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The relationship between self-reported adverse experiences and depressive symptoms among middle-aged and elderly individuals: A longitudinal study based on the CHARLS database

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ABSTRACT

Background: Adverse experiences are critical determinants of late-life depressive symptomatology. Understanding how these experiences influence later-life health outcomes remains a research priority. This study examines the longitudinal associations between self-reported adverse childhood experiences (ACEs) and adverse adult experiences (AAEs) with depressive symptoms in older adults, as well as the underlying mechanisms.
Methods: A sample of 3941 adults aged ≥45 years from the China Health and Retirement Longitudinal Study (CHARLS) was analyzed. K-means for Longitudinal Data (KML), Logistic regression, and Bayesian Kernel Machine Regression (BKMR) models were employed to assess the effects of adverse experiences. Subgroup and mediation analyses were also performed.
Results: The high depressive symptomatology cluster (n = 1432) demonstrated significant associations with six ACEs: childhood hunger (OR = 1.23, 95%CI:1.03–1.47), dangerous growth environments (OR = 1.34, 95% CI:1.09–1.65), childhood loneliness (OR = 1.45, 95%CI:1.20–1.74), bullying (OR = 1.2, 95%CI:1.01–1.43), parental depression (OR = 1.80, 95%CI:1.50–2.16), and parental disability (OR = 1.44, 95%CI:1.03–2.02). Comprehensive effect estimation of ACEs indicated an 85.9% probability of a high depression score for those with all adverse experiences. AAEs like prolonged bed rest (OR = 1.39, 95%CI:1.08–1.79), and lifetime discrimination (OR = 1.37, 95%CI:1.12–1.66) independently predicted symptom severity. Effect modification analysis revealed stronger ACE impacts among individuals with higher cognitive reserve (OR = 3.32, 95% CI:2.34–4.70). Mediation analysis identified arthritis or rheumatism as a partial mediator of the ACE-depression pathway (natural indirect effect = 1.04, 95%CI:1.02–1.05).
Conclusions: Self-reported ACEs and AAEs demonstrate persistent associations with depressive symptoms in later life, mediated by chronic morbidity and moderated by cognitive reserve.

1. Background

With the global population aging, mental health issues among older adults have emerged as a growing public health concern. As a prevalent psychiatric disorder, depression substantially impairs the quality of life, social functioning, and physical health in older populations (Alexopoulos, 2005). This condition imposes significant burdens on both familial caregivers and healthcare systems. According to World Health Organization projections, depression is anticipated to become the primary contributor to global disease burden by 2030, having currently ranked third (Malhi and Mann, 2018). Consequently, elucidating depression-related risk factors, investigating its developmental pathways, and examining the lifelong impacts of early-life experiences on geriatric mental health constitute essential research priorities in psychological and gerontological studies.

Adverse Childhood Experiences (ACEs) encompass traumatic exposures occurring before adulthood (age <18 years), comprising three principal domains: 1) abuse (physical, emotional, Genderual), 2) neglect

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(physical, emotional), and 3) household dysfunction (domestic violence, parental divorce, substance abuse, mental illness, incarceration) (Felitti et al., 1998). These adversities trigger biologically embedded toxic stress responses, resulting in chronic dysregulation of neuroendocrine-immune axis homeostasis (Bucci et al., 2016; Danese and McEwen, 2012; Pechtel and Pizzagalli, 2011). A dose-response relationship has been established, with meta-analytic evidence indicating 52% increased depression risk per additional ACE exposure during adulthood (Danielsdottir et al., 2024). Nevertheless, current measurement approaches predominantly rely on cumulative ACE counts (Bucci et al., 2016; Danielsdottir et al., 2024; Neves et al., 2021) or conventional regression models (e.g. linear regression, logistic regression). These methods inherently assume linear dose-response relationships and fail to quantitatively disentangle the complex, non-additive effects of multiple ACEs exposure, particularly when accounting for potential interactions or threshold effects among specific adversities.

Adverse Adult Experiences (AAEs), operationalized as traumatic exposures occurring during adulthood (≥18 years), encompass five principal categories: (1) economic hardship, (2) unemployment, (3) intimate partner violence, (4) major illness, and (5) bereavement (Wang et al., 2023a; Cao et al., 2022a). These exposures are associated with clinically significant psychiatric sequelae, including post-traumatic stress disorder (PTSD) and generalized anxiety disorder (Adams et al., 2024), with heightened vulnerability observed in populations with chronic stress exposure histories. Mechanistically, AAEs demonstrate robust associations with incident cardiometabolic disorders through persistent inflammation and dysregulation of stress pathways (Li et al., 2024a). When combined with ACEs, AAEs amplify the "double-hit" effect, significantly increasing the likelihood of long-term health complications and reduced resilience (Li et al., 2024a).

The association between ACEs and geriatric depression has been extensively documented in epidemiological studies. During later-life transitions involving retirement, widowhood, and chronic disease accumulation, latent effects of early-life trauma may manifest through epigenetic mechanisms and maladaptive coping patterns (Ege et al., 2015; Iob et al., 2020; Wang et al., 2024). Notably, exposure to ACEs may increase the risk of encountering adversity and perceiving greater stress in adulthood (Crielaard et al., 2021; Korkeila et al., 2010). AAEs may serve as triggers linking ACEs to adult health outcomes. Meanwhile, protective psychosocial factors including cognitive resilience and perceived social support demonstrate moderating effects, albeit with significant socioeconomic gradient (Ren et al., 2023).

The dual exposure framework necessitates an integrated investigation of ACEs and AAEs. Nevertheless, limited empirical evidence exists regarding the synergistic effects of ACEs-AAEs co-exposure on geriatric depression trajectories. Although prior research (Li et al., 2024b; Sun et al., 2024) has established depressive symptoms as mediators between ACEs and chronic comorbidities, the reverse mediation pathway through chronic conditions remains understudied. Furthermore, the moderating effects of psychosocial factors, including social engagement and cognitive reserve, require systematic examination.

Therefore, this study utilizes China Health and Retirement Longitudinal Study (CHARLS) data with Bayesian Kernel Machine Regression (BKMR) within a biopsychosocial framework to: (1) delineate independent, cumulative, and interactive effects of ACEs/AAEs on geriatric depression; (2) identify mediating roles of chronic diseases; (3) assess buffering effects of cognitive reserve and social engagement. The mechanistic insights from this analysis may inform multilevel interventions targeting developmental stressors across the life course in geriatric populations.

2. Methods

2.1. Study population

This study employed data from the CHARLS, a nationally representative survey covering adults aged ≥45 years across 150 counties/districts and 450 villages/urban communities in 28 Chinese provinces (including autonomous regions and municipalities). The survey methodology has been detailed in prior publications (Zhao et al., 2014). Five major survey waves were completed: a 2011 baseline followed by follow-ups in 2013, 2015, 2018, and 2020. Additionally, a 2014 Life History Survey captured retrospective life-course data from participants' birth onward. Data were drawn from the 2014 Life History Survey combined with the 2011–2020 CHARLS waves.

The Harmonized CHARLS dataset (2011–2018) provided the initial sample pool (n = 25,586). Through sequential 1:1 matching (first with 2014 Life History Survey data, then with 2020 CHARLS data), 19,098 participants with complete longitudinal records were retained.

Three sequential exclusion criteria were applied: First, 493 participants aged <45 years were excluded. Second, 7590 individuals with incomplete ACEs/AAEs records were removed. Third, 7074 cases lacking baseline covariates (including demographic characteristics, socioeconomic status, and health indicators) were excluded.

The exclusion process yielded a final analytical sample of 3941 participants (see Figure S1; All supplementary materials use "S" prefix notation, whereas main text elements employ numeric-only labels). The cohort had a mean age of 57.6±8.27 years, comprising 53.9% female and 46.1% male participants. Key baseline characteristics (e.g. smoking status, education level, chronic disease prevalence) are comprehensively summarized in the Supplementary Materials (see Table S1).

Missing data were addressed through complete-case analysis, where only participants with complete data on exposure variables (ACEs/AAEs) and outcome-related covariates were included.

2.2. Definition of ACEs and AAEs

Ten standardized ACE items were identified: parental divorce, childhood hunger, dangerous growth environment, childhood loneliness, bullying, parental depression, parental substance dependence, parental incarceration, parental disability, and parental physical abuse. Parental substance dependence was operationally defined as maternal/paternal engagement in ≥1 high-risk behavior including alcohol abuse, substance use, or pathological gambling. Parental incarceration encompassed any parental history of criminal conviction, arrest, or imprisonment. All ACE items were dichotomized. The BKMR modeling results informed the creation of a composite ACE score (0 = low risk, 1 = high risk)

Five AAE items were derived from the CHARLS dataset following established protocols (Cao et al., 2022b; Wang et al., 2023b): death of a child, lifetime discrimination, prolonged bed rest, extended hospitalization, and ever leaving a job due to health conditions. Operational definitions are provided in the Supplementary Materials (see Table S2). All items were dichotomized.

All adverse experience data were collected via standardized CHARLS self-report questionnaires. The retrospective recall validity was confirmed through previous CHARLS studies (Cao et al., 2022b; Wang et al., 2023b).

2.3. Assessment of depressive symptoms

Depressive symptoms were assessed using the 10-item Center for Epidemiologic Studies Depression Scale (CES-D 10) in CHARLS (Chen and Mui, 2014). Full item descriptions are available in the Supplementary Materials (see Table S3). Participants were asked to report symptom frequency during the preceding week. The scale evaluates core depressive domains including depressed mood, sleep difficulties, appetite changes, and concentration problems. Responses were coded as: 0 (rarely, <1 day), 1 (some, 1–2 days), 2 (occasionally, 3–4 days), or 3 (most, 5–7 days). Summed scores ranged from 0 to 30. A cutoff score >10 indicated probable depression per established criteria (Li et al., 2022).

2.4. Covariates

Demographic characteristics were collected, including age, Gender, residential location, educational attainment, and marital status. Health behaviors were assessed through smoking status, alcohol use patterns, and social engagement level. Health status was evaluated using cognitive function scores, self-rated health trajectory, and Self-reported physician-diagnosed diseases (including 12 diseases such as hypertension, diabetes, cancer, etc.). A complete list of covariates is provided in the Supplementary Materials (see Table S4)

Social engagement was assessed through an 11-item checklist querying participation in social activities during the preceding month ("Have you done any of these activities in the last month? (Check all that apply)"). Each endorsed activity received one point, yielding a maximum total score of 11. Higher scores reflected greater social engagement intensity.

Cognitive function was evaluated through both immediate and delayed word recall tests. Participants were administered a 10-word list recall task under two conditions: immediate and delayed recall. Correct responses were scored 1 point per word, yielding a maximum composite score of 20 (10 points per subtest). Higher total scores corresponded to superior cognitive performance.

Self-rated health trajectory was assessed through participant responses to the following question: "How has your health status changed since your last interview?". Responses were coded into three categories: improved (score = 1), stable (score = 2), or worsened (score = 3).

2.5. Statistical analysis

Continuous variables were summarized as medians with interquartile ranges (IQR), whereas categorical variables were presented as frequencies (percentages). Group comparisons employed three statistical tests: Kruskal-Wallis H test, χ^2 test, and Freedman-Diaconis test. A binary logistic regression model was constructed to examine the effects of ACEs, AAEs, chronic diseases, and other factors on depression score trajectories.

The K-means for Longitudinal Data (KML) (Genolini and Falissard, 2011) was implemented to analyze temporal patterns in depression scores, cognitive function, social engagement level, and self-rated health trajectories. This non-parametric method accommodates unequal measurement intervals and missing data while utilizing multiple information criteria for optimal cluster determination.

The Bayesian Kernel Machine Regression (BKMR) model was employed to assess the combined and interaction effects of ACEs in multivariable analyses. This approach accommodates high-dimensional exposures without linearity constraints, automatically identifying nonlinear associations and interaction patterns (Bobb et al., 2015; Valeri et al., 2017). Model parameters were estimated via Markov chain Monte Carlo (MCMC) algorithms with 5000 iterations.

Additionally, subgroup analyses (stratified by gender, self-rated health trajectories, cognitive function trajectories, etc.) were conducted to explore interaction effects. Associations were reassessed following adjustment for demographic confounders and chronic disease status. A causal mediation analysis evaluated potential pathways through which chronic diseases might mediate ACEs-depression associations. Technical details of KML and BKMR implementations are available in Supplementary Materials Section 6.

Sensitivity analyses were performed to address measurement bias from three sources: self-report inaccuracies, recall errors, and missing variables. These included: (1) logistic regression validation through k-fold cross-validation; (2) BKMR-based subgroup analysis; and (3) E-value quantification of unmeasured confounding resistance. Methodological details and sensitivity analysis results are provided in Supplementary Materials.

All statistical analyses were conducted using R 4.3.0, except mediation analysis performed in Stata 17.0. Two-sided tests were employed, with statistical significance defined as $P \leq 0.05$.

3. Results

3.1. Baseline population analysis

Baseline characteristics are detailed in Supplementary (see Table S1). Briefly, the cohort demonstrated a mean age of 57.57±8.27 years with near-equal Gender distribution (53.9% female). Current or former smokers comprised 30.7% of participants, while 9.9% attained secondary education.

Cluster analysis identified longitudinal trajectory patterns for depression, cognitive function, social engagement, and self-rated health (see Supplementary materials for details). Two distinct depression trajectories emerged: Low-Stable (63.7%) showing sustained low scores, and High-Rising (36.3%) demonstrating progressive elevation. Cognitive trajectories bifurcated into Low-Declining (52.9%) with accelerated deterioration and High-Stable (47.1%) preserving baseline function. Social engagement patterns comprised Low (74.6%: persistently minimal) and Medium (25.4%: transient moderate increase followed by decline). Six unique self-rated health trajectories were identified (detailed in Supplementary Materials Section 7).

When comparing depression trajectory groups, the High Rising Group exhibited a higher proportion of low cognitive function (66.1% vs. 43.8%) and worse self-rated health trajectories ("Same to Worse": 31.4% vs. 21.6%; "Keep Worse": 20.6% vs. 11.2%). Gender distribution differed markedly, with male representation at 31.3 % in High-Rising versus 54.6 % in Low-Stable. Lung disease and heart problems were more prevalent in the High Rising Group. Notably, ACEs and AAEs were more common in the High Rising Group, particularly childhood hunger, dangerous growth environments, childhood loneliness, bullying, parental depression, loss of a child, lifetime discrimination, prolonged bed rest, extended hospitalization, and health-related job loss.

3.2. Analysis of logistic regression

The final multivariate logistic regression model incorporated all variables demonstrating statistical significance in preliminary univariate analyses (Table 1).

Following full covariate adjustment, six ACEs retained statistical significance as depression trajectory predictors. The effect magnitudes decreased sequentially from parental depression (OR = 1.80, 95% CI:1.50–2.16) to bullying(OR = 1.20, 95%CI:1.01–1.43), with childhood loneliness (OR = 1.45, 95%CI:1.20–1.74), parental disability (OR = 1.44, 95%CI:1.03–2.02), dangerous growth environments (OR = 1.34, 95%CI:1.09–1.65), and childhood hunger (OR = 1.23, 95% CI:1.03–1.47) showing intermediate effects.

Three AAEs showed significant associations with elevated depression risk: prolonged bed rest (OR = 1.39, 95%CI:1.08–1.79), extended hospitalization (OR = 1.34, 95%CI:1.01–1.78), and lifetime discrimination (OR = 1.14, 95%CI:1.01–1.54)

In addition, participants maintaining stable high cognitive function demonstrated 51 % lower depression risk versus those with cognitive decline (OR = 0.49, 95%CI:0.42–0.58). Regarding self-rated health, all self-rated health trajectories except "Same to Worse" showed significantly reduced depression risk ($P < 0.05$).

Gender and residential location were significantly associated with depression risk. Females demonstrated nearly threefold increased risk versus males (OR = 2.87, 95%CI:2.31–3.56), while urban residents showed 40 % lower risk compared to rural areas (OR = 0.60, 95%CI: 0.50–0.71). Moreover, chronic conditions including heart disease, arthritis or rheumatism, liver disease, and particularly kidney disease (OR = 2.26, 95%CI:1.61–3.18), were statistically associated with elevated depression risk.

Table 1
Predictors of depression score trajectory in Logistic Regression.

Predictor	Reference level	Estimate	SE	z	*P*	OR	95 % CI	
							Lower	Upper
Intercept		−1.37	0.173	−7.921	<0.001	0.254	0.181	0.357
Childhood Hunger								
Yes	No	0.205	0.09	2.263	0.024	1.227	1.028	1.465
Dangerous growth environment								
Yes	No	0.292	0.106	2.768	0.006	1.34	1.089	1.648
Childhood loneliness								
Yes	No	0.369	0.096	3.861	<0.001	1.446	1.199	1.744
Bullying								
Yes	No	0.182	0.089	2.057	0.04	1.2	1.009	1.428
Parental depression								
Yes	No	0.588	0.093	6.34	<0.001	1.8	1.501	2.159
Parental disability								
Yes	No	0.364	0.173	2.102	0.036	1.439	1.025	2.019
Cognitive function								
Hihg Stable Group	Low Declining Group	−0.711	0.082	−8.629	<0.001	0.491	0.418	0.577
Self-rated health changes								
Same to Worse	Keep Worse	−0.216	0.12	−1.795	0.073	0.806	0.636	1.02
Same-Better-Worse	Keep Worse	−0.579	0.182	−3.191	0.001	0.56	0.392	0.8
Same-Worse-Same	Keep Worse	−1.018	0.131	−7.759	<0.001	0.361	0.279	0.467
Worse to Same	Keep Worse	−0.877	0.132	−6.651	<0.001	0.416	0.321	0.539
Worse-Same-Worse	Keep Worse	−0.329	0.148	−2.22	0.026	0.72	0.539	0.962
Gender								
Woman	Man	1.054	0.11	9.542	<0.001	2.868	2.31	3.562
Education								
Tertiary	Less than lower secondary	−13.885	208.346	−0.067	0.947	0	–	–
Upper secondary & Vocational training	Less than lower secondary	−0.318	0.169	−1.889	0.059	0.727	0.523	1.012
Marriage								
Divorced	Married	0.273	0.612	0.445	0.656	1.313	0.396	4.359
Never Married	Married	−0.291	0.973	−0.299	0.765	0.748	0.111	5.03
Partnered	Married	0.063	0.166	0.376	0.707	1.064	0.769	1.474
Separated	Married	0.466	0.672	0.693	0.488	1.594	0.427	5.952
Widowed	Married	0.305	0.14	2.172	0.03	1.356	1.03	1.785
resident								
Urban Community	Rural Village	−0.513	0.088	−5.832	<0.001	0.599	0.504	0.711
Lung disease								
Yes	No	−0.032	0.154	−0.204	0.838	0.969	0.716	1.312
Heart problem								
Yes	No	0.351	0.122	2.869	0.004	1.42	1.118	1.804
Arthritis or rheumatism								
Yes	No	0.626	0.081	7.754	<0.001	1.87	1.596	2.191
Liver disease								
Yes		0.566	0.223	2.535	0.011	1.762	1.137	2.73
Kidney disease	No							
Yes		0.815	0.174	4.696	<0.001	2.26	1.608	3.176
Stomach or other digestive disease								
Yes	No	0.391	0.094	4.141	<0.001	1.478	1.229	1.779
Asthma								
Yes	No	0.933	0.223	4.182	<0.001	2.541	1.641	3.934
drink								
Yes	No	−0.111	0.096	−1.157	0.247	0.895	0.741	1.08
smoke								
Yes	No	0.213	0.111	1.93	0.054	1.238	0.997	1.538
Death of a child								
Yes	No	0.136	0.111	1.218	0.223	1.145	0.921	1.425
Lifetime discrimination								
Yes	No	0.294	0.131	2.247	0.025	1.342	1.038	1.734
Prolonged bed rest								
Yes	No	0.329	0.13	2.532	0.011	1.389	1.077	1.791
Extended hospitalization								
Yes	No	0.374	0.138	2.714	0.007	1.454	1.11	1.905
ever leaving a job due to health conditions								
Yes	No	0.191	0.119	1.607	0.108	1.211	0.959	1.528

Note. Estimates represent the log odds of "depression score trajectory = High Rising Group" vs. " depression score trajectory = Low Stable Group".

3.3. BKMR—Analysis of cumulative and interaction effects

Six ACEs (childhood hunger, dangerous environments, loneliness, bullying, parental depression, and parental disability) were selected for BKMR modeling based on multivariate significance, adjusting for cognitive function, Gender, and covariates.

Cumulative ACE effects were assessed using zero exposure as a reference. Fig. 1 demonstrates dose-dependent risk escalation, where effects intensified with exposure accumulation. At lower percentiles (10th-20th), null exposure corresponded to baseline risk ($b = 0$). Childhood hunger alone (30th-70th percentiles) produced limited effects ($b = 0.13$). At higher exposures (80th-90th percentiles, excluding parental disability), effects escalated markedly ($b = 0.88$ and 0.94). Maximum cumulative risk ($b = 1.07$) emerged at full six-ACE exposure (100th percentile).

Effect sizes were translated into predicted probabilities of High-

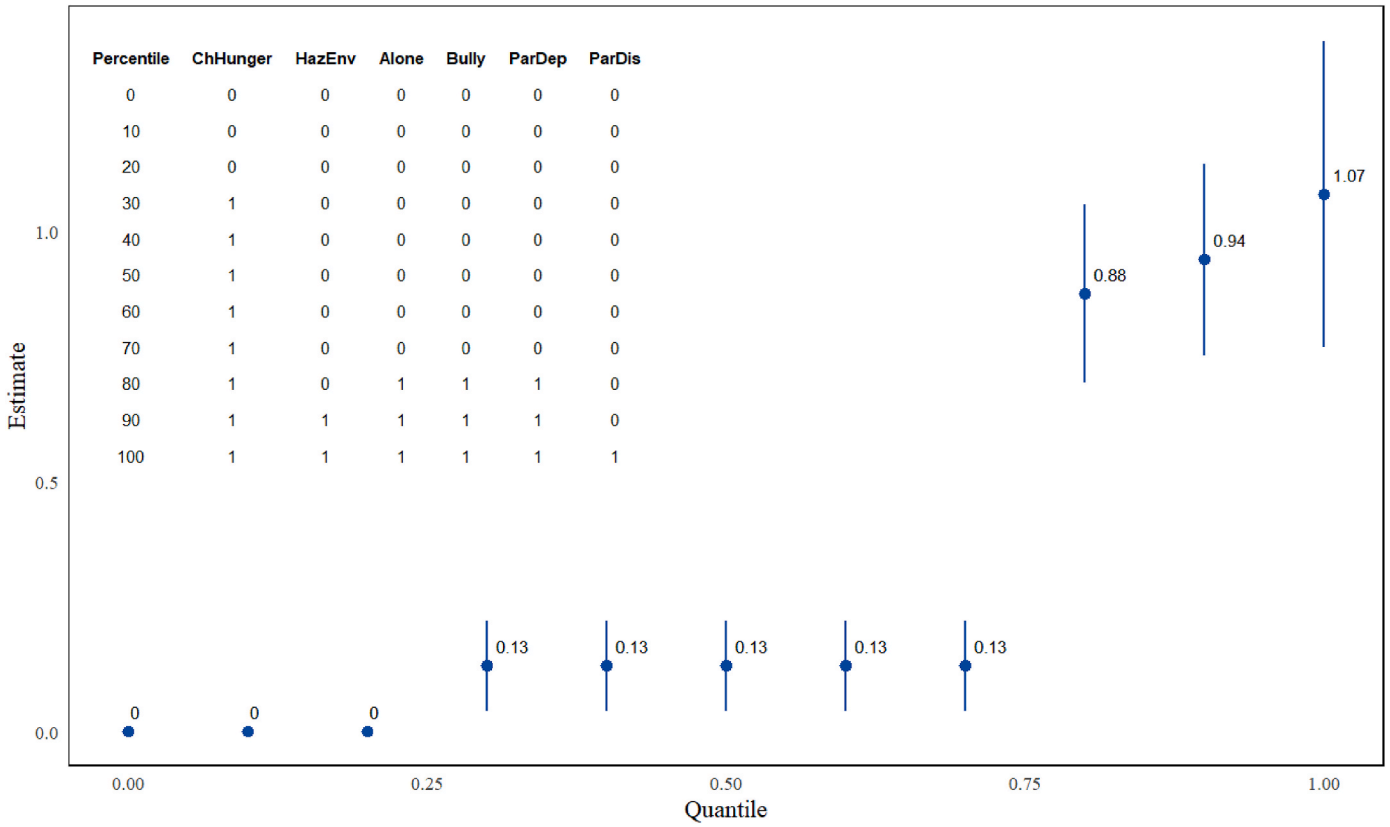

Fig. 1. Overall Effect Plot of the BKMR model.
Note:ChHunger means childhood hunger, HazEnv means dangerous growth environment, Alone means childhood loneliness, ParDep means parental depression, ParDis means parental disability.

Rising group membership (see Table S5). The probability rose from 55.2% (b = 0.13) to 80.9% (b = 0.88), peaking at 85.7% (b = 1.07), demonstrating significant exposure-response gradients.

Posterior inclusion probability (PIP) analyses revealed that parental depression and childhood loneliness had the highest importance among ACEs, followed by bullying (see Table S6). Although childhood hunger showed the lowest relative importance, all ACEs demonstrated PIP values exceeding 0.9, indicating strong statistical significance.

No statistically significant interaction effects were detected between ACE components (see Figure S4).

3.4. Moderation effect analysis

A composite ACE variable was constructed from BKMR results, dichotomized as 1 (≥4 ACEs) versus 0 (<4 ACEs). Consistent with the biopsychosocial framework, five moderators were identified: cognitive function, gender, self-rated health trajectory, social engagement level, and AAEs.

Fig. 2 demonstrates significant effect modification by cognitive function (P for interaction = 0.040) after adjusting for residence and chronic conditions (residential status, heart disease, arthritis or rheumatism, liver disease, kidney disease, stomach or other digestive disease, and asthma). No other subgroups showed moderation effects.

Specifically, the High-Stable Cognitive Group showed stronger ACE-depression associations (OR = 3.32, 95%CI:2.34–4.70) versus the Low-Declining Group (OR = 1.99, 95%CI:1.45–2.73). This pattern indicates amplified ACE effects in cognitively preserved individuals. The borderline interaction significance (P = 0.040) necessitates replication in independent cohorts.

3.5. Mediation effect analysis

Mediation pathways were quantified through counterfactual framework analysis, estimating Natural Direct Effects (NDE), Natural Indirect Effects (NIE), and Marginal Total Effects (MTE) for chronic disease mediators in ACE-depression associations.

Arthritis or rheumatism exhibited significant mediation (NIE = 1.04, 95%CI:1.02–1.05), indicating partial mediation of ACE-depression associations through this pathway (Table 2).

Other conditions showed marginal mediation: kidney disease (NIE = 1.01, 95%CI: 0.99–1.01), stomach or other digestive diseases (NIE = 1.01, 95%CI: 0.99–1.01), and asthma (NIE = 1.01, 95%CI: 0.99–1.011). These subthreshold effects warrant confirmation in expanded datasets.

Moreover, when chronic conditions were aggregated into a composite variable (encompassing heart disease, arthritis or rheumatism, liver disease, kidney disease, stomach or other digestive diseases, and asthma), the cumulative mediation effect remained significant (NIE = 1.03, 95%CI:1.02–1.05). This suggests the ACE-depression association was partially mediated through multimorbidity pathways.

3.6. Sensitivity analysis

Additional analyses presented in Supplementary Materials Section 9 confirmed the robustness of the primary findings. Cross-validation demonstrated consistent predictive accuracy across randomized partitions. Stratified BKMR analyses revealed consistent significant associations at higher exposure quantiles across population subgroups. E-value calculations further supported that key predictors (e.g. parental depression, and childhood loneliness) demonstrated strong robustness against unmeasured confounding.

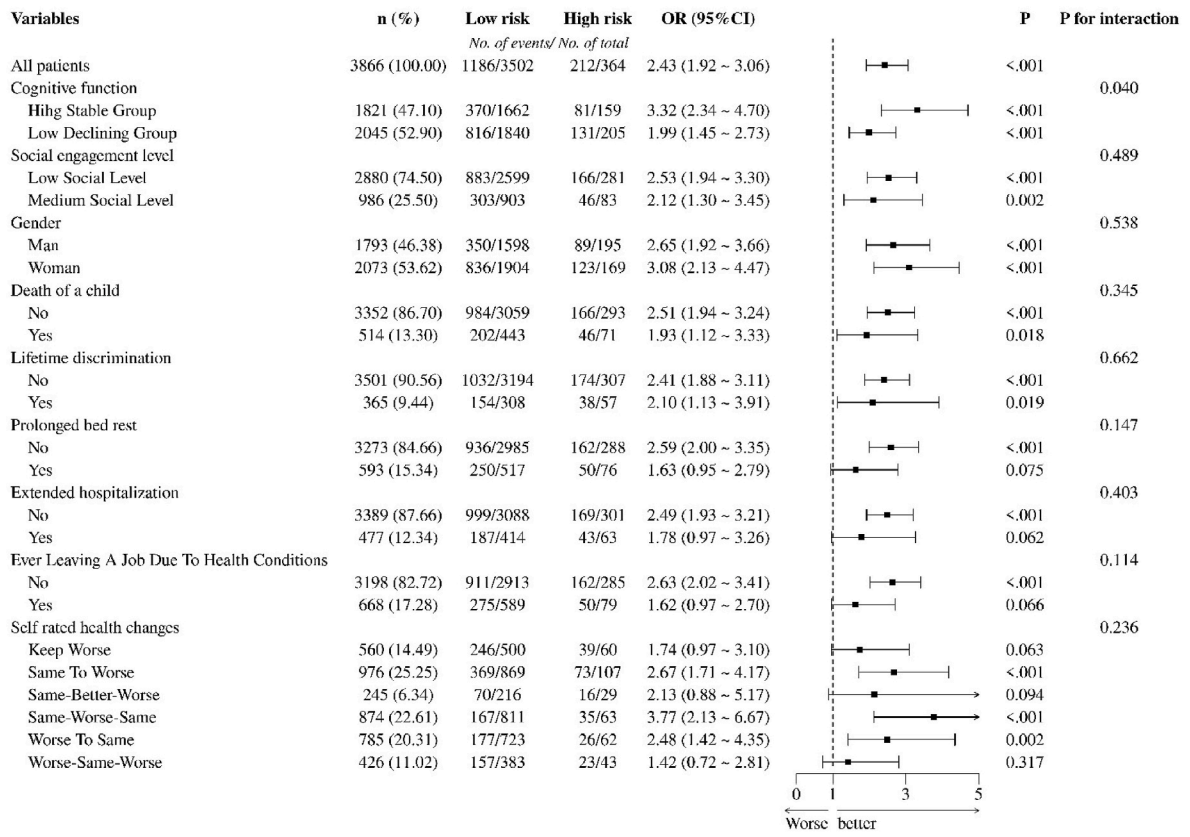

Fig. 2. Subgroup analysis forest plot.

4. Discussion

A dual-exposure model was developed as the core framework, integrating ACEs and AAEs through a unified analytical paradigm. This model systematically evaluates the cumulative and interactive effects of adverse exposures on depression risk from mid-to-late life. Adopting a life-course perspective, this approach surpasses previous studies that focused on isolated exposure periods, thereby improving the quantification of lifelong adversity accumulation. Methodologically, BKMR was applied to quantify and analyze joint exposures of multiple adversities. This approach elucidated not only independent effects but also potential interactions between risk factors. Subsequently, integrative analyses were performed across biopsychosocial domains, establishing a cross-dimensional explanatory framework that incorporates immune-inflammatory mechanisms, early emotional attachment patterns, and adaptive coping strategies. The findings demonstrate intervention paradigm implications: Identification of critical ACE/AAE mechanisms across life stages supports the development of precision prevention strategies, including (1) multi-biomarker screening protocols, (2) social support system optimization, and (3) personalized psychosocial rehabilitation programs, collectively aiming to reduce adverse experience impacts on late-life depression and enhance health outcomes.

After adjusting for biological, psychological, and social confounders, a significant positive association was observed between ACEs/AAEs and elevated depression scores in later life. A dose-response relationship was identified, with cumulative ACE exposure being significantly associated with heightened late-life depression risk. The reporting of multiple early adversities was strongly predictive of elevated depression scores, thereby emphasizing the necessity for early preventive measures and targeted interventions.

Among specific ACE subtypes, childhood loneliness, and parental depression were identified as having particularly strong associations with late-life depression risk. This association may originate from the disrupted development of early emotional attachment patterns and maladaptive coping mechanisms. Parental depression and psychosomatic disorders were shown to impair the establishment of secure child-caregiver attachment bonds. Furthermore, exposure to bullying, a dangerous growth environment, or childhood food insecurity revealed systemic deficiencies in familial and societal support structures. Consequently, preventive frameworks should therefore prioritize (1) early detection of emotional deprivation and (2) targeted interventions for populations with inadequate parental mental health support.

The U.S.-based longitudinal cohort study demonstrated a significant childhood adversity-midlife depression dose-response relationship (Sonu et al., 2019). Analysis of the European UK Biobank(UKB) cohort also revealed ACEs' dose-dependent associations with late-life depression, anxiety, and comorbidity (Yu et al., 2023). In Asian regions, Japanese (Wakuta et al., 2023) and South Korean (Bae, 2023) studies identified persistent childhood adversity effects on geriatric psychological health. Similar associations were replicated in an Australian longitudinal child cohort (Sahle et al., 2024). These findings demonstrate cross-national consistency with international research conclusions. Notably, while the dose-response patterns show cross-cultural consistency, the ACE subtype profiles exhibit cultural divergence. For instance, childhood loneliness—identified as a key risk factor in our cohort—may carry distinct social meanings in collectivist societies compared to Western individualistic contexts (Lykes and Kemmelmeier, 2014). In Chinese populations, perceived loneliness often stems from failing to meet familial role expectations rather than purely interpersonal isolation, suggesting cultural modulation of ACEs' psychological impacts.

Notably, consistent with McLaughlin et al.'s findings (McLaughlin et al., 2010), no significant inter-ACEs interactions were observed, supporting the cumulative adversity model wherein childhood adversities predominantly exert additive rather than interactive effects on adult mental health. AAEs, including prolonged discrimination and

Table 2
Mediation effect analysis of chronic diseases.

Mediate variable	item	Estimate	Std Err	P>|z|	95 %CI	
heart problem[a]						
	nde	1.404	0.033	0.000	1.316	1.497
	nie	0.996	0.003	0.161	0.991	1.002
	mte	1.398	0.033	0.000	1.310	1.492
Arthritis or rheumatism[a]						
	nde	1.405	0.032	0.000	1.318	1.497
	nie	1.035	0.007	0.000	1.022	1.049
	mte	1.454	0.032	0.000	1.365	1.550
liver disease[a]						
	nde	1.408	0.032	0.000	1.322	1.500
	nie	1.000	0.002	0.819	0.997	1.003
	mte	1.409	0.032	0.000	1.322	1.501
Kidney disease[a]						
	nde	1.402	0.033	0.000	1.314	1.495
	nie	1.006	0.003	0.086	0.999	1.013
	mte	1.410	0.033	0.000	1.322	1.504
Stomach or other digestive disease[a]						
	nde	1.404	0.033	0.000	1.318	1.497
	nie	1.005	0.003	0.080	0.999	1.011
	mte	1.412	0.033	0.000	1.324	1.505
Asthma[a]						
	nde	1.396	0.034	0.000	1.306	1.491
	nie	1.007	0.004	0.077	0.999	1.014
	mte	1.405	0.034	0.000	1.316	1.500
Chronic diseases[b]						
	nde	1.415	0.033	0.000	1.327	1.508
	nie	1.033	0.007	0.000	1.019	1.046
	mte	1.461	0.033	0.000	1.369	1.558

Note: nde: natural direct effect, nie: natural indirect effect, mte: marginal total effect.

[a] The models control for the effects of cognitive function, self-rated health changes, gender, residence, education level, lifetime discrimination, prolonged bed rest, extended hospitalization, heart problems, arthritis or rheumatism, liver disease, kidney disease, stomach or other digestive disease, and asthma. (If the mediator variable overlaps with the control variables, the current mediator variable is excluded from the control variables.)

[b] The model controls for the effects of cognitive function, self-rated health changes, gender, residence, education level, lifetime discrimination, prolonged bed rest, extended hospitalization. This variable is generated from heart problems, arthritis or rheumatism, liver disease, kidney disease, stomach or other digestive disease, and asthma. If the sample contains any of these conditions, it is assigned a value of 1; otherwise, it is assigned a value of 0.

recurrent hospitalization, were found to accelerate the erosion of social support systems. These exposures exhibited synergistic interactions with chronic stress-inflammatory coupling mechanisms, thereby amplifying late-life depression vulnerability. Crucially, the cumulative burden of AAEs and ACEs was shown to generate enduring biopsychosocial adversities throughout the lifespan, creating recursive depression risk accumulation pathways. This paradigm necessitates intervention frameworks spanning the lifespan, emphasizing healthcare access optimization and multi-level social support infrastructure development.

Three primary biological mechanisms have been proposed: (1) hypothalamic-pituitary-adrenal (HPA) axis dysregulation, (2) chronic inflammation, and (3) neurotransmitter imbalance. Specifically, chronic HPA axis dysregulation was shown to induce glucocorticoid resistance and hippocampal neuroplasticity impairment, thereby reducing emotional regulation capacity (Su et al., 2025). The chronic inflammation hypothesis has been proposed to involve cytokine-mediated mechanisms: ACEs-triggered epigenetic modifications promote persistent pro-inflammatory gene activation (Soares et al., 2021; Hirano, 2021); these inflammatory mediators subsequently cross the blood-brain barrier, disrupting limbic system function (Huang et al., 2021). Regarding neurotransmitter systems, animal studies have demonstrated that early-life stress causes permanent alterations in prefrontal cortex serotonin transporter density and dopamine D2 receptor expression (Adjimann et al., 2021; Wakeford et al., 2024), creating neurochemical vulnerability to late-life depression.

It has been demonstrated that ACEs/AAEs compromise social support systems and coping capacities, with individuals exhibiting impaired support mechanisms showing elevated depressive symptomatology following adverse exposures (Cheong et al., 2017; Kobrinsky and Siedlecki, 2023). Three synergistic psychosocial pathways have been proposed: (1) The attachment framework posits that childhood trauma generates insecure attachment patterns, limiting adult supportive relationship formation (Watters et al., 2024); (2) The stress accumulation model suggests that early adversity reduces psychological resilience, enhancing depression vulnerability to later stressors (Elrefaay and Elyzal, 2024); (3) The social cognitive perspective indicates that trauma-induced negative self-schemas magnify catastrophic health interpretations via cognitive biases (Gvion and Fachler, 2015). These pathways dynamically interact with biological mechanisms. Chronic stress was shown to enhance somatic symptom perception through HPA-immune axis interactions (Mbiydzenyuy and Qulu, 2024), establishing self-perpetuating psychobiological dysregulation cycles.

Extensive research has established ACEs' associations with multiple comorbidities that elevate depression risk and symptom severity in older populations (Wang et al., 2023b). Therefore, the mediating role of chronic diseases was investigated. Arthritis or rheumatism was identified as a significant mediator in the ACEs-depression trajectory association. This finding has been corroborated by mechanistic studies demonstrating inflammatory pathway mediation, where ACEs exert partial effects on depression via chronic low-grade inflammation induction (Zagaria et al., 2024). Gut dysbiosis linked to rheumatoid arthritis has been shown to directly provoke depression-like behaviors. Animal studies have revealed that fecal microbiota transplantation from rheumatoid arthritis patients induces abnormal T-cell activation and pro-inflammatory cytokine release in mice, suggesting gut-brain-immune axis involvement in arthritis-mediated ACEs-depression pathways (Pu et al., 2022).

Moreover, cognitive function was found to significantly moderate the ACEs-depression score association among middle-aged and older adults. Specifically, Stronger ACEs-depression associations were observed in the High Stable cognitive group, compared with significantly attenuated effects in the Low Declining group. These results indicate that while elevated baseline cognition may indicate neurocompensatory capacity, its regulatory effects on ACEs-related pathways exhibit bidirectional complexity. Enhanced associations in high-functioning individuals could originate from: (1) psychosocial stress level elevation (Anda et al., 2006); (2) heightened biological embedding of cumulative childhood-adulthood adversity among cognitively resilient subgroups (Felitti et al., 1998; Shonkoff and Garner, 2012); and (3) improved retrospective ACEs reporting validity mitigating exposure misclassification (Felitti et al., 1998). Conversely, diminished associations among low-functioning individuals may reflect exposure misclassification due to memory impairment and cognitive constraints (Shonkoff and Garner, 2012). These mechanisms require verification via prospective cohort designs.

Significant geographic disparities in geriatric depression risk were observed, potentially attributable to urban residents' enhanced access to healthcare systems, social security provisions, and community support networks. Rural older adults were found to experience compounded burdens, including elevated physical comorbidity rates, economic constraints, and limited access to mental health services and social networks. These findings underscore the necessity for public health initiatives focusing on (1) equitable healthcare resource allocation and (2) rural social support infrastructure development to effectively address depression risk in this population.

A higher depression prevalence was observed in females relative to males, consistent with documented gender disparities in mental health epidemiology (Chapman et al., 2004; Rivara et al., 2019). However, subgroup analyses did not detect statistically significant gender differences in ACEs-depression associations, although elevated OR was noted among females. This contrasts with UKB and Danish cohort reports (Yu

et al., 2023; Kofman et al., 2024) of stronger ACEs-depression associations in females. Several potential explanations emerge: (1) Cultural modulation of gender-related vulnerability – Western populations' gender-specific coping strategies (e.g. heightened social support utilization by females) may amplify ACEs impacts, whereas sociocultural contexts in our cohort might activate alternative resilience mechanisms; (2) Limited statistical power for detecting interaction effects in subgroup analyses, potentially compounded by gender-specific ACEs exposure prevalence.

Lower depression risk was observed in older adults with stable/improving self-rated health, suggesting an interaction between positive health perceptions and emotional regulation capacity. Positive health perceptions were associated with both favorable physical status and enhanced psychological resilience, thereby decreasing stress-induced depression vulnerability. These findings highlight the need for interventions targeting self-rated health maintenance via (1) health literacy programs, (2) chronic disease control, and (3) psychosocial support systems. This aligns with existing evidence demonstrating self-rated health's protective effects against depressive symptoms (Hazel et al., 2008).

A three-tier prevention strategy is proposed to address intergenerational adversity transmission and ACEs-related health sequelae. Primary: Integrate ACEs screening into maternal-child/primary care to disrupt intergenerational transmission via rural support networks; Secondary: Develop inflammatory biomarker/cognitive-based stratification for ACEs-related comorbidities (e.g. arthritis), combining anti-inflammatory diets, CBT, and trauma reprocessing for cognitively intact subgroups; Tertiary: Incorporate gut microbiome modulation into chronic disease protocols and trauma-informed peer-mentored networks. The policy mandates interagency data-sharing platforms and insurance-covered biobehavioral interventions to establish life-course depression prevention.

Several limitations warrant acknowledgment. First, the ACEs assessment lacked validated measures of emotional abuse/neglect and Genderual abuse (Huang et al., 2024), potentially underestimating cumulative burden and obscuring subtype-specific mechanisms. Second, retrospective self-reports risk nondifferential misclassification, despite probabilistic bias adjustments. Third, CES-D10-based depression measures may inflate prevalence estimates, albeit consistent with epidemiological conventions. Fourth, absent pre-baseline depression history precluded controlling for recurrence/chronicity effects. Fifth, residual confounding persists from unmeasured variables (e.g. socioeconomic status). Lastly, cultural differences, such as social stigma and unique interpretations of adversity in China, may lead to cross-cultural variations in ACEs/AAEs reporting, potentially limiting the generalizability of findings to Western populations. Future studies should expand sample sizes, adopt more refined clinical indicators, implement WHO ACE-IQ instruments, integrate neuroimaging biomarkers, and collect lifetime psychiatric histories to clarify the temporal dynamics and mechanistic pathways through which adverse experiences contribute to mental health outcomes.

5. Conclusion

In conclusion, exposure to ACEs or AAEs was associated with elevated depression scores in middle-aged and elderly populations. A dose-response relationship was specifically observed for ACEs. Furthermore, cognitive functioning was identified as a moderating factor in the ACEs-depression association, with the detrimental effects of ACEs demonstrating greater magnitude among individuals with higher cognitive reserves. Importantly, arthritis or rheumatism emerged as a significant mediator between ACEs and depression scores. These findings underscore the necessity of lifespan health management strategies that integrate both early-life adversity prevention and adult chronic disease control for depression mitigation. Prospective randomized controlled trials are required to validate these causal pathways through longitudinal intervention designs.

CRediT authorship contribution statement

Feng Jiang: Writing – original draft, Visualization, Methodology, Formal analysis. **Xifei Guan:** Writing – original draft, Methodology, Conceptualization. **Zhixin Zhu:** Writing – review & editing, Conceptualization. **Nawen Liu:** Writing – review & editing, Visualization. **Hua Gu:** Writing – review & editing, Conceptualization. **Xiuyang Li:** Writing – review & editing, Methodology.

Ethics approval and consent to participate

All methods were performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants. The CHARLS study was approved by the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015), and ethics approval for the use of CHARLS data was obtained from the University of Newcastle Human Research Ethics Committee. This study was conducted following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Data access

The data that support the findings of the study are available through the website of CHARLS: http://charls.pku.edu.cn/index/en.html. To access and use the day for research purpose, approval should be obtained from the CHARLS team at Peking University.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

ACEs: Adverse Childhood Experiences; AAEs: Adverse Adulthood Experiences; KML:K-means for Longitudinal Data; BKMR: Bayesian Kernel Machine Regression; CHARLS: China Health and Retirement Longitudinal Study; NDE: Natural Direct Effect; NIE: Natural Indirect Effect; MTE: Marginal Total Effect; OR: Odds ratio; CI: Confidence interval; PIP: Posterior Inclusion Probability.

Appendix ASupplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bbih.2025.101001.

Data availability

Data will be made available on request.

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