; (2) birth-year information was available from any of the 2011-2018 waves; (3) provided valid data on the measurement of early life adversity and history of chronic conditions; and (4) aged ≥ 60 years in 2018. In addition, we excluded respondents aged over 85 in 2018 because the oldest-old group was not well represented in the CHARLS (the proportion of respondents aged over 85 in the 2018 CHARLS survey was 1.6%). The final analytical sample included 9,112 respondents (please see *Figure 1* for details about the sample selection process).

<insert Figure 1 about here>

Variables

Development of chronic conditions

We obtained information about each respondent's history of chronic conditions from the 2011-2018 CHRALS survey. In each survey, respondents were asked if they had been diagnosed by a healthcare provider with any of the following 14 chronic conditions: hypertension, dyslipidemia, diabetes, cancer or malignant tumor, chronic lung diseases, liver disease, heart disease, stroke, kidney disease, stomach or other digestive diseases, arthritis or rheumatism, asthma, emotional or psychiatric problems, and memory-related disorders. For each condition, respondents who answered in the affirmative were then asked to report the year when this condition was first diagnosed. Using the self-reported information on the starting year of each condition, we calculated the age at onset of each chronic condition for each respondent. Given that most studies on chronic conditions used age 50 as a starting point and the high prevalence of chronic conditions in people over 50, we tracked each individual's chronic conditions from the age of 50 [28][29]. Then, the time-varying variable "development of chronic conditions" was generated for each respondent, indicating his or her total number of chronic conditions being diagnosed in each year between the age of 50 and the current age when participating in the 2018 CHARLS survey. For more details about the distribution of this time-varying variable, please see *eFigure 1*. This variable was further used for the identification of distinctive long-term multimorbidity trajectories within this population.

Early Life Adversity

We extracted eight indicators of early life adversity (ELA) from the CHARLS 2014 survey, including parental illness, parental death, parental quarrel/divorce, relative poverty, food insufficiency, domestic violence, and bullying. The detailed questionnaire items and definitions of each ELA indicator are available in *eTable1*. Responses to each item were dichotomized and summed to generate a cumulative ELA score for each respondent, ranging from 0 to 7. Higher scores indicated more experience with ELA. To investigate the relationship between the accumulation of different ELA experiences and the long-term trajectories of multimorbidity, we further categorized the accumulation of ELA experiences according to ELA scores: none, 1-2, 3-4, and 5-7 types of ELA experience accumulation. The measurement has been accepted and widely used in empirical studies [30].

Covariates

This study included the following covariates: (1) demographic characteristics included gender, residence area (urban versus rural), and marital status (married versus other status (unmarried/divorced/separated/widowed)); (2) socioeconomic characteristics included educational attainment (below high school versus high school and above), whether receiving *Dibao* assistance, and types of medical insurance (none, urban employee, urban and rural resident, and others); and (3) health behaviors included smoking, drinking, and physical activity (no-, light-, moderate- and vigorous-intensity physical activity).

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Analytical Strategy

The group-based trajectory modeling (GBTM) approach was used to model progression in the number of chronic conditions over time (i.e., from late adulthood to old age) [31][32][33]. The fundamental concept of interest is the distribution of outcomes (in our study, the number of chronic conditions) conditional on age. Maximum-likelihood methods were used for the estimation of the model parameters, and a censored normal (CNORM) model was selected given the continuous nature of targeted outcomes [34][35]. Following the standard procedure for applying this approach, we conducted a sequence of GBTM models. For model selection, we used the following model-fit indices and statistical criteria in combination with conceptual considerations of group distinctiveness and interpretability: (a) the Bayesian Information Criteria (BIC) values were compared between the different models, with a smaller BIC value indicating a better-fit model; (b) the average posterior probability of group assignment that measures the probability of a group individual belonging to this specific trajectory group was set at greater than 0.7; and (c) according to the posterior probability of the group member, a minimum membership of 5% is required in each trajectory group[36]. After identifying the optimal number of trajectory groups, univariate analysis was used to test the differences in trajectory groups from

the final model among a range of individual characteristics at baseline. Multivariate logistic models were used to assess the association between ELA and trajectory group memberships.

RESULTS

Sample Characteristics by ELA Number in Older Adults

Table 1 shows the characteristics of individuals (measured in the 2018 CHARLS survey) by the accumulation of ELA experiences (none, 1 to 2 types, 3 to 4 types, and 5 to 7 types). Among individuals with three or more chronic conditions, the proportion of individuals who reported 5 to 7 types of ELA accumulation (57.2%) was significantly higher than that of those who reported less types of ELA accumulation (none, 1 to 2, and 3 to 4 types). Individuals from the four accumulation groups of ELA experiences significantly differ in their demographic, socioeconomic characteristics and health behaviors.

<insert Table 1 about here>

Long-term Trajectories of Multimorbidity among Older Adults

We used the GBTM approach to identify distinct groups of individuals sharing a similar long-term trajectory of multimorbidity from age 50 to 85. Models were estimated with one to six groups (Table 2). For Groups 1-4, the BICs were consistently close to 0. The entropy in group 4 was 0.976. Based on considerations of changes in BIC and entropy, a logit model with four trajectory groups was the most

suitable fit for the data.

<insert Table 2 about here>

Figure 2 illustrates the distribution of older individuals from the four identified long-term trajectories of multimorbidity. The number of chronic conditions in Group 1 ("maintaining-low") was consistently low, with most remaining free of chronic conditions until age 75. Older individuals in Group 2 ("low onset-rapidly increasing") had no chronic condition at the starting point, but their number of chronic conditions showed a rapid increase after age 65. Older individuals in Group 3 ("middle onset-moderately increasing") had one chronic condition at the starting point, and their number of chronic conditions increased steadily with age. Older adults in Group 4 ("chronically-high") had two chronic conditions at the starting point, with the number of chronic conditions increasing rapidly with age. Please see the *Supplemental Tables* for more information on the characteristics of the long-term trajectory distribution of multimorbidity.

<insert Figure 2 about here>

Early Life Adversity Predicts Long-term Trajectories of Multimorbidity

Model 1 in Table 3 presents the results of the multinomial logistic regressions for the relationship between specific types of ELA and multimorbidity trajectories. Exposure to parental illness, parental quarrel/divorce, relative poverty, food insufficiency, domestic violence, and bullying were associated with more severe long-term trajectories of multimorbidity. Individuals who had experienced parental

quarrel/divorce reported a higher relative risk of being in the "low onset-rapidly increasing" group, the "middle onset-moderately increasing" group, and the "chronically-high" group than in the "maintaining-low" group. Similar results have also been found among individuals who reported childhood food insufficiency.

Model 2 presents the results of the multinomial logistic regressions for the relationship between the accumulation of different ELA experiences and multimorbidity trajectories. Individuals who had accumulated 1 to 2 types, 3 to 4 types, and 5-7 types of ELA experiences reported a higher relative risk of being in the "low onset-rapidly increasing" group, the "middle onset-moderately increasing" group, and the "chronically-high" group than in the "maintaining-low" group.

Sensitivity Analyses

Supplemental Tables (*eTables 2 and 4-8*) show the results of sensitivity analyses that included restricting the GBTM analyses to 12 chronic conditions (excluding memory-related and emotional/psychiatric problems given their low prevalence in the study population), using a different set of ELA indicators or different categorization for the accumulation of ELA, and stratifying by gender and urban-rural residence.

<insert Table 3 about here>

DISCUSSION

Using population-based longitudinal data, we identified four distinct long-term

trajectories of multimorbidity development among Chinese older adults and linked different types and accumulation of ELA experiences with these long-term multimorbidity trajectories. The most prominent health-deteriorating impact of ELA has been found among individuals who reported exposure to food insufficiency and parental quarrel/divorce. Individuals who had accumulated different ELA experiences had a significantly higher relative risk of developing more severe multimorbidity trajectories over time.

The development of multimorbidity in older adults has been widely reported, but only a few studies have examined the heterogeneity of multimorbidity trajectories in older adults[37][12]. Our findings confirmed the existence of heterogeneous long-term multimorbidity trajectories in Chinese older adults. The "maintaining-low" (19.1%) group and the "low onset-rapidly increasing" (22%) group were both characterized by a low starting point, whereas the "low onset-rapidly increasing" group reported the onset of diseases around the age of 65 and a faster development of new disease diagnosis since the age of 80. A similar trajectory of health development in later life has been consistently reported in previous studies among older Chinese populations across a variety of health outcomes, including frailty and functional disability (e.g.,[38][39]). Individuals from the largest group "middle onset-moderately increasing" (40.2%) were characterized by an average of one condition in their 50 s and a gradual progression of new condition diagnosis over time. Female and individuals with below high school education were more likely to be located in this

group. The “chronically-high” group comprised individuals with the highest number of conditions throughout the age range from 50 to 85, accounting for approximately 20% of the study population. Such a similar group has also been found in several previous studies [12][13], with an estimated proportion ranging between 7.5% and 27.8%.

Our findings indicated that exposure to specific types of ELA was associated with more severe long-term multimorbidity trajectories. The most prominent health-deteriorating impact of ELA on multimorbidity progression was found among individuals who had experienced childhood food insufficiency and parental quarrel/divorce. Specifically, our finding was consistent with previous studies linking childhood food insufficiency with a variety of adverse health outcomes in later life, such as a higher risk of hyperglycemia, cognitive decline, and frailty[40][41][42][43]. Additionally, our finding of the harmful effects of parental quarrel/divorce on long-term multimorbidity trajectories extended the literature on the importance of early-life dysfunctional family relationships for physical and mental health in adulthood[44][45]. By linking specific types of ELA experiences with the longitudinal development of multimorbidity, our study provided new evidence for the critical-period model that childhood adverse experiences may exert long-lasting, irreversible health-damaging effects that lead to significant health disparities in old age [22][24][27].

Previous studies have also documented associations between the accumulation of different ELA experiences and an increased risk of multimorbidity[46] [23]. The current study makes a further contribution by linking the accumulation of different ELA experiences with distinctive long-term trajectories of multimorbidity. Our findings supported our hypothesis that individuals who experienced more accumulated ELA were more likely to develop a more severe multimorbidity trajectory over time. This finding was consistent with the accumulation of risk model [47], suggesting that cumulative disadvantages of ELA may contribute to the persistent widening of health inequalities [29]. Initial disadvantages may contribute to how individuals are exposed to subsequent risk factors, thus leading to greater disparities in health status in later life[48] [49]. For example, family socioeconomic vulnerabilities and maladaptation may cause interruption of education in adolescence, which subsequently increases the risk of exposure to new adversities in adulthood, such as unemployment, and limits the potential opportunities for upward mobility [49].

Our study has some key strengths. First, taking advantage of time-varying data on the history of chronic conditions, we captured the entire course of individuals' development of multimorbidity from the first chronic disease onset to old age, with the longest time spanning 35 years. Second, our study is among the first to empirically establish the longitudinal association between ELA and long-term differential multimorbidity trajectories. Third, our study linked two important aspects of ELA

experiences (specific types and accumulation of ELA) with multimorbidity trajectories, offering a more nuanced picture for testing the life-course models concerning the pathways through which ELA influences health development. Nevertheless, this study also has some limitations. First, our measures of ELA and multimorbidity were retrospective and based on self-reports, which may introduce recall bias into the data. Second, we did not consider the frequency and intensity of ELA, which was limited by data unavailability. Additionally, there may be other protective factors (e.g., resilience) related to multimorbidity could not be included in our study.

In conclusion, our study indicated that the development of multimorbidity shows considerable heterogeneity within the older Chinese population with respect to the onset and increased rate of conditions, and such heterogeneity can be explained by ELA experiences. The findings highlight the role of a supportive early-life family environment in promoting health development across the adult lifespan. Practitioners and clinicians should pay more attention to the upstream factors in which adult disease development is rooted when delivering health care services and psychosocial interventions serving older people in the community[50].

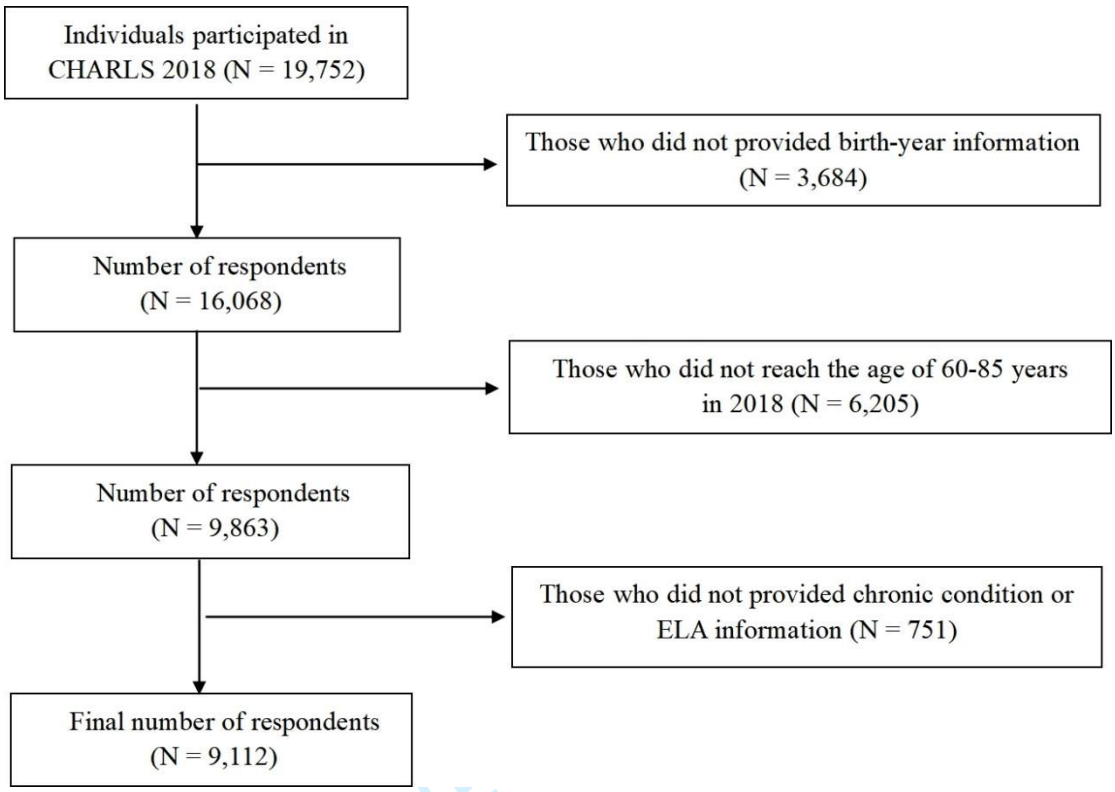

Figure 1 Flow of Respondents and Study Inclusion.

N = number; CHARLS = China Health and Retirement Longitudinal Survey

Table 1 Sample Characteristics by ELA Number in CHARLS 2018 (*N*=9,112)

Variables (%)	ELA Number				*P*-value
	0	1-2	3-4	5-7	
Number of Chronic Conditions					<0.001
0-1 condition	38.2	33.7	28.2	21.8	
2 conditions	19.5	22.8	21.5	21.1	
≥ 3 conditions	42.3	43.5	50.3	57.2	
Female	63.2	56.2	46.3	44.7	<0.001
Rural	57.7	60.8	65.7	70.8	<0.001
Marital Status					<0.001
married	71.7	78.1	80.3	81.3	
other status	28.3	21.9	19.7	18.8	
Educational Attainment					0.001
below high school	87.2	88.8	91.0	92.1	
high school and above	12.8	11.2	9.0	7.9	
Receiving *Dibao* Assistance	89.2	91.7	89.1	87.6	<0.001
Types of Medical Insurance					0.001
none	3.9	2.9	2.7	2.8	
urban employee	16.1	13.4	13.2	9.3	
urban and rural resident	76.6	81.1	81.9	86.3	
others	3.5	2.6	2.2	1.6	
Smoking	65.1	58.4	51.4	51.1	<0.001
Drinking	72.6	67.9	63.1	61.5	<0.001
Physical Activity					<0.001
none	15.7	14.2	11.8	9.5	
low intensity	40.0	35.5	31.1	26.8	
moderate intensity	29.3	27.5	26.9	26.4	
high intensity	15.0	22.8	30.2	37.2	

Notes: ELA = early life adversity. The information is from the China Health and Retirement Longitudinal Study 2018. Other status of marriage includes unmarried/divorced/separated/widowed. Urban and rural resident medical insurance integrated urban resident medical insurance and new rural cooperative medical insurance.The results of the chi-square test for variables.

Table 2 Tabulated BIC and 2ΔBIC

Number of Groups	BIC	Entropy	2(Δ BIC)
1	-308557.37	--	--
2	-253000.24	0.967	-55557.13
3	-226640.40	0.975	-26359.84
4	-213163.38	0.976	-13477.02
5	-201166.33	0.973	-11997.05
6	-193334.26	0.941	-7832.07

Notes: N=9,112. BIC = Bayesian Information Criterion. The closer the entropy is to 1, the better the model fits.

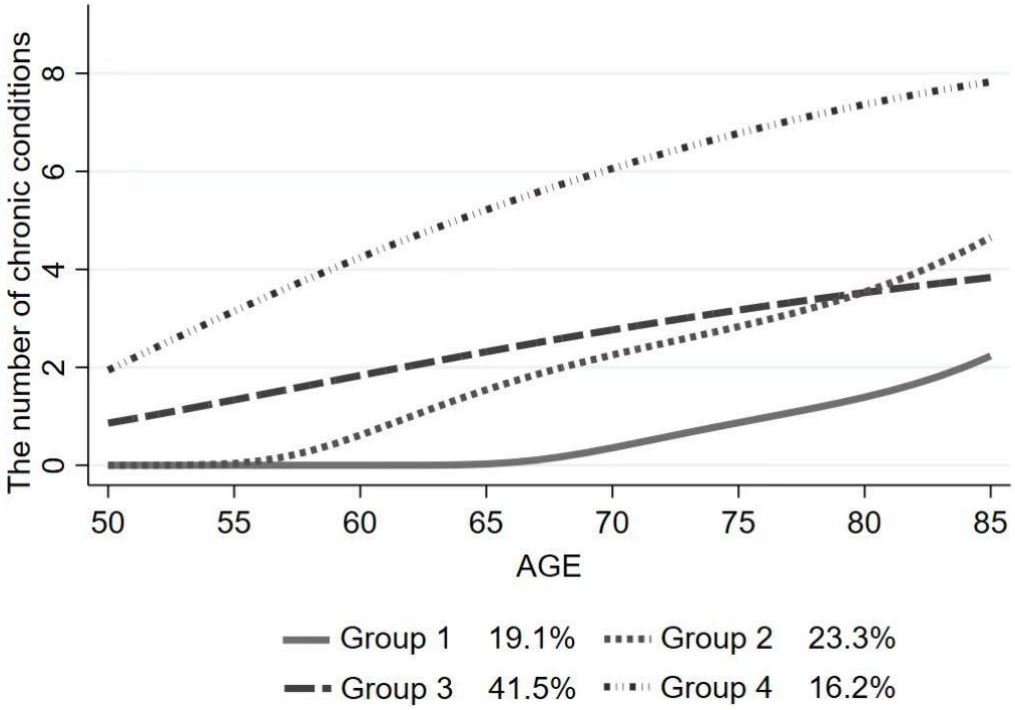

Figure 2 Long-term Trajectories Distribution of Multimorbidity

Table 3 Multinomial Logistic Regressions for ELA Experiences and Multimorbidity Trajectories

Variables	Group 2 Low onset-rapidly increasing	Group 3 Middle onset-moderately increasing	Group 4 Chronically-high
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Model 1			
Parental Illness	1.059 (0.891-1.258)	1.230 (1.054-1.435)**	1.885 (1.578-2.251)***
Parental Death	1.032 (0.876-1.215)	1.013 (0.874-1.174)	0.980 (0.816-1.176)
Parental Quarrel/Divorce	1.214 (1.011-1.458)*	1.181 (1.000-1.394)*	1.262 (1.038-1.536)*
Relative Poverty	1.092 (0.944-1.264)	1.210 (1.061-1.379)**	1.333 (1.136-1.564)***
Food Insufficiency	1.403 (1.197-1.645)***	1.372 (1.190-1.582)***	1.780 (1.472-2.152)***
Domestic Violence	1.132 (0.982-1.305)	1.340 (1.178-1.523)***	1.597 (1.360-1.876)***
Bullying	1.051 (0.889-1.243)	1.215 (1.046-1.411)*	1.443 (1.208-1.724)***
Model 2			
ELA (ref: none)			
1-2	1.694 (1.284-2.233)***	1.512 (1.189-1.922)**	1.975 (1.384-2.819)***
3-4	2.066 (1.557-2.741)***	2.148 (1.680-2.746)***	3.746 (2.621-5.355)***
5-7	2.625 (1.836-3.755)***	3.427 (2.505-4.690)***	7.555 (4.993-11.431)***

Notes: Reference category was Group 1 ("maintaining-low"). RRR = relative risk ratios. CI = confidence interval. ELA = early life adversity. ref =reference. *p < .05; **p < .01; ***p < .001. Model adjusted for gender, residence area, marital status, educational attainment, types of medical insurance, and whether receive *Dibao* assistance, smoking, drinking, and physical activity.

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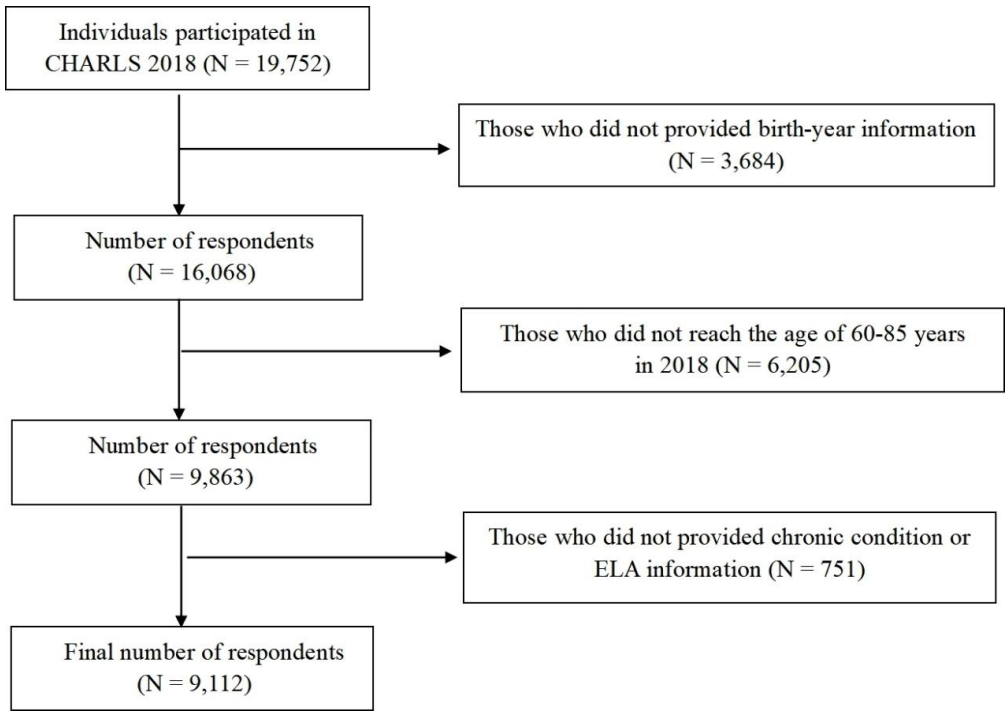


Figure 1 Flow of Respondents and Study Inclusion.
N = number; CHARLS = China Health and Retirement Longitudinal Survey

146x103mm (220 x 220 DPI)

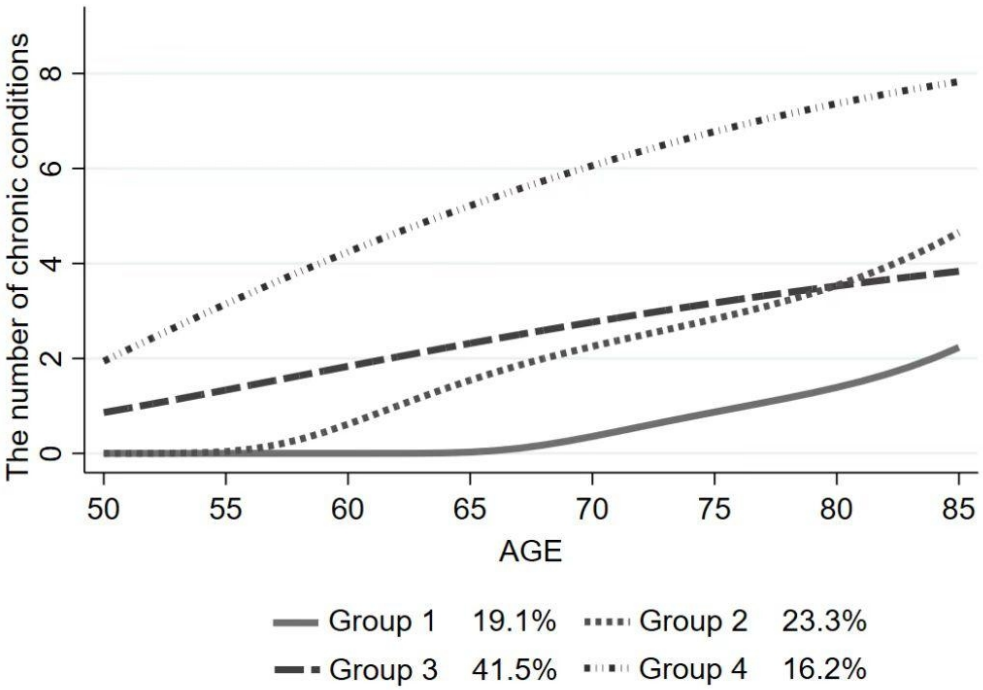
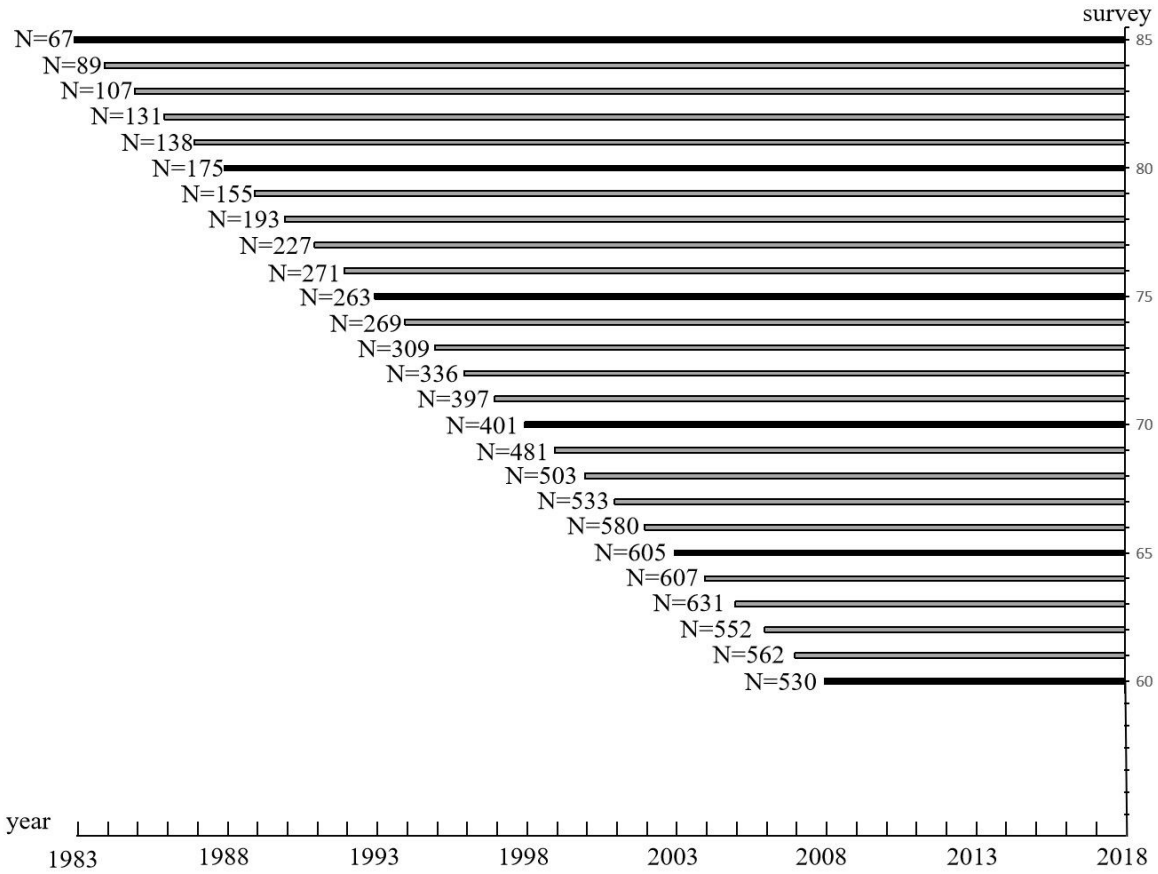


Figure 2 Long-term Trajectories Distribution of Multimorbidity.

136x99mm (192 x 192 DPI)

Supplemental Figures

eFigure 1 Retracing the Development of Chronic Disease in the Sample



eFigure 1 Retracing the Development of Chronic Disease in the Sample.

N = number; The total number of respondents was 9,112.

Supplemental Tables

eTable 1 Questionnaire Items and Prevalence of Each ELA Indicator

eTable 2 Tabulated BIC and 2ΔBIC (using 12 chronic conditions)

eTable 3 Sample Characteristics by Multimorbidity Trajectories in CHARLS 2018 (N=9,112)

eTable 4 Multinomial Logistic Regression Models for nine types of ELA Experiences and Multimorbidity Trajectories

eTable 5 Multinomial Logistic Regressions for ELA Experiences (Male, N=4,440)

eTable 6 Multinomial Logistic Regressions for ELA Experiences (Female, N=4,672)

eTable 7 Multinomial Logistic Regressions for ELA Experiences (Urban, N=3,305)

eTable 8 Multinomial Logistic Regressions for ELA Experiences (Rural, N=5,807)

eTable 1 Questionnaire Items and Prevalence of Each ELA Indicator

Types of ELA	Questionnaire Items	Prevalence (%)
Parental Illness	Did your female/male guardian have a long time be sick on bed when you were young? (yes[a], no) Did your female/male guardian have a serious deformity when you were young? (yes[a], no) Did your female/male guardian have abnormality of mind when you were young? (yes[a], no)	23.5%
Parental Death	Is your biological mother/biological father alive? (yes[a], no)	23.0%
Parental Quarrel/Divorce	Did your parents often quarrel? (often[a], sometimes[a], not very often[a], never) Were your biological parents divorced? (yes[a], no)	19.3%
Relative Poverty	When you were a child before age 17, compared to the average family in the same community/village at that time, how was your family's financial situation? (a lot better off than them, somewhat better off than them, same as them, somewhat worse off than them[a], a lot worse off than them[a])	41.1%
Food Insufficiency	When you were a child before age 17 was there ever a time when your family did not have enough food to eat? (yes[a], no)	77.9%
Domestic Violence	When you were growing up, did your female/male guardian ever hit you? Was that often, sometimes, rarely, or never? (often[a], sometimes[a], rarely[a], never)	56.9%
Bullying	When you were a child, how often were you picked on or bullied by kids in your neighborhood? Is it often, sometimes, rarely or never? (often[a], sometimes[a], not very often[a], never) When you were a child, how often were you picked on or bullied by kids in your school? Is it often, sometimes, rarely or never? (often[a], sometimes[a], not very often[a], never)	26.5%
Poor Physical Health	Before you were 15 years old (including 15 years old), would you say that compared to other children of the same age, you were (much healthier, somewhat healthier, about average, somewhat less healthy[a], much less healthy[a])	13.1%
Loneliness	When you were a child, how often did you feel lonely for not having friends? Is it often, sometimes, not very often or never? (often[a], sometimes[a], not very often[a], never)	13.4%

Notes: ELA = early life adversity. [a] Answers indicate thresholds for ELA. Prevalence indicates the proportion of individuals who have experienced ELA. "Poor

Physical Health" and "Loneliness" are two additional indicators of ELA added for sensitivity analysis.

eTable 2 Tabulated BIC and 2ΔBIC (using 12 chronic conditions)

Number of Groups	BIC	Entropy	2(ΔBIC)
1	-302678.31	.	.
2	-245853.85	0.972	-56824.46
3	-219850.02	0.976	-26003.83
4	-206847.93	0.980	-13002.09
5	-194196.80	0.979	-12651.13
6	-186460.39	0.945	-7736.41

Notes: The GBTM analyses using 12 chronic conditions (excluding memory-related and emotional/psychiatric problems given their low prevalence in the study population). N=9,112. BIC = Bayesian Information Criterion. The closer the entropy is to 1, the better the model fits.

eTable 3 Sample Characteristics by Multimorbidity Trajectories in CHARLS 2018 (N=9,112)

Variables (%)	Multimorbidity Trajectories				*P*-value
	Group I	Group2	Group 3	Group 4	
Female	45.8	51.0	51.7	57.1	<0.001
Rural	65.1	63.6	63.0	64.3	0.464
Marital Status					<0.001
married	72.3	77.3	81.2	83.6	
other status	27.7	22.7	18.8	16.4	
Educational Attainment					0.116
below high school	90.4	90.9	89.8	88.5	
high school and above	9.6	9.1	10.2	11.5	
Receiving *Dibao* Assistance	92.0	90.6	90.1	86.8	<0.001
Types of Medical Insurance					0.656
none	3.3	3.2	2.8	2.3	
urban employee	12.2	12.5	13.2	14.1	
urban and rural resident	82.0	82.0	81.7	81.2	
others	2.6	2.3	2.3	2.4	
Smoking	52.2	55.3	55.6	56.9	0.038
Drinking	63.2	65.3	65.2	69.3	0.004
Physical Activity					0.020
none	13.6	12.6	12.1	13.7	
low intensity	35.7	33.0	31.9	32.8	
moderate intensity	23.8	27.6	28.7	26.9	
high intensity	26.9	26.7	27.4	26.6	

Notes: ELA = early life adversity. The information is from the China Health and Retirement Longitudinal Study 2018. Other status of marriage includes unmarried/divorced/ separated/widowed. Urban and rural resident medical insurance integrated urban resident medical insurance and new rural cooperative medical insurance.The results of the chi-square test for variables.

eTable 4 Multinomial Logistic Regression Models for nine types of ELA Experiences and Multimorbidity Trajectories

Variables	Group 2 Low onset-rapidly increasing	Group 3 Middle onset-moderately increasing	Group 4 Chronically-high
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Model 1			
Parental Illness	1.050 (0.883-1.250)	1.220 (1.044-1.425)*	1.816 (1.517-2.173)***
Parental Death	1.015 (0.860-1.197)	0.994 (0.856-1.154)	0.935 (0.777-1.125)
Parental Quarrel/Divorce	1.206 (1.003-1.449)*	1.166 (0.986-1.377)	1.230 (1.010-1.499)*
Relative Poverty	1.069 (0.922-1.238)	1.176 (1.030-1.344)*	1.229 (1.045-1.446)*
Food Insufficiency	1.413 (1.204-1.659)***	1.366 (1.183-1.576)***	1.768 (1.461-2.141)***
Domestic Violence	1.128 (0.978-1.302)	1.343 (1.180-1.528)***	1.586 (1.349-1.865)***
Bullying	1.046 (0.882-1.239)	1.188 (1.021-1.383)*	1.377 (1.149-1.650)**
Poor Physical Health	1.333 (1.050-1.692)*	1.613 (1.302-1.998)***	2.317 (1.827-2.939)***
Loneliness	0.973 (0.785-1.207)	1.028 (0.848-1.246)	1.160 (0.924-1.458)
Model 2			
ELA (ref: none)			
1-2	1.668 (1.248-2.229)**	1.483 (1.151-1.910)**	2.119 (1.430-3.138)***
3-4	2.088 (1.556-2.803)***	2.205 (1.706-2.851)***	4.088 (2.760-6.054)***
5-9	2.278 (1.632-3.180)***	3.016 (2.254-4.035)***	7.862 (5.173-11.947)***

Notes: Reference category was Group 1 ("maintaining-low"). RRR = relative risk ratios. CI = confidence interval. ELA = early life adversity. ref =reference. *p < .05; **p < .01; ***p < .001. Model adjusted for gender, residence area, marital status, educational attainment, types of medical insurance, and whether receive *Dibao* assistance, smoking, drinking, and physical activity.

eTable 5 Multinomial Logistic Regressions for ELA Experiences (Male, N=4,440)

Variables	Group 2 Low onset-rapidly increasing	Group 3 Middle onset-moderately increasing	Group 4 Chronically-high
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Model 1			
Parental Illness	0.884 (0.693-1.128)	1.140 (0.923-1.407)	1.756 (1.363-2.261)***
Parental Death	1.028 (0.820-1.288)	1.052 (0.860-1.286)	1.045 (0.808-1.351)
Parental Quarrel/Divorce	1.111 (0.862-1.433)	1.172 (0.935-1.469)	1.134 (0.855-1.505)
Relative Poverty	1.053 (0.861-1.288)	1.216 (1.016-1.454)*	1.343 (1.069-1.687)*
Food Insufficiency	1.444 (1.151-1.812)**	1.548 (1.263-1.897)***	1.873 (1.404-2.499)***
Domestic Violence	1.056 (0.864-1.290)	1.196 (0.998-1.434)	1.440 (1.130-1.835)**
Bullying	0.957 (0.769-1.190)	1.124 (0.928-1.362)	1.324 (1.042-1.683)*
Model 2			
ELA (ref: none)			
1-2	2.145 (1.365-3.370)**	1.621 (1.108-2.372)*	1.919 (1.072-3.435)*
3-4	2.241 (1.425-3.524)***	2.249 (1.539-3.287)***	3.018 (1.695-5.374)***
5-7	2.284 (1.341-3.891)**	3.214 (2.058-5.020)***	6.224 (3.316-11.683)***

Notes: Reference category was Group 1 ("maintaining-low"). RRR = relative risk ratios. CI = confidence interval. ELA = early life adversity. ref =reference. *p < .05; **p < .01; ***p < .001. Model adjusted for residence area, marital status, educational attainment, types of medical insurance, and whether receive *Dibao* assistance, smoking, drinking, and physical activity.

eTable 6 Multinomial Logistic Regressions for ELA Experiences (Female, N=4,672)

Variables	Group 2 Low onset-rapidly increasing	Group 3 Middle onset-moderately increasing	Group 4 Chronically-high
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Model 1			
Parental Illness	1.273 (0.993-1.633)	1.351 (1.076-1.696)*	2.061 (1.599-2.656)***
Parental Death	1.030 (0.810-1.308)	0.965 (0.775-1.201)	0.905 (0.697-1.176)
Parental Quarrel/Divorce	1.321 (1.012-1.724)*	1.194 (0.934-1.527)	1.374 (1.041-1.815)*
Relative Poverty	1.128 (0.912-1.395)	1.217 (1.003-1.477)*	1.332 (1.061-1.670)*
Food Insufficiency	1.350 (1.078-1.690)**	1.234 (1.009-1.509)*	1.699 (1.315-2.195)***
Domestic Violence	1.219 (0.993-1.497)	1.521 (1.263-1.831)***	1.777 (1.426-2.215)***
Bullying	1.254 (0.959-1.640)	1.401 (1.098-1.789)**	1.692 (1.286-2.227)***
Model 2			
ELA (ref: none)			
1-2	1.412 (0.991-2.013)	1.445 (1.057-1.975)*	1.949 (1.241-3.060)**
3-4	2.013 (1.390-2.916)***	2.147 (1.546-2.983)***	4.408 (2.784-6.979)***
5-7	3.588 (2.120-6.074)***	4.212 (2.601-6.819)***	9.444 (5.237-17.030)***

Notes: Reference category was Group 1 ("maintaining-low"). RRR = relative risk ratios. CI = confidence interval. ELA = early life adversity. ref =reference. *p < .05; **p < .01; ***p < .001. Model adjusted for residence area, marital status, educational attainment, types of medical insurance, and whether receive *Dibao* assistance, smoking, drinking, and physical activity.

eTable 7 Multinomial Logistic Regressions for ELA Experiences (Urban , N=3,305)

Variables	Group 2 Low onset-rapidly increasing	Group 3 Middle onset-moderately increasing	Group 4 Chronically-high
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Model 1			
Parental Illness	1.086 (0.794-1.484)	1.198 (0.905-1.585)	1.673 (1.210-2.313)**
Parental Death	1.060 (0.793-1.416)	1.021 (0.786-1.327)	1.031 (0.746-1.425)
Parental Quarrel/Divorce	1.207 (0.889-1.639)	1.110 (0.841-1.465)	1.195 (0.860-1.662)
Relative Poverty	1.111 (0.858-1.438)	1.324 (1.049-1.670)*	1.419 (1.072-1.879)*
Food Insufficiency	1.518 (1.170-1.970)**	1.415 (1.123-1.784)**	1.837 (1.355-2.490)***
Domestic Violence	1.166 (0.917-1.484)	1.385 (1.115-1.722)**	1.640 (1.249-2.154)***
Bullying	1.069 (0.800-1.429)	1.250 (0.965-1.619)	1.689 (1.246-2.291)**
Model 2			
ELA (ref: none)			
1-2	1.709 (1.118-2.614)*	1.821 (1.245-2.663)**	2.378 (1.365-4.143)**
3-4	2.113 (1.359-3.285)**	2.652 (1.788-3.933)***	4.394 (2.497-7.732)***
5-7	3.195 (1.718-5.944)***	4.463 (2.546-7.824)***	9.875 (4.867-20.032)***

Notes: Reference category was Group 1 ("maintaining-low"). RRR = relative risk ratios. CI = confidence interval. ELA = early life adversity. ref =reference. *p < .05; **p < .01; ***p < .001. Model adjusted for gender, marital status, educational attainment, types of medical insurance, and whether receive *Dibao* assistance, smoking, drinking, and physical activity.

eTable 8 Multinomial Logistic Regressions for ELA Experiences (Rural, N=5,807)

Variables	Group 2 Low onset-rapidly increasing	Group 3 Middle onset-moderately increasing	Group 4 Chronically-high
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Model 1			
Parental Illness	1.049 (0.852-1.290)	1.244 (1.034-1.496)*	2.009 (1.623-2.486)***
Parental Death	1.022 (0.837-1.246)	1.011 (0.845-1.209)	0.963 (0.772-1.202)
Parental Quarrel/Divorce	1.214 (0.965-1.526)	1.218 (0.990-1.498)	1.294 (1.013-1.653)*
Relative Poverty	1.086 (0.910-1.296)	1.160 (0.989-1.360)	1.304 (1.072-1.584)**
Food Insufficiency	1.337 (1.093-1.636)**	1.339 (1.117-1.605)**	1.761 (1.379-2.250)***
Domestic Violence	1.118 (0.937-1.334)	1.321 (1.126-1.549)**	1.586 (1.298-1.936)***
Bullying	1.040 (0.846-1.279)	1.203 (1.001-1.446)*	1.337 (1.073-1.666)*
Model 2			
ELA (ref: none)			
1-2	1.693 (1.173-2.442)**	1.325 (0.971-1.810)	1.762 (1.107-2.803)*
3-4	2.037 (1.405-2.954)***	1.856 (1.354-2.545)***	3.429 (2.156-5.453)***
5-7	2.426 (1.547-3.804)***	2.917 (1.983-4.291)***	6.606 (3.920-11.132)***

Notes: Reference category was Group 1 ("maintaining-low"). RRR = relative risk ratios. CI = confidence interval. ELA = early life adversity. ref =reference. *p < .05; **p < .01; ***p < .001. Model adjusted for gender, marital status, educational attainment, types of medical insurance, and whether receive *Dibao* assistance, smoking, drinking, and physical activity.

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Exposure to early-life adversity and long-term trajectories of multimorbidity among older adults in China: analysis of longitudinal data from the China Health and Retirement Longitudinal Study

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ABSTRACT

Objectives: This study aimed to identify long-term distinct trajectories of multimorbidity with ageing from 50 to 85 years among Chinese older adults and examine the relationship between exposure to early-life adversity (ELA; including specific types of adversity and accumulation of different adversities) with these long-term multimorbidity trajectories.

Design: Group-based trajectory models identified long-term multimorbidity trajectories. Multinomial logistic regression models were used to examine the relationship between ELA and the identified multimorbidity trajectories.

Setting： This study used data from the China Health and Retirement Longitudinal Study (CHARLS, 2011–2018) and the 2014 Life History Survey**.**

Participants： We used data from 9,112 respondents (aged 60 and above) of the 2018 wave of CHARLS.

Outcome measures: Each respondent's history of chronic conditions and experiences of ELA were collected from the 2011-2018 waves of CHARLS and the 2014 Life History Survey.

Results: Four heterogeneous long-term trajectories of multimorbidity development were identified: "maintaining-low" (19.1%), "low onset-rapidly increasing" (23.3%), "middle onset-moderately increasing" (41.5%), and "chronically-high" (16.2%). Our findings indicated that the heterogeneity can be explained by ELA experiences. Across various types of different ELA experiences, exposure to food insufficiency (relative risk ratios: 1.372 [95% CI 1.190-1.582] to 1.780 [1.472-2.152]) and parental

quarrel/divorce (1.181 [1.000-1.394] to 1.262 [1.038-1.536]) had the most prominent associations with health deterioration. The accumulation of more different ELA experiences was associated with a higher relative risk of developing more severe multimorbidity trajectories (relative risk ratio for 5-7 ELAs and chronically-high trajectory: 7.555 [95% CI 4.993-11.431]).

Conclusions: There are heterogeneous long-term trajectories of multimorbidity in Chinese older adults and the risk of multimorbidity associated with ELA accumulates over the lifespan. Our findings highlight the role of a supportive early-life family environment in promoting health development across the lifespan, advocating for the integration of life-course approaches to implementing health disparity interventions.

Keywords: chronic disease development; childhood adversity; Chinese older adults; longitudinal trajectory

Strengths and limitations of this study

- Taking advantage of time-varying data on the history of chronic conditions, we captured the entire course of individuals' development of multimorbidity from the first chronic disease onset to old age, with the longest time spanning 35 years.
- Our study investigated the longitudinal association between ELA and long-term differential multimorbidity trajectories.
- Our study linked two important aspects of early-life adversity (ELA) experiences (specific types and accumulation of ELA) with multimorbidity trajectories,

offering a more nuanced picture for testing the life-course models concerning the pathways through which ELA might influence health development.

- Our measures of ELA and multimorbidity were retrospective and based on self-reports, which may introduce recall bias into the data.
- We did not consider the frequency and intensity of ELA, which was limited by data unavailability; additionally, there may be other protective factors (e.g., resilience) related to multimorbidity that could not be included in our study.

INTRODUCTION

Chronic diseases are one of the leading causes of death, placing a huge burden on healthcare systems worldwide [1]. Multimorbidity, defined as the coexistence of two or more chronic conditions, has been observed at an extremely high prevalence in old age[2]. More than half of Chinese older adults are estimated to have two or more chronic conditions [3], and this number is expected to increase with the continuing population aging and improvements in the survival of people with chronic diseases. Extensive studies have documented a range of adverse outcomes resulting from multimorbidity, including a higher risk of mortality, disability, and increased healthcare use [4].

Despite the growing interest in studying multimorbidity and its associated factors, previous research has mostly focused on a list of arbitrarily chosen conditions at a single point or period in time and thus does not cover the complete time-varying picture of multimorbidity [5][6]. Recent research has indicated that older individuals not only show variations in the timing of disease onset but also develop multimorbidity at different rates over time [7][8]. In particular, several studies have successfully identified distinct subgroups of multimorbidity within study populations [9][10][11]. Similar groups emerged across these studies, including a group of older individuals maintaining few conditions, a group characterized by a consistently high number of conditions, and a group of individuals reporting a rapidly increasing number of conditions [12][13]. To our knowledge, however, no study has examined heterogeneous

multimorbidity trajectories by longitudinally capturing the accumulation of chronic conditions throughout the whole period starting from an individual's first-onset condition to his or her very old age. Identifying such long-term trajectories will not only enhance the understanding of the development of multimorbidity but also help prognostic studies better target people at risk of more severe multimorbidity progression and associated adverse outcomes.

Early-life adversity (ELA) has been documented as a potential risk factor for worse health outcomes, including an increased risk of multimorbidity in old age [14][15][16]. ELA is commonly defined as exposure to traumatic events such as parental death, parental divorce, or abuse during childhood [17][18].The life-course perspective provides two important theoretical models explaining the mechanisms underlying the association between ELA and health development [19]. The critical period model asserts that exposure to ELA has long-lasting influence on individuals' developmental trajectories of health. This influence could vary across different types of ELA experiences, and operate by shaping the structural aspects of individuals' brain architecture and behavioral development [20][21]. Existing studies supporting this model have demonstrated that exposure to specific types of ELA (e.g., domestic violence and food deprivation) could increase the risk of multimorbidity in various older populations through the dysregulation of centrally mediated stress-response processes [22][23]and the promotion of detrimental behaviors or poor social ties [24][25]. Alternatively, the accumulation of risk model suggests that early-life

disadvantages increase one's exposure to later health risks, contributing to the development of the adulthood health "chain of risk", wherein ELA experiences at different life stages tend to sequentially compound [19][20]. Empirical evidence supporting this model has revealed that individuals who experienced four or more accumulated ELA reported increased risks of multimorbidity and developing specific chronic conditions (e.g., dyslipidemia and psychiatric disease) compared with those who did not experience ELA [26].

In addition to the life-course perspective, the cumulative disadvantage (CDA) framework also provides important viewpoints for understanding the impact of ELA on later-life health disparities highlighting the mechanism of path dependence. It posits that initial disparities can be linked to later-life health outcomes indirectly through influencing adulthood exposure to environmental risks and health opportunities [27]. Empirical studies have revealed that disadvantaged early environment (e.g., lower educational attainment) may lead to poorer socioeconomic status in adulthood (e.g., placement in the occupational hierarchy), subsequently exerting significant effects on later-life health through the influence of lifestyle choices or access to medical services [28].

To our knowledge, no existing studies have incorporated the life-course theory and the CDA framework for understanding the impact of ELA experiences on health development in later life, particularly by linking the two aspects of ELA experiences

(types and accumulation) with long-term distinct trajectories of multimorbidity. Using population-based longitudinal data, the present study aimed to identify long-term heterogeneous trajectories of multimorbidity among Chinese older adults starting in late adulthood and followed up to 35 years and to examine the relationship between exposure to ELA (including specific types of adversity and accumulation of different adversities) and these long-term multimorbidity trajectories. Drawing from the existing literature, we expected that exposure to certain types of ELA and the accumulation of more different ELA types would be associated with a higher likelihood of more severe multimorbidity trajectories. Clarifying the impact of ELA experiences on later-life health will provide a basis for health care providers to develop comprehensive lifecycle health interventions.

METHODS

Data and sampling

The present study utilized data from the four waves (2011-2018) of the China Health and Retirement Longitudinal Study (CHARLS) and the 2014 Life History Survey. The 2011 baseline survey collected data from 17,706 respondents aged 45 and above on their demographic, socioeconomic and health characteristics. The 2014 Life History Survey interviewed respondents who participated in the 2011 and 2013 surveys and collected information on their early-life experiences, including living environment, family socioeconomic status, and health history. For the purpose of the present study, we restricted our analytical sample to respondents who met the following inclusion

criteria: (1) participated in the 2018 wave and the 2014 Life History survey; (2) birth-year information was available from any of the 2011-2018 waves; (3) provided valid data on the measurement of ELA and history of chronic conditions; and (4) aged ≥ 60 years in 2018. In addition, we excluded respondents aged over 85 in 2018 because the oldest-old group was not well represented in the CHARLS (the proportion of respondents aged over 85 in the 2018 CHARLS survey was 1.6%). The final analytical sample included 9,112 respondents (see *Figure 1* for details about the sample selection process). To validate that the sample size in this study enabled subgrouping analyses, a power analysis using Stata 17 determined that, given an α level of 0.05 and a power of 0.8, the sample size required to achieve the detection of significant relationships between study variables would be approximately 863 respondents.

Variables

Development of chronic conditions

We obtained information about each respondent's history of chronic conditions from the 2011-2018 CHARLS survey. In each survey, respondents were asked if they had been diagnosed by a healthcare provider with any of the following 14 chronic conditions: hypertension, dyslipidemia, diabetes, cancer or malignant tumor, chronic lung diseases, liver disease, heart disease, stroke, kidney disease, stomach or other digestive diseases, arthritis or rheumatism, asthma, emotional or psychiatric problems, and memory-related disorders [29]. For each condition, respondents who answered in the affirmative were then asked to report the year when this condition was first

diagnosed. Using the self-reported information on the starting year of each condition, we calculated the age at onset of each chronic condition for each respondent. Given that most studies on chronic conditions used age 50 as a starting point and the high prevalence of chronic conditions in people over 50, we tracked each individual's chronic conditions from the age of 50 [30][31]. Then, the time-varying variable "development of chronic conditions" was generated for each respondent, indicating his or her total number of chronic conditions being diagnosed in each year between the age of 50 and the current age when participating in the 2018 CHARLS survey. For more details about the distribution of this time-varying variable, please see **Supplemental Figure 1**. This variable was further used for the identification of distinctive long-term multimorbidity trajectories within this population.

Early-life adversity

We extracted eight indicators of ELA from the CHARLS 2014 survey, including parental illness, parental death, parental quarrel/divorce, relative poverty, food insufficiency, domestic violence, and bullying. The detailed questionnaire items and definitions of each ELA indicator are available in **Supplemental Table 1**. Responses to each item were dichotomized and summed to generate a cumulative ELA score for each respondent, ranging from 0 to 7. Higher scores indicated more experience with ELA. To investigate the relationship between the accumulation of different ELA experiences and the long-term trajectories of multimorbidity, we further categorized the accumulation of ELA experiences according to ELA scores: none, 1-2, 3-4, and 5-7

types of ELA experience accumulation. The measurement has been accepted and widely used in empirical studies [32].

Covariates

We controlled for a number of confounding factors identified in previous studies that may contribute to the association between ELA and multimorbidity [10] [33] [34]. These factors include (1) demographic characteristics: gender, residence area (urban versus rural), and marital status (married versus other status including unmarried/divorced/separated/widowed); (2) socioeconomic characteristics: educational attainment (below high school versus high school and above), whether receiving Dibao assistance, and types of medical insurance (none, urban employee, urban and rural resident, and others); and (3) health behavior factors: smoking, drinking, and physical activity (no-, light-, moderate- and vigorous-intensity physical activity).

Analytical strategy

The group-based trajectory modeling (GBTM) approach was used to model progression in the number of chronic conditions over time (i.e., from late adulthood to old age) [35][36][37]. The GBTM approach is designed to identify distinctive groups of individuals sharing a similar trajectory using finite mixtures of suitably defined probability distributions [35]. Applied to this study, this approach enables the assignment of individuals into distinct trajectories based on the similarity of multimorbidity trajectories as they age. In specific, each individual was assigned to a

single group in which they have the highest posterior probability of membership [6]. The fundamental concept of interest is the distribution of outcomes (in our study, the number of chronic conditions) conditional on age. We examined a series of foundational assumptions of GBTM [38][39]. First, GBTM assumes that the data follow continuous distribution with finite starting and ending points (in this study, the chronic conditions data are continuous, ranging from 0 to 14). Given the slight skewness in the data, we examined the applicability of the censored normal (cnorm) model and the zero-inflated Poisson(zip) model. The results indicated a better fit for the cnorm model. Second, GBTM assumes that heterogeneity between groups arises from differences in trajectory development rather than other variables. We compared the model with random effects, including gender, to the model without random effects, and the results did not show significant differences. Third, GBTM posits that all trajectories exhibit steady changes (in this study, the number of chronic conditions in individuals increased over time). Fourth, GBTM assumes that the sample size of each subgroup should not be less than 5% of the total sample size. In this study, the smallest subgroup constituted 16.2% of the total sample (the sample sizes of the four groups were 1743, 2119, 3779, and 1471, respectively), exceeding the model requirements significantly.

Following the standard procedure for applying this approach, we conducted a sequence of GBTM models. A small amount of missingness occurred due to no-response or incomplete responses to the chronic conditions and ELA information; these missing data were treated as missing at random. For model selection, we used the following

model-fit indices and statistical criteria in combination with conceptual considerations of group distinctiveness and interpretability: (a) the Bayesian Information Criteria (BIC) values. The BIC is the most widely used criteria for model selection, with a BIC closer to 0 indicating better model fit. (b) relative entropy estimates the accuracy (convergence) of classification of individuals into the different latent classes. Entropy values close to 1 indicate lower classification uncertainty. (c) the average posterior probability of group assignment that measures the probability of a group individual belonging to this specific trajectory group was set at greater than 0.7; and (d) according to the posterior probability of the group member, a minimum membership of 5% is required in each trajectory group[40]. These criteria were applied iteratively, and the final model was chosen based on a comprehensive evaluation of statistical fit and conceptual coherence, striking a balance between model complexity and interpretability. After identifying the optimal number of trajectory groups, univariate analysis was used to test the differences in trajectory groups from the final model among a range of individual characteristics at baseline. Multivariate logistic models were used to assess the association between ELA and trajectory group memberships after controlling for various confounding factors including demographic features, socioeconomic factors, and health behavior factors.

We performed a series of sensitivity analyses: (1) We reran the GBTM analyses using 12 chronic conditions (excluding memory-related and emotional/psychiatric problems given their low prevalence in the study population). (2) We also reran the main analyses

using a different set of ELA indicators (including two additional indicators that have been suggested as having a potential influence on health in later life) and using different categorizations for the accumulation of ELA. (3) All the analyses were stratified by gender and urban-rural residence.

We followed the STROBE checklist for reporting observational studies (see **Supplemental Table 2**).

Patient and public involvement

None.

RESULTS

Sample characteristics by ELA number in older adults

Table 1 shows the characteristics of individuals (measured in the 2018 CHARLS survey) by the accumulation of ELA experiences (none, 1 to 2 types, 3 to 4 types, and 5 to 7 types). Among individuals with three or more chronic conditions, the proportion of individuals who reported 5 to 7 types of ELA accumulation (57.2%) was significantly higher than that of those who reported less types of ELA accumulation (none, 1 to 2, and 3 to 4 types). Individuals from the four accumulation groups of ELA experiences significantly differ in their demographic, socioeconomic characteristics and health behaviors.

Long-term trajectories of multimorbidity among older adults

We used the GBTM approach to identify distinct groups of individuals sharing a similar long-term trajectory of multimorbidity from age 50 to 85. Models were estimated with one to six groups (*Table 2*). Comparatively, the BIC and entropy indicated that Group 4 and Group 6 were more suitable than the other groups. The optimal BIC was found in Group 6 (closest to 0), and Group 4 exhibited the highest entropy (closest to 1, at 0.976). Meanwhile, we observed a diminished rate of BIC reduction after Group 4, suggesting that further increasing model complexity no longer yields significant benefits [40]. Based on considerations of changes in BIC and entropy, a logit model with four trajectory groups was the most suitable fit for the data.

Figure 2 illustrates the distribution of older individuals from the four identified long-term trajectories of multimorbidity. The number of chronic conditions in Group 1 ("maintaining-low") was consistently low, with most remaining free of chronic conditions until age 75. Older individuals in Group 2 ("low onset-rapidly increasing") had no chronic condition at the starting point, but their number of chronic conditions showed a rapid increase after age 65. Older individuals in Group 3 ("middle onset-moderately increasing") had one chronic condition at the starting point, and their number of chronic conditions increased steadily with age. Older adults in Group 4 ("chronically-high") had two chronic conditions at the starting point, with the number of chronic conditions increasing rapidly with age. Please see the **Supplemental Table 3** for more information on the characteristics of the long-term trajectory distribution of

multimorbidity.

ELA predicts long-term trajectories of multimorbidity

Model 1 in *Table 3* presents the results of the multinomial logistic regressions for the relationship between specific types of ELA and multimorbidity trajectories. Exposure to parental illness, parental quarrel/divorce, relative poverty, food insufficiency, domestic violence, and bullying were associated with more severe long-term trajectories of multimorbidity. Individuals who had experienced parental quarrel/divorce reported a higher relative risk of being in the "low onset-rapidly increasing" group, the "middle onset-moderately increasing" group, and the "chronically-high" group than in the "maintaining-low" group. Similar results have also been found among individuals who reported childhood food insufficiency.

Model 2 in *Table 4* presents the results of the multinomial logistic regressions for the relationship between the accumulation of different ELA experiences and multimorbidity trajectories. Individuals who had accumulated 1 to 2 types, 3 to 4 types, and 5-7 types of ELA experiences reported a higher relative risk of being in the "low onset-rapidly increasing" group, the "middle onset-moderately increasing" group, and the "chronically-high" group than in the "maintaining-low" group.

Sensitivity analyses

The results remained generally consistent when restricting the GBTM analyses to only

12 chronic conditions, when using a different set of ELA indicators or different categorization for the accumulation of ELA, and when stratifying by gender and urban-rural residence (see **Supplemental Table 3 and Supplemental Tables 5-9** for details).

DISCUSSION

Using population-based longitudinal data, we identified four distinct long-term trajectories of multimorbidity development among Chinese older adults and linked different types and accumulation of ELA experiences with these long-term multimorbidity trajectories. Exposure to food insufficiency and parental quarrel/divorce had the most prominent associations with health deterioration. Individuals who had accumulated different ELA experiences had a significantly higher relative risk of developing more severe multimorbidity trajectories over time.

The development of multimorbidity in older adults has been widely reported, but only a few studies have examined the heterogeneity of multimorbidity trajectories in older adults[41][12]. Our findings confirmed the existence of heterogeneous long-term multimorbidity trajectories in Chinese older adults. The "maintaining-low" (19.1%) group and the "low onset-rapidly increasing" (22%) group were both characterized by a low starting point, whereas the "low onset-rapidly increasing" group reported the onset of diseases around the age of 65 and a faster development of new disease diagnosis since the age of 80. A similar trajectory of health development in later life has been consistently reported in previous studies among older Chinese populations

across a variety of health outcomes, including frailty and functional disability [42][43]. This might because that increasing life expectancy and decreasing incidence of infectious diseases have led to an increase in chronic disease in old age [44]. Individuals from the largest group "middle onset-moderately increasing" (40.2%) were characterized by an average of one condition in their 50s and a gradual progression of new condition diagnosis over time. The "chronically-high" group comprised individuals with the highest number of conditions throughout the age range from 50 to 85, accounting for approximately 20% of the study population. Such a similar group has also been found in several previous studies [12][13], with an estimated proportion ranging between 7.5% and 27.8%.

Our findings indicated that exposure to specific types of ELA was associated with more severe long-term multimorbidity trajectories. Experience of childhood food insufficiency and parental quarrel/divorce had the most prominent associations with health deterioration. Specifically, our finding was consistent with previous studies linking childhood food insufficiency with a higher risk of chronic conditions in middle and old age [45][25][46]. This might due to the fact that individuals shape physiological characteristics in early life that make them be capable of maintaining homeostasis in metabolism when challenged by a metabolic load [47][25]. Food insufficiency in childhood may lead to malnutrition, which may impair the development of metabolic capacity and increase the susceptibility to chronic diseases in the long term [47]. Additionally, our finding of the harmful effects of parental quarrel/divorce on long-

term multimorbidity trajectories extended the literature on the importance of early-life dysfunctional family relationships for physical and mental health in adulthood[48][49]. One possible explanation might be that parental quarrel/divorce would cause psychological stress in childhood [48], which causes behavioral proclivities (such as unhealthy lifestyle choices) and hormonal dysregulation (such as altered endocrine patterns) over the life span [50], and thereby giving rising to increased risks of chronic diseases [44]. By linking specific types of ELA experiences with the longitudinal development of multimorbidity, our study provided new evidence for the critical-period model that childhood adverse experiences may exert long-lasting, irreversible health-damaging effects that lead to significant health disparities in old age [22][26].

Previous studies have also documented associations between the accumulation of different ELA experiences and an increased risk of multimorbidity[51] [23]. The current study makes a further contribution by linking the accumulation of different ELA experiences with distinctive long-term trajectories of multimorbidity. Our findings supported our hypothesis that individuals who experienced more accumulated ELA were more likely to develop a more severe multimorbidity trajectory over time. This finding was consistent with the accumulation of risk model [52], suggesting that cumulative disadvantages of ELA may contribute to the persistent widening of health inequalities [31]. Initial disadvantages may cause individuals to be exposed to subsequent risk factors, such as interrupted education in adolescence, employment disadvantages and unhealthy lifestyles in adulthood, leading to greater disparities in

health status in old age [53] [54]. On the one hand, ELA such as poverty and food insufficiency may cause excessive wear and tear in the body. As people age, they are at increasing risks of chronic diseases such as arthritis. On the other hand, since China's reform and opening up in the late 1970s, with socioeconomic development, individuals who have experienced childhood adversity may have more compensatory energy intake [55], leading to hypertension, diabetes, and other cardiometabolic diseases. Notably, the influence of ELA on the multimorbidity trajectories observed above remained significant even after adjusting for demographic features, socioeconomic factors, and health behavior factors. Consistent with the existing literature linking a range of individual difference factors with later-life health development [10] [33], our result revealed that factors such as gender, marital status, educational attainment, Dibao assistance, smoking or not smoking, and physical activity exerted independent effect on multimorbidity trajectories. In specific, being female, married, having high school and above educational attainment, receiving Dibao assistance, smoking, and engaging in moderate physical activity intensity were significantly associated with a higher risk of developing more severe multimorbidity trajectories. Our study contributed to the literature by providing new evidence that ELA served as an explanatory factor influencing long-term trajectories of multimorbidity. Future research could build upon our study by further examining the impact of ELA on multimorbidity trajectories in interaction with various confounders (e.g., gender and marital status).

Our study has some key strengths. First, taking advantage of time-varying data on the

history of chronic conditions, we captured the entire course of individuals' development of multimorbidity from the first chronic disease onset to old age, with the longest time spanning 35 years. Second, our study is among the first to empirically establish the longitudinal association between ELA and long-term differential multimorbidity trajectories. Third, our study linked two important aspects of ELA experiences (specific types and accumulation of ELA) with multimorbidity trajectories, offering a more nuanced picture for testing the life-course models concerning the pathways through which ELA influences health development. Nevertheless, this study also has some limitations. First, our measures of ELA and multimorbidity were retrospective and based on self-reports, which may introduce recall bias into the data. Second, we did not consider the frequency and intensity of ELA, which was limited by data unavailability. Additionally, the issue of omitted variables may persist in our study, and future research was encouraged to employ more comprehensive datasets to investigate the relationship between potentially influential confounders (e.g., genetic inheritance and resilience) with multimorbidity trajectories. Third, our sample excluded individuals over 85 years old, which may have incurred some sample selection bias. Our research findings should thus be interpreted with caution regarding the possible underestimation of multimorbidity prevalence and trajectories in the oldest segments of the population. Considering this limitation, future research could focus on developing inclusive sampling strategies to ensure a more comprehensive representation of individuals aged 85 and above. This approach would contribute to a more comprehensive view of multimorbidity across the full age spectrum.

CONCLUSION

In conclusion, our study indicated that the development of multimorbidity shows considerable heterogeneity within the older Chinese population with respect to the onset and increased rate of conditions, and such heterogeneity can be explained by ELA experiences. The findings highlight the critical role of childhood in an individual's physical and psychological development, as childhood adversity can even influence the trajectory of multimorbidity in old age. Our findings could have the following implications. First, poverty alleviation programs or rural revitalization programs should pay specific attention to poor children and endeavor to provide them with better living conditions, thereby reducing the burden of multimorbidity in later life. Second, expanding existing child health services to include child support interventions that advance nurturing care is essential for a multisectoral effort to support families and benefit children [56]. For example, services that improve the nutritional status of infant and young children, as well as social work practice that identifies and intervenes in children's unfavorable developmental environments (e.g., family violence and parental quarrels) may be helpful. Third, clinicians should develop early preventive interventions for susceptible middle-aged and older adults (such as those with ELA experience, female gender, lower education, etc.) so as to alleviate the rapid increases in chronic diseases in later adulthood. The integral treatment or management of multimorbidity to mitigate the deleterious health consequences of ELA. Moreover, future studies that identify mechanisms linking ELA with multimorbidity is needed to

inform health management strategies and social policies that support long-term health in middle-aged and older adults.

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Competing interests

We have no conflicts of interest to disclose.

Contributors

Huiying Liu: Conceptualization, Methodology, Writing - original draft, Writing - review & editing. Mi Zhang: Writing - original draft, Formal analysis. Xinyan Zhang: Writing - original draft, Formal analysis. Xinyi Zhao: Conceptualization, Methodology, Writing - original draft, Writing - review & editing. All authors contributed to the planning, conduct and reporting of this study. All authors had full access to all data and can take responsibility for the integrity of the data analysis.

Data availability statement

Data are available in a public, open access repository. Data were derived from the China Health and Retirement Longitudinal Study (CHARLS). Researchers who want to use

these data can visit http://charls.pku.edu.cn/.

Ethics approval

The CHARLS was approved by the Peking University Ethical Review Committee. The current study is a secondary analysis of the deidentified CHARLS public data. The Ethics Review Committee granted an exempt research determination to the current study.

Table 1. Sample characteristics by ELA number in CHARLS 2018 (*N*=9,112)

Variables (%)	ELA Number				*P*-value
	0	1-2	3-4	5-7	
Number of Chronic Conditions					<0.001
0-1 condition	38.2	33.7	28.2	21.8	
2 conditions	19.5	22.8	21.5	21.1	
≥ 3 conditions	42.3	43.5	50.3	57.2	
Female	63.2	56.2	46.3	44.7	<0.001
Rural	57.7	60.8	65.7	70.8	<0.001
Marital Status					<0.001
married	71.7	78.1	80.3	81.3	
other status	28.3	21.9	19.7	18.8	
Educational Attainment					0.001
below high school	87.2	88.8	91.0	92.1	
high school and above	12.8	11.2	9.0	7.9	
Receiving *Dibao* Assistance	10.8	8.3	10.9	12.4	<0.001
Types of Medical Insurance					0.001
none	3.9	2.9	2.7	2.8	
urban employee	16.1	13.4	13.2	9.3	
urban and rural resident	76.6	81.1	81.9	86.3	
others	3.5	2.6	2.2	1.6	
Smoking	65.1	58.4	51.4	51.1	<0.001
Drinking	72.6	67.9	63.1	61.5	<0.001
Physical Activity					<0.001
none	15.7	14.2	11.8	9.5	
low intensity	40.0	35.5	31.1	26.8	
moderate intensity	29.3	27.5	26.9	26.4	
high intensity	15.0	22.8	30.2	37.2	

Notes: ELA = early life adversity. The information is from the China Health and Retirement Longitudinal Study 2018. Other status of marriage includes unmarried/divorced/separated/widowed. Urban and rural resident medical insurance integrated urban resident medical insurance and new rural cooperative medical insurance. The results of the chi-square test for variables.

Table 2. Tabulated BIC and 2ΔBIC

Number of Groups	BIC	Entropy	2(Δ BIC)
1	-308557.37	--	--
2	-253000.24	0.967	111114.26
3	-226640.40	0.975	52719.68
4	-213163.38	0.976	26954.04
5	-201166.33	0.973	23994.10
6	-193334.26	0.941	15664.14

Notes: N=9,112. BIC = Bayesian Information Criterion. The closer the entropy is to 1, the better the model fits.

Table 3. Multinomial logistic regressions for ELA experiences and multimorbidity trajectories (model 1)

Variables	Group 2 Low onset-rapidly increasing	Group 3 Middle onset-moderately increasing	Group 4 Chronically-high
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
ELA Experiences			
Parental Illness	1.059 (0.891-1.258)	1.230 (1.054-1.435)	1.885 (1.578-2.251)
Parental Death	1.032 (0.876-1.215)	1.013 (0.874-1.174)	0.980 (0.816-1.176)
Parental Quarrel/Divorce	1.214 (1.011-1.458)	1.181 (1.000-1.394)	1.262 (1.038-1.536)
Relative Poverty	1.092 (0.944-1.264)	1.210 (1.061-1.379)	1.333 (1.136-1.564)
Food Insufficiency	1.403 (1.197-1.645)	1.372 (1.190-1.582)	1.780 (1.472-2.152)
Domestic Violence	1.132 (0.982-1.305)	1.340 (1.178-1.523)	1.597 (1.360-1.876)
Bullying	1.051 (0.889-1.243)	1.215 (1.046-1.411)	1.443 (1.208-1.724)
Covariates			
Female	1.384 (1.127-1.698)	1.573 (1.308-1.893)	2.499 (1.981-3.154)
Rural	0.932 (0.797-1.089)	0.921 (0.800-1.061)	0.976 (0.819-1.162)
Marital status (ref: other status)	1.337 (1.135-1.574)	1.700 (1.464-1.974)	2.309 (1.897-2.811)
Educational attainment (ref: below high school)	0.925 (0.720-1.190)	1.085 (0.869-1.355)	1.421 (1.089-1.855)
Receiving *Dibao* Assistance (ref: no)	1.261 (0.982-1.619)	1.422 (1.134-1.783)	2.026 (1.565-1.721)
Types of Medical Insurance (ref: none)			
urban employee	1.075 (0.689-1.679)	1.241 (0.826-1.865)	1.516 (0.907-2.534)
urban and rural resident	1.019 (0.691-1.502)	1.130 (0.791-1.615)	1.166 (0.739-1.839)
others	1.084 (0.602-1.951)	1.154 (0.676-1.972)	1.347 (0.686-2.646)
Smoking (ref: no)	1.059 (0.872-1.286)	1.120 (0.941-1.335)	1.381 (1.108-1.721)
Drinking (ref: no)	0.980 (0.837-1.149)	0.952 (0.825-1.098)	0.840 (0.702-1.004)
Physical activity (ref: none)			
low intensity	0.966 (0.774-1.206)	1.009 (0.825-1.233)	0.863 (0.676-1.101)

moderate intensity	1.186 (0.938-1.498)	1.297 (1.049-1.603)	1.047 (0.811-1.352)
high intensity	1.016 (0.805-1.283)	1.082 (0.877-1.337)	0.824 (0.638-1.064)

Notes: Reference category was Group 1 ("maintaining-low"). RRR = relative risk ratios. CI = confidence interval. ELA = early life adversity. ref =reference. *p < .05; **p < .01; ***p < .001.

Table 4. Multinomial logistic regressions for ELA experiences and multimorbidity trajectories (model 2)

Variables	Group 2 Low onset-rapidly increasing	Group 3 Middle onset-moderately increasing	Group 4 Chronically-high
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
ELA (ref: none)			
1-2	1.694 (1.284-2.233)	1.512 (1.189-1.922)	1.975 (1.384-2.819)
3-4	2.066 (1.557-2.741)	2.148 (1.680-2.746)	3.746 (2.621-5.355)
5-7	2.625 (1.836-3.755)	3.427 (2.505-4.690)	7.555 (4.993-11.431)
Covariates			
Female	1.377 (1.129-1.679)	1.540 (1.287-1.841)	2.435 (1.946-3.046)
Rural	0.937 (0.805-1.090)	0.922 (0.804-1.058)	0.974 (0.822-1.154)
Marital status (ref: other status)	1.362(1.163-1.595)	1.743 (1.508-2.014)	2.362 (1.953-2.856)
Educational attainment (ref: below high school)	0.943 (0.737-1.207)	1.133 (0.912-1.408)	1.480 (1.142-1.918)
Receiving *Dibao* Assistance (ref: no)	1.256 (0.990-1.595)	1.370 (1.104-1.700)	1.962 (1.534-2.510)
Types of Medical Insurance (ref: none)			
urban employee	1.054 (0.682-1.629)	1.183 (0.794-1.762)	1.495 (0.902-2.477)
urban and rural resident	1.002 (0.684-1.466)	1.101 (0.775-1.562)	1.162 (0.714-1.822)
others	1.007 (0.565-1.793)	1.071 (0.635-1.809)	1.170 (0.602-2.275)
Smoking (ref: no)	1.065 (0.882-1.288)	1.104 (0.931-1.310)	1.381 (1.116-1.710)
Drinking (ref: no)	0.974 (0.834-1.137)	0.965 (0.839-1.109)	0.869 (0.731-1.035)

Physical activity (ref: none)			
low intensity	0.990 (0.800-1.226)	0.991 (0.817-1.201)	0.893 (0.706-1.130)
moderate intensity	1.227 (0.978-1.538)	1.270 (1.035-1.557)	1.058 (0.826-1.355)
high intensity	1.049 (0.837-1.315)	1.074 (0.877-1.317)	0.888 (0.693-1.138)

Notes: Reference category was Group 1 ("maintaining-low"). RRR = relative risk ratios. CI = confidence interval. ELA = early life adversity. ref =reference. *p < .05; **p < .01; ***p < .001.

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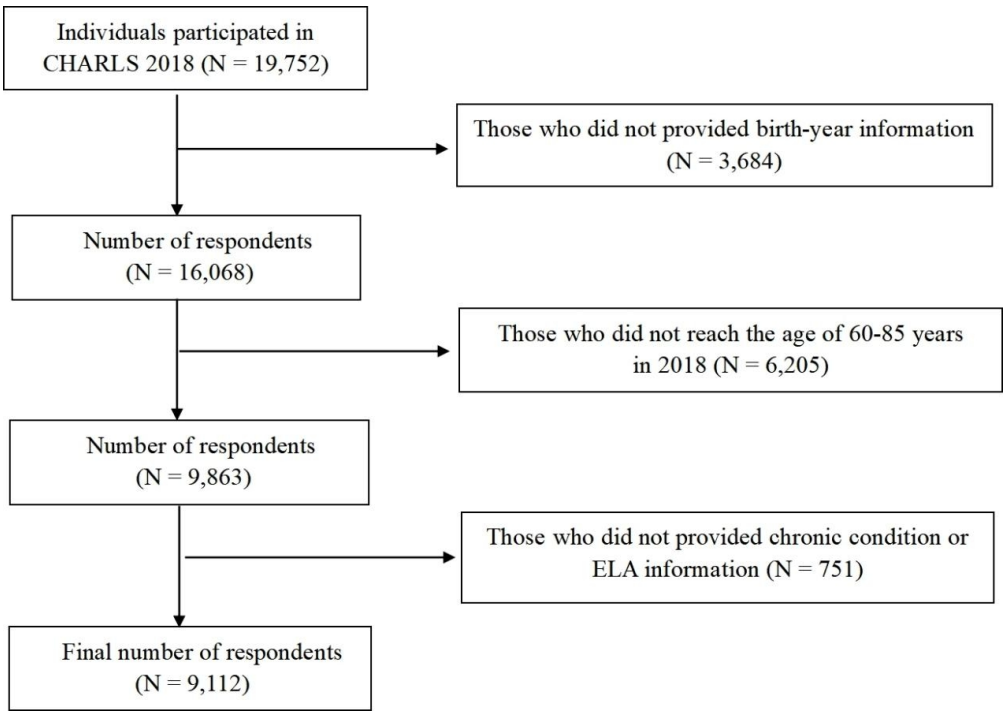
FIGURE TITLES

Figure 1. Sample selection

Figure 2. Long-term trajectories of multimorbidity



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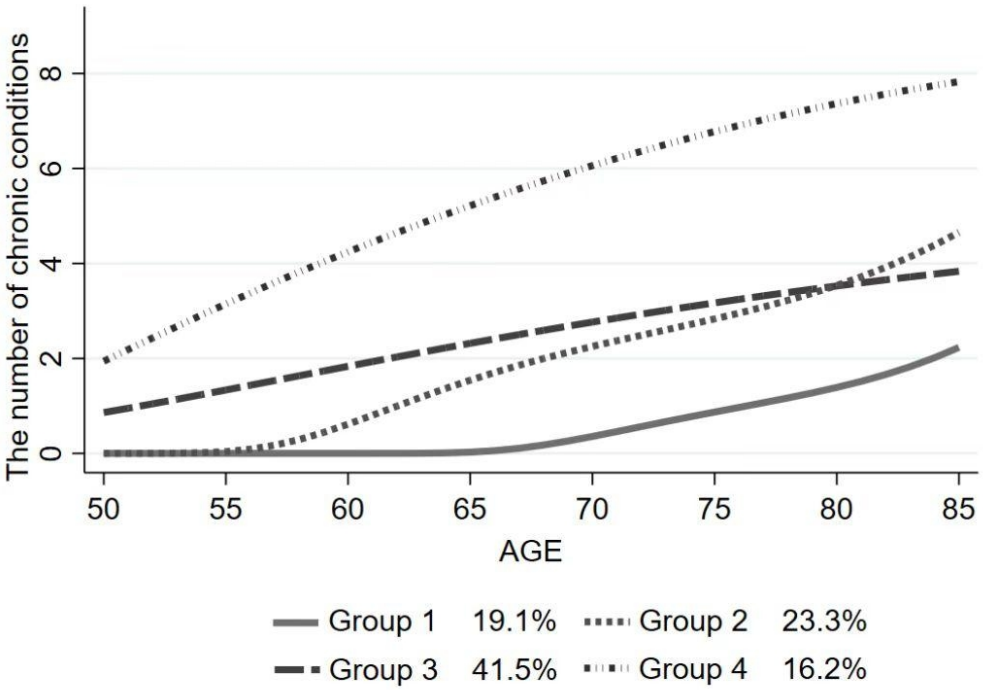

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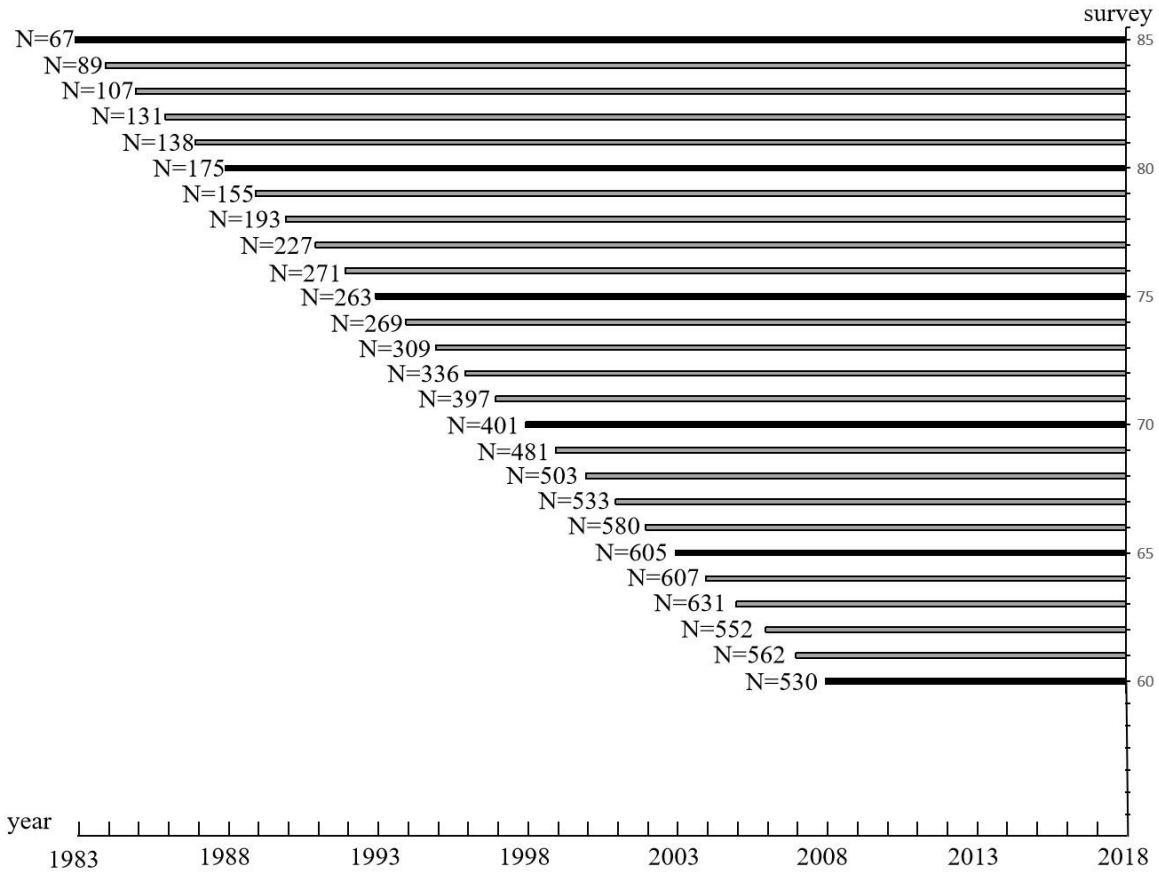
Supplemental Figures

eFigure 1 Retracing the Development of Chronic Disease in the Sample



eFigure 1 Retracing the Development of Chronic Disease in the Sample.

N = number; The total number of respondents was 9,112.

Supplemental Table1, 3-9

eTable 1 Questionnaire Items and Prevalence of Each ELA Indicator

eTable 3 Tabulated BIC and 2ΔBIC (using 12 chronic conditions)

eTable 4 Sample Characteristics by Multimorbidity Trajectories in CHARLS 2018 (N=9,112)

eTable 5 Multinomial Logistic Regression Models for nine types of ELA Experiences and Multimorbidity Trajectories

eTable 6 Multinomial Logistic Regressions for ELA Experiences (Male, N=4,440)

eTable 7 Multinomial Logistic Regressions for ELA Experiences (Female, N=4,672)

eTable 8 Multinomial Logistic Regressions for ELA Experiences (Urban, N=3,305)

eTable 9 Multinomial Logistic Regressions for ELA Experiences (Rural, N=5,807)

eTable 1 Questionnaire Items and Prevalence of Each ELA Indicator

Types of ELA	Questionnaire Items	Prevalence (%)
Parental Illness	Did your female/male guardian have a long time be sick on bed when you were young? (yes[a], no) Did your female/male guardian have a serious deformity when you were young? (yes[a], no) Did your female/male guardian have abnormality of mind when you were young? (yes[a], no)	23.5%
Parental Death	Is your biological mother/biological father alive? (yes[a], no)	23.0%
Parental Quarrel/Divorce	Did your parents often quarrel? (often[a], sometimes[a], not very often[a], never) Were your biological parents divorced? (yes[a], no)	19.3%
Relative Poverty	When you were a child before age 17, compared to the average family in the same community/village at that time, how was your family's financial situation? (a lot better off than them, somewhat better off than them, same as them, somewhat worse off than them[a], a lot worse off than them[a])	41.1%
Food Insufficiency	When you were a child before age 17 was there ever a time when your family did not have enough food to eat? (yes[a], no)	77.9%
Domestic Violence	When you were growing up, did your female/male guardian ever hit you? Was that often, sometimes, rarely, or never? (often[a], sometimes[a], rarely[a], never)	56.9%
Bullying	When you were a child, how often were you picked on or bullied by kids in your neighborhood? Is it often, sometimes, rarely or never? (often[a], sometimes[a], not very often[a], never) When you were a child, how often were you picked on or bullied by kids in your school? Is it often, sometimes, rarely or never? (often[a], sometimes[a], not very often[a], never)	26.5%
Poor Physical Health	Before you were 15 years old (including 15 years old), would you say that compared to other children of the same age, you were (much healthier, somewhat healthier, about average, somewhat less healthy[a], much less healthy[a])	13.1%
Loneliness	When you were a child, how often did you feel lonely for not having friends? Is it often, sometimes, not very often or never? (often[a], sometimes[a], not very often[a], never)	13.4%

Notes: ELA = early life adversity. [a] Answers indicate thresholds for ELA. Prevalence indicates the proportion of individuals who have experienced ELA. "Poor

Physical Health" and "Loneliness" are two additional indicators of ELA added for sensitivity analysis.

eTable 3 Tabulated BIC and 2ΔBIC (using 12 chronic conditions)

Number of Groups	BIC	Entropy	2(ΔBIC)
1	-302678.31	.	.
2	-245853.85	0.972	113648.92
3	-219850.02	0.976	52007.66
4	-206847.93	0.980	26004.18
5	-194196.80	0.979	25302.26
6	-186460.39	0.945	15472.82

Notes: The GBTM analyses using 12 chronic conditions (excluding memory-related and emotional/psychiatric problems given their low prevalence in the study population). N=9,112. BIC = Bayesian Information Criterion. The closer the entropy is to 1, the better the model fits.

eTable 4 Sample Characteristics by Multimorbidity Trajectories in CHARLS 2018 (N=9,112)

Variables (%)	Multimorbidity Trajectories				*P*-value
	Group I	Group2	Group 3	Group 4	
Female	45.8	51.0	51.7	57.1	<0.001
Rural	65.1	63.6	63.0	64.3	0.464
Marital Status					<0.001
married	72.3	77.3	81.2	83.6	
other status	27.7	22.7	18.8	16.4	
Educational Attainment					0.116
below high school	90.4	90.9	89.8	88.5	
high school and above	9.6	9.1	10.2	11.5	
Receiving *Dibao* Assistance	92.0	90.6	90.1	86.8	<0.001
Types of Medical Insurance					0.656
none	3.3	3.2	2.8	2.3	
urban employee	12.2	12.5	13.2	14.1	
urban and rural resident	82.0	82.0	81.7	81.2	
others	2.6	2.3	2.3	2.4	
Smoking	52.2	55.3	55.6	56.9	0.038
Drinking	63.2	65.3	65.2	69.3	0.004
Physical Activity					0.020
none	13.6	12.6	12.1	13.7	
low intensity	35.7	33.0	31.9	32.8	
moderate intensity	23.8	27.6	28.7	26.9	
high intensity	26.9	26.7	27.4	26.6	

Notes: ELA = early life adversity. The information is from the China Health and Retirement Longitudinal Study 2018. Other status of marriage includes unmarried/divorced/ separated/widowed. Urban and rural resident medical insurance integrated urban resident medical insurance and new rural cooperative medical insurance.The results of the chi-square test for variables.

eTable 5 Multinomial Logistic Regression Models for nine types of ELA Experiences and Multimorbidity Trajectories

Variables	Group 2 Low onset-rapidly increasing	Group 3 Middle onset-moderately increasing	Group 4 Chronically-high
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Model 1			
Parental Illness	1.050 (0.883-1.250)	1.220 (1.044-1.425)*	1.816 (1.517-2.173)***
Parental Death	1.015 (0.860-1.197)	0.994 (0.856-1.154)	0.935 (0.777-1.125)
Parental Quarrel/Divorce	1.206 (1.003-1.449)*	1.166 (0.986-1.377)	1.230 (1.010-1.499)*
Relative Poverty	1.069 (0.922-1.238)	1.176 (1.030-1.344)*	1.229 (1.045-1.446)*
Food Insufficiency	1.413 (1.204-1.659)***	1.366 (1.183-1.576)***	1.768 (1.461-2.141)***
Domestic Violence	1.128 (0.978-1.302)	1.343 (1.180-1.528)***	1.586 (1.349-1.865)***
Bullying	1.046 (0.882-1.239)	1.188 (1.021-1.383)*	1.377 (1.149-1.650)**
Poor Physical Health	1.333 (1.050-1.692)*	1.613 (1.302-1.998)***	2.317 (1.827-2.939)***
Loneliness	0.973 (0.785-1.207)	1.028 (0.848-1.246)	1.160 (0.924-1.458)
Model 2			
ELA (ref: none)			
1-2	1.668 (1.248-2.229)**	1.483 (1.151-1.910)**	2.119 (1.430-3.138)***
3-4	2.088 (1.556-2.803)***	2.205 (1.706-2.851)***	4.088 (2.760-6.054)***
5-9	2.278 (1.632-3.180)***	3.016 (2.254-4.035)***	7.862 (5.173-11.947)***

Notes: Reference category was Group 1 ("maintaining-low"). RRR = relative risk ratios. CI = confidence interval. ELA = early life adversity. ref =reference. *p < .05; **p < .01; ***p < .001. Model adjusted for gender, residence area, marital status, educational attainment, types of medical insurance, and whether receive *Dibao* assistance, smoking, drinking, and physical activity.

eTable 6 Multinomial Logistic Regressions for ELA Experiences (Male, N=4,440)

Variables	Group 2 Low onset-rapidly increasing	Group 3 Middle onset-moderately increasing	Group 4 Chronically-high
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Model 1			
Parental Illness	0.884 (0.693-1.128)	1.140 (0.923-1.407)	1.756 (1.363-2.261)***
Parental Death	1.028 (0.820-1.288)	1.052 (0.860-1.286)	1.045 (0.808-1.351)
Parental Quarrel/Divorce	1.111 (0.862-1.433)	1.172 (0.935-1.469)	1.134 (0.855-1.505)
Relative Poverty	1.053 (0.861-1.288)	1.216 (1.016-1.454)*	1.343 (1.069-1.687)*
Food Insufficiency	1.444 (1.151-1.812)**	1.548 (1.263-1.897)***	1.873 (1.404-2.499)***
Domestic Violence	1.056 (0.864-1.290)	1.196 (0.998-1.434)	1.440 (1.130-1.835)**
Bullying	0.957 (0.769-1.190)	1.124 (0.928-1.362)	1.324 (1.042-1.683)*
Model 2			
ELA (ref: none)			
1-2	2.145 (1.365-3.370)**	1.621 (1.108-2.372)*	1.919 (1.072-3.435)*
3-4	2.241 (1.425-3.524)***	2.249 (1.539-3.287)***	3.018 (1.695-5.374)***
5-7	2.284 (1.341-3.891)**	3.214 (2.058-5.020)***	6.224 (3.316-11.683)***

Notes: Reference category was Group 1 ("maintaining-low"). RRR = relative risk ratios. CI = confidence interval. ELA = early life adversity. ref =reference. *p < .05; **p < .01; ***p < .001. Model adjusted for residence area, marital status, educational attainment, types of medical insurance, and whether receive *Dibao* assistance, smoking, drinking, and physical activity.

eTable 7 Multinomial Logistic Regressions for ELA Experiences (Female, N=4,672)

Variables	Group 2 Low onset-rapidly increasing	Group 3 Middle onset-moderately increasing	Group 4 Chronically-high
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Model 1			
Parental Illness	1.273 (0.993-1.633)	1.351 (1.076-1.696)*	2.061 (1.599-2.656)***
Parental Death	1.030 (0.810-1.308)	0.965 (0.775-1.201)	0.905 (0.697-1.176)
Parental Quarrel/Divorce	1.321 (1.012-1.724)*	1.194 (0.934-1.527)	1.374 (1.041-1.815)*
Relative Poverty	1.128 (0.912-1.395)	1.217 (1.003-1.477)*	1.332 (1.061-1.670)*
Food Insufficiency	1.350 (1.078-1.690)**	1.234 (1.009-1.509)*	1.699 (1.315-2.195)***
Domestic Violence	1.219 (0.993-1.497)	1.521 (1.263-1.831)***	1.777 (1.426-2.215)***
Bullying	1.254 (0.959-1.640)	1.401 (1.098-1.789)**	1.692 (1.286-2.227)***
Model 2			
ELA (ref: none)			
1-2	1.412 (0.991-2.013)	1.445 (1.057-1.975)*	1.949 (1.241-3.060)**
3-4	2.013 (1.390-2.916)***	2.147 (1.546-2.983)***	4.408 (2.784-6.979)***
5-7	3.588 (2.120-6.074)***	4.212 (2.601-6.819)***	9.444 (5.237-17.030)***

Notes: Reference category was Group 1 ("maintaining-low"). RRR = relative risk ratios. CI = confidence interval. ELA = early life adversity. ref =reference. *p < .05; **p < .01; ***p < .001. Model adjusted for residence area, marital status, educational attainment, types of medical insurance, and whether receive *Dibao* assistance, smoking, drinking, and physical activity.

eTable 8 Multinomial Logistic Regressions for ELA Experiences (Urban , N=3,305)

Variables	Group 2 Low onset-rapidly increasing	Group 3 Middle onset-moderately increasing	Group 4 Chronically-high
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Model 1			
Parental Illness	1.086 (0.794-1.484)	1.198 (0.905-1.585)	1.673 (1.210-2.313)**
Parental Death	1.060 (0.793-1.416)	1.021 (0.786-1.327)	1.031 (0.746-1.425)
Parental Quarrel/Divorce	1.207 (0.889-1.639)	1.110 (0.841-1.465)	1.195 (0.860-1.662)
Relative Poverty	1.111 (0.858-1.438)	1.324 (1.049-1.670)*	1.419 (1.072-1.879)*
Food Insufficiency	1.518 (1.170-1.970)**	1.415 (1.123-1.784)**	1.837 (1.355-2.490)***
Domestic Violence	1.166 (0.917-1.484)	1.385 (1.115-1.722)**	1.640 (1.249-2.154)***
Bullying	1.069 (0.800-1.429)	1.250 (0.965-1.619)	1.689 (1.246-2.291)**
Model 2			
ELA (ref: none)			
1-2	1.709 (1.118-2.614)*	1.821 (1.245-2.663)**	2.378 (1.365-4.143)**
3-4	2.113 (1.359-3.285)**	2.652 (1.788-3.933)***	4.394 (2.497-7.732)***
5-7	3.195 (1.718-5.944)***	4.463 (2.546-7.824)***	9.875 (4.867-20.032)***

Notes: Reference category was Group 1 ("maintaining-low"). RRR = relative risk ratios. CI = confidence interval. ELA = early life adversity. ref =reference. *p < .05; **p < .01; ***p < .001. Model adjusted for gender, marital status, educational attainment, types of medical insurance, and whether receive *Dibao* assistance, smoking, drinking, and physical activity.

eTable 9 Multinomial Logistic Regressions for ELA Experiences (Rural, N=5,807)

Variables	Group 2 Low onset-rapidly increasing	Group 3 Middle onset-moderately increasing	Group 4 Chronically-high
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Model 1			
Parental Illness	1.049 (0.852-1.290)	1.244 (1.034-1.496)*	2.009 (1.623-2.486)***
Parental Death	1.022 (0.837-1.246)	1.011 (0.845-1.209)	0.963 (0.772-1.202)
Parental Quarrel/Divorce	1.214 (0.965-1.526)	1.218 (0.990-1.498)	1.294 (1.013-1.653)*
Relative Poverty	1.086 (0.910-1.296)	1.160 (0.989-1.360)	1.304 (1.072-1.584)**
Food Insufficiency	1.337 (1.093-1.636)**	1.339 (1.117-1.605)**	1.761 (1.379-2.250)***
Domestic Violence	1.118 (0.937-1.334)	1.321 (1.126-1.549)**	1.586 (1.298-1.936)***
Bullying	1.040 (0.846-1.279)	1.203 (1.001-1.446)*	1.337 (1.073-1.666)*
Model 2			
ELA (ref: none)			
1-2	1.693 (1.173-2.442)**	1.325 (0.971-1.810)	1.762 (1.107-2.803)*
3-4	2.037 (1.405-2.954)***	1.856 (1.354-2.545)***	3.429 (2.156-5.453)***
5-7	2.426 (1.547-3.804)***	2.917 (1.983-4.291)***	6.606 (3.920-11.132)***

Notes: Reference category was Group 1 ("maintaining-low"). RRR = relative risk ratios. CI = confidence interval. ELA = early life adversity. ref =reference. *p < .05; **p < .01; ***p < .001. Model adjusted for gender, marital status, educational attainment, types of medical insurance, and whether receive *Dibao* assistance, smoking, drinking, and physical activity.

STROBE Statement—checklist of items that should be included in reports of observational studies (Page numbers refer to those on original submitted word document)

For manuscript: "Early-Life Adversity Predicts Distinct Trajectories of Multimorbidity with Ageing from 50 to 85 years: A Nationwide Longitudinal Study" , submitted by Huiying Liu et al., 075834

	Item No	Recommendation	Item page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-8
Objectives	3	State specific objectives, including any prespecified hypotheses	7-8
Methods			
Study design	4	Present key elements of study design early in the paper	8-14
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8-9
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8-9
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	10-11
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	8-14
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	8-9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11-13
		(*b*) Describe any methods used to examine subgroups and interactions	11-13
		(*c*) Explain how missing data were addressed	N/A
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	14

Continued on next page

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	8-9 (plus Figure 1)
		(b) Give reasons for non-participation at each stage	8-9 (plus Figure 1)
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	14-15
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	14-17
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	17
Discussion			
Key results	18	Summarise key results with reference to study objectives	17-23
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	21-22
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17-23
Generalisability	21	Discuss the generalisability (external validity) of the study results	17-23
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	23-24

*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.