# Childhood Socioeconomic Disadvantages versus Adverse Care Experiences: Mediation and Moderation Impacts on Late-Life Depressive Symptoms

**Short running title: Childhood Adversities and Depression**

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## Abstract

**Background:** Whether material deprivation-related childhood socioeconomic disadvantages (CSD) and care-related adverse childhood experiences (ACE) have different impacts on depressive symptoms in middle-aged and older people is unclear.

**Methods:** In Guangzhou Biobank Cohort Study, CSD and ACE were assessed by 7 and 5 culturally sensitive questions respectively on 8,716 participants aged 50+. Depressive symptoms were measured by 15-item Geriatric Depression Scale (GDS). Multivariable linear regression, stratification analyses and mediation analyses were done.

**Results:** Higher CSD and ACE scores were associated with higher GDS score in dose-response manner (P for trend < 0.001). Participants with one point increment in CSD and ACE had higher GDS score by 0.11 (95% CI, 0.09 to 0.14) and 0.41 (95% CI, 0.35 to 0.47) respectively. The association of CSD with GDS score was significant in women only (P for sex interaction < 0.001; women: β (95% CI)=0.14 (0.11 to 0.17), men: 0.04 (-0.01 to 0.08)). The association between ACE and GDS score was stronger in participants with high social deprivation index (SDI) (P for interaction = 0.01; low SDI: β (95% CI)=0.36 (0.29 to 0.43), high SDI: 0.64 (0.48 to 0.80)). The proportion of association of CSD and ACE scores with GDS score mediated via education was 20.11% and 2.28%.

**Conclusions:** CSD and ACE were associated with late-life depressive symptoms with dose-response patterns, especially in women and those with low adulthood




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socioeconomic status. Education was a major mediator for CSD but not ACE. Eliminating ACE should be a top priority.

**Key words:** Childhood socioeconomic disadvantages; Adverse care experiences; Late-life depressive symptoms; Mediation; Moderation



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## Introduction

Depression has become increasingly common in older people with heavy disease burden [1]. A 2021 meta-analysis by Tang et al. showed that the prevalence of depressive symptoms in adults aged ≥60 years in mainland China was 20%, and the prevalence increased with age [2]. A 2020 systematic review by Worrall et al. showed that health behaviours and socioeconomic status (SES) were associated with depressive symptoms in older people, but the study did not consider childhood variables [3]. Similar to this systematic review, most reports were on later-life behavioural, social and health status, while childhood variables had not been included. A 2017 meta-analysis by Nelson et al. showed that childhood maltreatment was a risk factor for depressive symptoms in older adults [4]. However, most of the studies in this meta-analysis were from high-income Western countries, and none from low-to-middle income countries. Moreover, this meta-analysis examined direct childhood adversity and ignored indirect childhood adversity such as household difficulties [4]. A 2021 meta-analysis by Hughes et al. showed that childhood adversity, including both direct (e.g., maltreatment) and indirect (e.g., household difficulties) types, increased risk of depressive symptoms in older adults [5]. However, this meta-analysis included only European countries and assumed each type of childhood adversity had same adverse effect on health. Note that the magnitude of the associations above may vary across socioeconomic and political contexts [6, 7]. Whether these associations exist in other settings and ethnic groups and whether



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different types of childhood adversity have different impacts on depressive symptoms have not been reported.

Before and during the early years of the People's Republic of China, most older Chinese experienced harsh social and family environments during their childhood. During adulthood due to the open-door policy started about 40+ years ago, their livelihood and socioeconomic status has continued to improve greatly. Such changes are quite different from people born in the same period in developed Western countries. Therefore, examining the associations between childhood adversity and late-life depressive symptoms in China may provide new insights for our understanding of depressive symptoms and early-life risk factors.

Several conceptual models have been introduced to explain the associations of childhood adversity with late-life depressive symptoms, suggesting that adulthood socioeconomic and health-related factors might be involved in the pathway. Nevertheless, the effect modifiers and underlying mechanisms remain unclear [8]. Moreover, most previous European studies used a cumulative measure of childhood adversities [5], which could not separate potentially differential effects of different types of childhood adversities on depressive symptoms [7, 9, 10]. Hence, in the present study, we used data from the Guangzhou Biobank Cohort Study (GBCS) to examine the associations of different types of childhood adversities separately,



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including material deprivation-related childhood socioeconomic disadvantages (CSD) and care-related adverse childhood experiences (ACE), with depressive symptoms in middle-aged and older people, and potential moderation effect of sex, SES and chronic diseases and mediations by socioeconomic factors, health behaviours and stressful life events (SLE) in adulthood. We hypothesised that the number of CSD items and ACE items were positively associated with depressive symptoms in older people, and the associations, if any, might differ by sex and SES and involve different pathways.

## Materials and methods

*Study participants*

The GBCS is a three-way collaboration among the Guangzhou Twelfth People's Hospital and the Universities of Hong Kong, China, and Birmingham, UK. Details of the GBCS have been described previously [11]. Briefly, participants were recruited from the Guangzhou Health and Happiness Association for the Respective Elders, which is a community social and welfare organization with branches in all ten districts of Guangzhou. Permanent residents in Guangzhou aged 50 years or above were eligible to participate. The baseline examination included a face-to-face interview by trained nurses using a computer-assisted standardized questionnaire. The study was approved by the Guangzhou Medical Ethics Committee of the Chinese Medical Association, and all participants provided written informed consent prior to



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participation. In phase 3 (2006-2008), the questionnaire included the validated Chinese version of the 15-item Geriatric Depression Scale (GDS) [12], thus in the present study, participants from phase 3 were included.

*Exposures*

CSD and ACE were exposure variables. Given the specific socio-historical context of China during the mid-20th century, standard tools for measuring CSD and ACE may not fully capture the range of experiences relevant to our study population. Therefore, we used measures developed from sociological accounts and prior research relevant to this context. While these measures have been used in our previous studies, we acknowledge that they are not widely validated, which may limit the direct comparability of our findings.

We took into account parental possession and childhood material deprivation in CSD measurement. Parental possession included three simple and easily notable items, i.e., a bicycle, a sewing machine and a watch, based on sociologic accounts of life in southern China in the mid-20th century and were used in our previous GBCS papers [13, 14]. Each item was coded as 0 for present or 1 for absent. Childhood material deprivation was assessed by four questions: ‘Did you usually have shoes when you were a child?’, ‘Did you usually get new clothes at Chinese New Year?’, ‘How often do you remember being hungry as a child?’ and ‘How often did you eat meat as a



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child?' Each item was coded as zero when the answer was 'Yes', 'Yes', 'Never' and 'Daily' for the four questions above, respectively, or as one otherwise. Then the cumulative CSD score was calculated. The CSD score ranged from 0 to 7, with higher CSD score indicating greater childhood socioeconomic disadvantages. Participants were further classified into two categories as low CSD (CSD score < 4) and high CSD (CSD score ≥ 4) based on the median CSD score of 4.

ACE was assessed by the following five culturally sensitive questions before the age of 18 years as we reported previously [13, 15]: separation from mother for more than one year continuously, an experience so frightening as to be thought about years afterwards, being sent away from home because of wrongdoing, frequent quarrelling of parents, and early parental death. One point was assigned for a positive response of each question and zero point otherwise. The cumulative ACE score was calculated. The ACE score ranged from 0 to 5, with higher ACE score indicating more care-related adverse childhood experiences. Participants were further classified into two categories as absence of ACE (ACE score = 0) and presence of ACE (ACE score ≥ 1) based on the median ACE score of 0.

*Outcomes*

The main outcome was the score of the 15-item GDS [12]. GDS was analysed as a continuous score, with higher scores indicating more negative symptoms. We also



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dichotomized the variable into presence or absence of depressive symptoms as another outcome. The presence of depressive symptoms was defined by a GDS score of 8 or more, which is the standard cut-off score for Chinese population [16] and has been widely used elsewhere, and reported in our previous papers [17-19].

*Potential confounders, mediators and effect modifiers*

Sex and age (in years) were included as potential confounders in regression model 1 (main model). To further examine potential mediators of the associations of CSD and ACE with GDS score, we included socioeconomic factors, health behaviours and SLE in adulthood in regression model 2. Socioeconomic factors included education (primary or below, secondary and college or above), occupation (manual, non-manual and others), marital status (never married, married, separated and widowed) and household income (< 30 000 CNY/year, ≥ 30 000 CNY/year and not known; US$1 = 7 CNY). Health behaviours included smoking status (never, former and current smoker) and alcohol drinking status (never, former and current user), physical activity (inactive, moderate and active), and body mass index (BMI) (continuous variable). SLE in adulthood were defined as at least one of ten major life events in the last year including separation or divorce, unemployment or retirement, business bankruptcy, physical assault, major conflict within family, major injury or traffic accident, death of spouse, major illness or death of a close family member, major natural disaster (such as flood or drought) and loss of all sources of income or living on debt, as reported in



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our previous papers [13, 20]. Moreover, CSD and ACE were also mutually adjusted in the regression model 3.

As women [2, 21], those with greater social deprivation [22, 23] and with chronic diseases [24] might be more vulnerable to depressive symptoms, sex, SES in adulthood and history of chronic diseases were considered as potential effect modifiers. According to previous studies [25, 26], we derived a social deprivation index (SDI) as proxy for adult SES by summing the presence of the following four indicators, with one point assigned to each: never-married status, primary school or below, unemployment, and household income < 30 000 CNY/year. The SDI score ranged from 0 to 4, with higher SDI scores indicating greater social deprivation and lower SES. Participants were further classified into low SDI (score 0-1) and high SDI (score 2-4) based on half of the maximum SDI score. History of chronic diseases was defined by the presence of any of the following 20 diseases: hypertension, dyslipidemia, type 2 diabetes mellitus, coronary heart disease, stroke, angina, rheumatic heart disease, arrhythmia, heart failure, cancer, liver disease, gastrointestinal disease, chest disease, genitourinary disease, neurological disease, eye disease, arthritis, thyroid disease, fracture history and mental disease [27].

*Statistical analysis*



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Chi-square test and analysis of variance was used respectively to compare characteristics of categorical and continuous variables according to low/high CSD (< 4 or ≥ 4) and ACE (0 or ≥ 1) score. Multivariable linear regression and logistic regression was used to analyse the associations of CSD and ACE with GDS score and the presence of depressive symptoms, respectively, giving adjusted regression coefficients (βs), odds ratios (ORs) and 95% confidence intervals (CIs). Multivariable linear regression was also used to analyse the associations of each CSD and ACE item with GDS score. To analyse the potential moderation effect, interaction terms by multiplying CSD or ACE score and potential effect modifiers were generated, and the heterogeneity of models with and without interaction term was compared. If a moderation effect exists, the interaction term would be statistically significant [28]. When significant interaction was found, we conducted stratification analyses. To estimate the contribution of potential mediators to the association of CSD and ACE score with GDS score, we used causal mediation analysis under the counterfactual framework, which can decompose the averaged total effect into indirect effect (average causal mediation effect) and direct effect (average direct effect) [29]. For mediation analyses, potential mediators were dichotomized, i.e., education (secondary or above vs primary or below), occupation (unemployment vs employment), marital status (never married vs married), household income (≥ 30 000 CNY/year vs < 30 000 CNY/year), smoking status (ever vs never), alcohol drinking status (ever vs never), physical activity (moderate or above vs inactive) and SLE in adulthood (yes vs no).



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The "medeff" package in STATA was used to perform mediation analysis. All analyses were performed using STATA (Version 16.0; StataCorp LP, College Station, TX, USA). All tests were two-sided, and statistical significance was indicated by $P < 0.05$.

## Results

*Characteristics of participants*

Of 10 088 participants recruited from 2006 to 2008, after excluding those with duplicate information (N=39), and missing information on CSD (N=353), ACE (N=687), GDS score (N=97) and potential mediators (N=429), 8 716 participants (86.4%) were included in the current study. Figure 1 shows an overview of the present study models.

Table 1 shows that participants with high CSD or ACE score had greater GDS score and higher prevalence of depressive symptoms (all $P < 0.001$). Participants with high CSD score were older, had higher proportions of men and current smokers, and had higher ACE score (all $P < 0.001$). They had lower proportions of married people, current alcohol users and those with stressful life events in adulthood, and lower socioeconomic position (lower education and household income and with manual occupation) (P from <0.001 to 0.003). Participants with high ACE score were also older, had higher proportions of men and current smokers, had higher CSD score but



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more with stressful life events in adulthood (P from <0.001 to 0.01). They had lower proportions of married people and those with lower education and manual occupation, and lower household income (P from <0.001 to 0.04). No significant differences were found for physical activity and BMI (P from 0.07 to 0.70).

*Childhood adversities and GDS score in adulthood*

Table 2 shows that higher CSD and ACE scores were associated with higher GDS score after adjusting for sex and age, with significant dose-response patterns (all P for trend < 0.001). Participants with one point increment in CSD had GDS score increased by 0.11 (95% CI, 0.09 to 0.14) after adjusting for sex and age (Model 1). Moreover, GDS score increased by 0.41 (95% CI, 0.35 to 0.47) per ACE score (Model 1). After additionally adjusting for potential mediators and ACE or CSD, almost all the results remained significant with slightly attenuated associations (Model 2 and 3). Each item of CSD and ACE was associated with GDS score (Tables S1 and S2). Of the CSD items, the associations of new clothes at Chinese New Year and hungry with GDS score appeared stronger than other items (adjusted mean differences, β (95% CI): 0.49 (0.39 to 0.59) and 0.43 (0.32 to 0.54), respectively) (Model 1). Of the ACE items, the associations of frightening experience thought about years afterwards, sent away from home because of wrongdoing and parents quarrelling frequently with GDS score were stronger than other items (β (95% CI): 0.97 (0.81 to 1.13), 0.88 (0.55 to 1.20) and 0.98 (0.80 to 1.16), respectively) (Model 1). The mean differences for these



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263 3 ACE items were also greater than the 7 CSD items. After additionally adjusting for
264 potential mediators and ACE or CSD, the associations of CSD items with GDS score
265 attenuated greatly, while the associations of ACE items with GDS score attenuated
266 slightly (Model 2 and 3). Moreover, higher CSD and ACE scores were also associated
267 with higher odds of depressive symptoms (all P for trend < 0.001) and the ORs per
268 ACE score were greater than those per CSD score (Model 1-3) (Table S3).
269
270 *Childhood adversities and GDS score in adulthood by sex*
271 Table 3 shows a significant moderation effect of sex on the association between CSD
272 score and GDS score in Model 1 (P for interaction < 0.001). Subgroup analyses by sex
273 showed that the associations of CSD with GDS score became stronger with a
274 significant trend (P < 0.001) in women. However, men showed no significant
275 associations (except for those with 2 and 7 items) and trend (P = 0.14). The GDS
276 score increased by 0.14 (95% CI, 0.11 to 0.17) in women per CSD score, but the small
277 increase in men was not significant. After additionally adjusting for potential
278 mediators and ACE, the associations for CSD in men and women much attenuated
279 (Model 2 and 3). Although no significant moderation effect of sex was observed for
280 the association between ACE score and GDS score (P for interaction = 0.22 in Model
281 1), the associations of ACE score with GDS score also appeared to be stronger in
282 women. After additionally adjusting for potential mediators and CSD, the results for
283 ACE in men and women were similar (Model 2 and 3).



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*Childhood adversities and GDS score in adulthood by SDI and chronic diseases*

Table 4 shows no significant moderation effect of SDI on the association between CSD score and GDS score in Model 1 (P for interaction = 0.30), but when CSD score was dichotomized into good (CSD score 0-3) and poor (CSD score 4-7) childhood socioeconomic conditions (Table S4 Model 1), a significant moderation effect was found (P for interaction = 0.01). Those with poor childhood socioeconomic conditions and high SDI in adulthood had the highest GDS score. A significant moderation effect of adulthood SDI on the ACE score and GDS score association was found (P for interaction = 0.01). Compared with participants with low SDI, the association between ACE score and GDS score was stronger in those with high SDI. The GDS score increased by 0.36 (95% CI, 0.29 to 0.43) per ACE score for low SDI, but by 0.64 (95% CI, 0.48 to 0.80) for high SDI. After additionally adjusting for potential mediators and ACE or CSD, the results were similar for per ACE score but much attenuated for per CSD score (Model 2 and 3). Chronic diseases did not significantly moderate the association of CSD/ACE with GDS score (P for interaction = 0.62 and 0.96 respectively in Model 1) (Table not shown).

*Mediation analyses*

Table 5 shows that the association of CSD score with GDS score was partly mediated by education, household income and smoking status after adjusting for sex and age,



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and the proportion of mediation was 20.11% (95% CI, 15.88% to 25.93%), 12.19% (95% CI, 9.32% to 16.32%) and 2.17% (95% CI, 1.75% to 2.72%), respectively (all P < 0.05). However, occupation, marital status, alcohol drinking status, physical activity, BMI and SLE showed no mediation. For ACE, the proportions via mediation to GDS by education, physical activity and SLE in adulthood were significant but small, being 2.28% (95% CI, 1.98% to 2.63%), 1.29% (95% CI, 1.12% to 1.49%) and 1.72% (95% CI, 1.48% to 1.97%), respectively. Alcohol drinking status (ever vs never) showed a suppressive effect on the association of ACE score with adulthood GDS score (-1.14%, 95% CI, -1.31% to -0.99%). Occupation, marital status, household income, smoking status and BMI showed no significant mediation.

## Discussion

We have first reported that both material deprivation-related childhood socioeconomic disadvantages and care-related adverse childhood experiences showed dose-response associations with depressive symptoms in middle to older age, the associations were stronger for adverse childhood experiences than childhood socioeconomic disadvantages (CSD), in women and those with low adulthood socioeconomic status, and education was the main and important mediator of the associations of childhood socioeconomic disadvantages with Geriatric Depression Scale score (20% mediation) but was the main but small mediator of the associations of adverse childhood experiences (ACE) with Geriatric Depression Scale score (2% mediation).



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Our findings in a setting with social development patterning very different from Western populations are consistent with previous studies mostly from Western countries showing that childhood adversities were associated with late-life depressive symptoms with dose-response patterns [5, 30-32]. The associations of childhood adversities, mainly maltreatment or care-related ACE, with depressive symptoms assessed by the Short Form of the Center for Epidemiologic Studies Depression Scale were also reported by two recent Chinese studies [33, 34]. Note that consistent findings across different settings with different socioeconomic and political contexts will provide more robust evidence to support causation. However, no previous studies distinguished and compared different types of childhood adversities in China and other countries. Previous Chinese studies just reported the associations of famine or deprivation [35, 36] or maltreatment or care-related ACE [33, 37, 38], or integrated childhood starvation or food deprivation and ACE into one variable [34, 39] with late-life depressive symptoms. Our study has shown new results that both material deprivation-related CSD and care-related ACE were associated with late-life depressive symptoms even after mutual adjustment, but the associations for ACE were stronger than CSD, indicating that the deleterious effect of psychological adverse events might be greater than childhood poverty. Moreover, we have shown that the dose-response relationships persisted after adjusting for potential mediators, indicating that childhood adversities may have direct long-lasting effects on late-life



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depression. Hence, our results could help identifying children or adults at risk of depression at older age.

We have also first reported on the different results of individual CSD and ACE items. Among CSD items, not receiving new clothes at Chinese New Year and experiencing hunger were particularly strong predictors of GDS scores. This might be attributed to the deep cultural importance of New Year traditions in Chinese society, where new clothes symbolize renewal and familial care, making the absence of such a tradition especially memorable. Additionally, hunger, being a direct threat to physical well-being, likely has a profound and lasting psychological impact, distinguishing these experiences from other forms of material deprivation such as the lack of shoes or less frequent meat consumption. Under ACE, the associations of frightening experience thought about years afterwards, having been sent away from home because of wrongdoing and parents quarrelling frequently with GDS score were the strongest, and stronger than the 2 CSD items above. However, while some studies, including a systematic review and meta-analysis by Simbi et al. (2020) [40], have highlighted early parental death as a risk factor for later-life depression, our study did not find a significant association between early parental death and GDS scores in our older adult population. As shown in Table S1, the GDS score for middle-aged and older individuals with early parental death increased by 0.14 (95% CI, 0.02 to 0.26) after adjusting for sex and age in Model 1. However, this association was attenuated to null



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(β (95% CI): 0.12 (-0.0004 to 0.24)) after further adjustments for socioeconomic factors, health behaviors, and stressful life events in adulthood (Model 2). This non-significant result could be attributed to several factors, including the unique socio-cultural and historical context of our study population, where the traditional structure of Chinese families might have provided additional support and resilience. Moreover, the meta-analysis by Simbi et al. (2020) [40] primarily focused on individuals aged 18-65, which might not fully represent the middle-aged and older populations in our study. The potential for the deleterious effects of early parental death on mental health to weaken over time due to the quality of other relationships and socio-economic positions in adulthood further complicates the direct comparison. This highlights the necessity of a nuanced approach in understanding the potential impact of early-life adversities, taking into account the specific characteristics of the population under study and the multifaceted nature of depression.

Our findings could be explained by human brain development. Childhood is a key period when there are major advances in the brain to develop skills in learning, reasoning and understanding, which are essential in subsequent social success [10]. Childhood adversity may lead to structural variation in brain grey and white matter, functional variation in brain activity and functional connectivity, and altered neurotransmitter metabolism or production, which could subsequently increase vulnerability to depression in adulthood [41]. Moreover, as young children have little



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awareness of social structures, psychosocial stress such as the feelings of inferiority, subordination or lack of control might emerge mainly due to the adverse feelings and behaviours of their caregivers, which in turn could influence mental health via neuroendocrine pathways [42]. And needs theory suggests that once basic needs that can be bought with money are met, increasing levels of wealth do not add any more to the overall levels of happiness [43]. Thus, care-related ACE might be more harmful for mental health than material deprivation-related CSD.

Depression is more common among women than men [21], but whether the associations between childhood adversities and late-life depressive symptoms vary by sex has been inconclusive. Previous studies showed mixed results, with some reporting stronger associations in women [44-46], some reporting similar associations in men and women [33, 47, 48], and some reporting stronger associations in men [49, 50]. We have reported the first result that although men might have more CSD and ACE, the associations of childhood adversities, especially material deprivation-related CSD, with late-life depressive symptoms were much stronger in women. Deeply ingrained patriarchal traditions in China might explain the sex differences. Historically, daughters were treated as ‘‘lost investment’’ in China [51], which might result in unequal treatment and opportunities for women compared to men, leading to women with childhood poverty more vulnerable to depression due to the cumulative effects of societal discrimination, limited opportunities, and unequal access to



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resources. However, although we observed significant sex interactions in the association between CSD and GDS scores, such interactions were not evident between ACE and GDS scores. This finding suggests that the impact of ACE on depressive symptoms in later life may not differ markedly between men and women. We hypothesize that this could be due to the pervasive nature of ACEs, which often involve emotional and interpersonal dynamics that might equally affect individuals regardless of sex. Additionally, cultural and social norms surrounding gender roles and emotional expression could influence the reporting and processing of ACEs, potentially contributing to the observed results. Further studies exploring these cultural and social dimensions could provide deeper insights into the mechanisms underlying these associations.

Moreover, our results that the associations of childhood adversities, mainly care-related ACE, with late-life depressive symptoms also varied by adulthood SES, corroborate results of previous studies from Japan [52] and China Health and Retirement Longitudinal Study [38]. The Japanese study defined adult SES based on educational attainment and annual household income [52], and the Chinese study used annual per capita household consumption expenditure to indicate participants' current economic status [38]. Both studies found that achieving high adulthood SES could ameliorate the adverse effects of childhood adversities, mainly psychological adverse events, on late-life depression. This might be explained by the social mobility model, suggesting that the adverse effects of childhood adversity may be mitigated or



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reversed by upward mobility, i.e., improved SES in adulthood [53], due to less economic pressure and more access to health resources related to individuals with high adulthood SES [54]. Our study used a composite indicator, i.e., SDI, to assess SES in adulthood, and suggested that high adult SES might also potentially mitigate the adverse effects of childhood poverty on late-life depression. However, the absence of a significant interaction between CSD and SDI warrants a cautious interpretation of the potential buffering effect of high adult SES. It is possible that factors not captured by our SDI, such as psychological resilience, social support, or access to mental health resources, may play critical roles in mitigating the impact of childhood poverty. Additionally, the uniform measure of SES represented by SDI may not fully capture the diverse aspects of socioeconomic status and their nuanced effects on mental health outcomes.

Consistent with previous studies [34, 45, 55-57], our study found that education might act as a mediator against adverse effects of childhood adversities on late-life depressive symptoms, indicating that expanding coverage of universal secondary education including females equally might be the most important intervention to reduce socioeconomic disparities and late-life depression symptoms in people with childhood adversities. However, previous studies did not compare the mediating effects of education on different types of childhood adversities. We first found that the mediating effect of education was much greater for CSD (20%) than ACE (2%), and



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we also found that the association of CSD with depressive symptoms could be partly mediated by higher household income (10%). Because ACE showed strong and almost 100% direct effect with very small proportion of effect via mediators, if such associations are causal, eliminating or reducing ACE and related psychological traumas in childhood should be a top priority to promote childhood mental health and prevent mental ill health in adult life.

Our study had some limitations. First, as information of CSD and ACE was collected by self-report like a case-cohort study, recall errors might have led to random and systemic errors. Random errors would result in underestimation of the strength of associations. Participants with depressive symptoms might have reported more childhood adversities than those without depressive symptoms. However, we used relatively objective and specific indicators to assess childhood adversities, such as parental possession and parental death, which might be hard to forget and have been supported in our previous papers [13-15]. Second, as our study used specific measures for CSD and ACE rather than a widely-used and validated standard tool, direct comparability of our results with those of previous studies may be limited. However, it is worth noting that the items of CSD were tailored to mid-20th century China, based on sociologic accounts of life in southern China during that era [14]. Similarly, the ACE items have been considered in other studies, including the National Population Health Survey of the Canadian population and the China Health and



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Retirement Longitudinal Study [58-60]. Third, we were unable to ascertain the timing of onset for depressive symptoms and other health conditions. But the timing of the data on childhood adversities should most likely precede depressive symptoms. Fourth, our CSD score and ACE score were self-reported subjective measures of cumulative childhood adversities [61]. Future studies using objective and documented childhood exposure data are warranted. Finally, underlying mechanisms through genetics, pathology or biomarker-related factors were not examined but such factors are unclear or unknown.

In conclusion, both material deprivation-related CSD and care-related ACE were associated with late-life depressive symptoms with dose-response patterns. The associations were stronger in women and those with low adulthood SES. Education was a major mediator for CSD but not ACE, highlighting the role of improving and equitable access to education in mitigating adverse effects of childhood socioeconomic disadvantages. With rapid development in economy and popularization of basic compulsory education in China and many low- and middle-income countries, some CSD items could have been reduced but ACE might not. But eliminating care-related adverse childhood experiences should be a top priority to prevent mental ill health in adulthood. Further studies are needed to clarify the mechanisms and examine the consequences of current CSD and ACE on future depression.



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**Conflicts of Interest**

The authors declare that they have no competing interests.

**Author Contribution**

YYH, WSZ, CQJ, FZ, YLJ, SLAY, JW, KKC, THL and LX have substantial contributions to conception and design, acquisition of funding, data and interpretation

of data; YYH and LX analysed the data, YYH drafted the article, LX, THL, JW, WSZ, CQJ, FZ, YLJ, SLAY and KKC revised it critically for important intellectual content. All authors read and approved the final manuscript.

## Data Availability

Data that support findings are restricted to researchers who have permission from the Guangzhou Biobank Cohort Study, and so are not publicly available.

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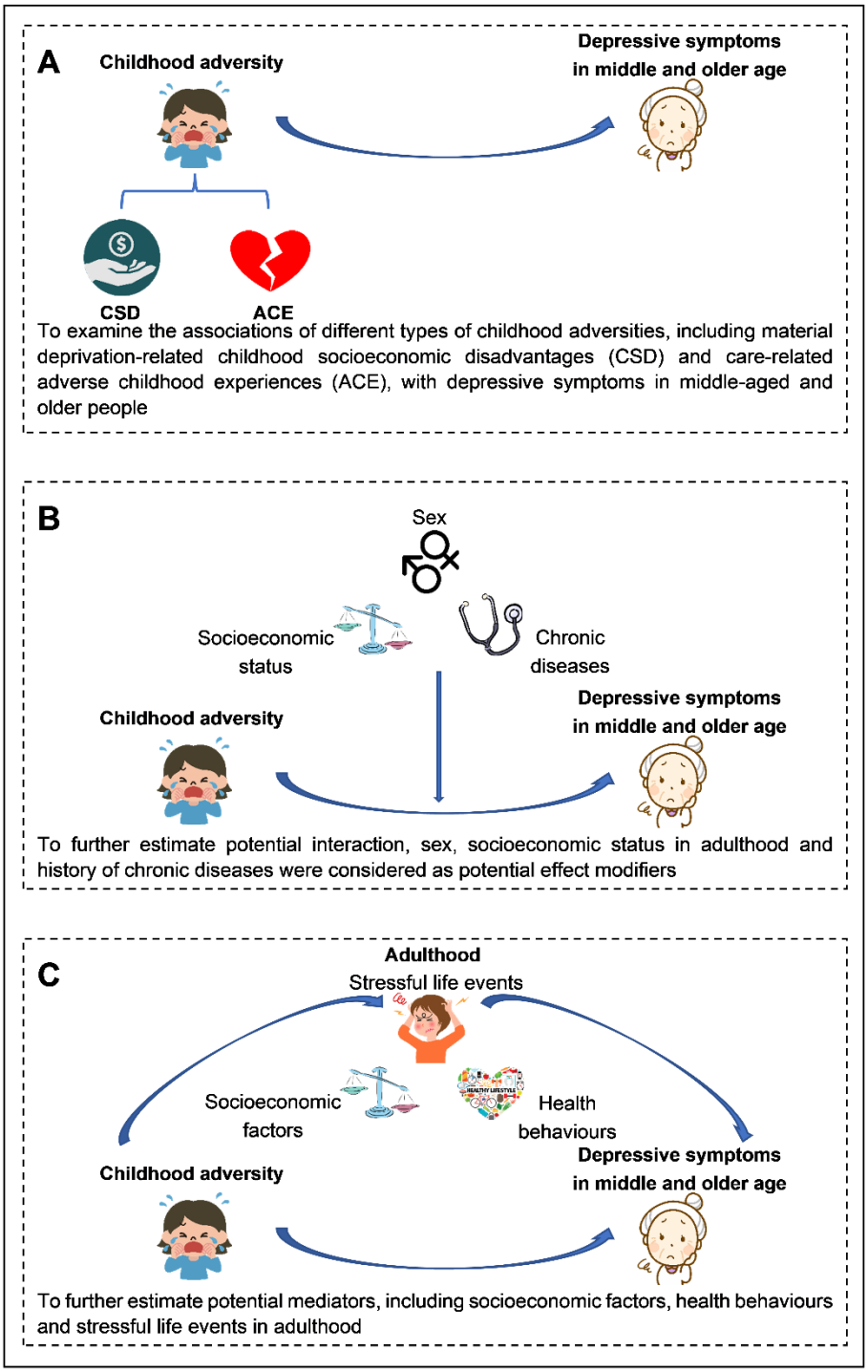
Figure Legend

Figure 1. Overview of the present study models.



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709 Table 1. Characteristics of the study sample by childhood socioeconomic disadvantages or adverse
710 childhood experiences.

| | Number of childhood socioeconomic disadvantage (CSD) items (score) | | P-value | Number of adverse childhood experience (ACE) items (score) | | P-value |
|---|---|---|---|---|---|---|
| | < 4 | ≥ 4 | | 0 | ≥ 1 | |
| Number of participants (row percentage) | 3 331 (38.22%) | 5 385 (61.78%) | | 4 822 (55.32%) | 3 894 (44.68%) | |
| Sex, % men | 20.41 | 28.38 | <0.001 | 22.40 | 28.97 | <0.001 |
| Age, years, mean (SD) | 57.33 (6.27) | 62.21 (7.77) | <0.001 | 59.07 (7.02) | 61.93 (8.01) | <0.001 |
| Education (%) | | | | | | |
| Primary or below | 18.43 | 48.64 | <0.001 | 34.22 | 40.65 | <0.001 |
| Secondary | 69.35 | 45.24 | | 57.55 | 50.62 | |
| College or above | 12.22 | 6.13 | | 8.23 | 8.73 | |
| Occupation (%) | | | | | | |
| Manual | 55.36 | 66.57 | <0.001 | 63.40 | 60.91 | 0.04 |
| Non-manual | 26.27 | 17.44 | | 19.97 | 21.85 | |
| Others | 18.37 | 15.99 | | 16.63 | 17.23 | |
| Marital status (%) | | | | | | |
| Never married | 0.93 | 0.54 | <0.001 | 0.75 | 0.62 | <0.001 |
| Married | 87.69 | 80.72 | | 86.21 | 79.89 | |
| Separated | 1.98 | 1.26 | | 1.31 | 1.82 | |
| Widowed | 9.40 | 17.47 | | 11.74 | 17.67 | |
| Household income, CNY/year (%) | | | | | | |
| < 30,000 | 29.48 | 39.35 | <0.001 | 34.26 | 37.21 | 0.001 |
| ≥ 30,000 | 60.25 | 41.00 | | 50.08 | 46.22 | |
| Don’t know | 10.27 | 19.65 | | 15.66 | 16.56 | |
| Smoking status (%) | | | | | | |
| Never | 86.52 | 79.78 | <0.001 | 84.32 | 79.92 | <0.001 |
| Former | 5.16 | 9.17 | | 6.18 | 9.45 | |
| Current | 8.32 | 11.05 | | 9.50 | 10.63 | |
| Alcohol drinking (%) | | | | | | |
| Never | 51.91 | 55.06 | <0.001 | 54.65 | 52.88 | 0.06 |
| Former | 4.77 | 5.81 | | 4.96 | 5.98 | |
| Current | 43.32 | 39.13 | | 40.40 | 41.14 | |
| Physical activity (%) | | | | | | |
| Inactive | 7.87 | 7.86 | 0.62 | 7.55 | 8.24 | 0.07 |
| Moderate | 27.98 | 27.04 | | 26.67 | 28.30 | |
| Active | 64.15 | 65.11 | | 65.78 | 63.46 | |



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| | | | | | | |
|---|---|---|---|---|---|---|
| Body mass index, kg/m$^2$, mean (SD) | 23.84 (3.29) | 23.81 (3.36) | 0.70 | 23.86 (3.40) | 23.77 (3.26) | 0.19 |
| Stressful life events in adulthood (%) | | | | | | |
| No | 89.34 | 91.29 | 0.003 | 91.25 | 89.68 | 0.01 |
| Yes | 10.66 | 9.71 | | 8.75 | 10.32 | |
| ACE/CSD score, mean (SD) | 0.50 (0.74) | 0.71 (0.86) | <0.001 | 3.50 (2.02) | 4.05 (1.94) | <0.001 |
| GDS score, mean (SD) | 2.19 (2.08) | 2.57 (2.35) | <0.001 | 2.17 (2.09) | 2.74 (2.42) | <0.001 |
| Depressive symptoms (%) | | | | | | |
| Absent (GDS < 8) | 97.42 | 95.06 | <0.001 | 97.10 | 94.56 | <0.001 |
| Present (GDS ≥ 8) | 2.58 | 4.94 | | 2.90 | 5.44 | |

US$1 = 7 CNY; GDS, Geriatric Depression Scale: higher scores indicating more negative symptoms; SD, standard deviation.



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714 Table 2. Associations of childhood socioeconomic disadvantages and adverse childhood
715 experiences with GDS score in adulthood.

| | *N* | Adjusted mean differences β (95% CI) in GDS score | | |
|---|---|---|---|---|
| | | Model 1 | Model 2 | Model 3 |
| **Number of childhood socioeconomic disadvantage (CSD) items (score)** | | | | |
| 0 | 517 | Ref. (0) | Ref. (0) | Ref. (0) |
| 1 | 1 215 | 0.17 (-0.06 to 0.40) | 0.11 (-0.11 to 0.34) | 0.11 (-0.11 to 0.34) |
| 2 | 751 | 0.42 (0.17 to 0.67)** | 0.33 (0.08 to 0.58)** | 0.30 (0.05 to 0.54)* |
| 3 | 848 | 0.37 (0.13 to 0.62)** | 0.27 (0.02 to 0.51)* | 0.24 (0.003 to 0.48)* |
| 4 | 2 085 | 0.38 (0.17 to 0.60)** | 0.23 (0.02 to 0.45)* | 0.20 (-0.02 to 0.41) |
| 5 | 1 469 | 0.75 (0.52 to 0.98)*** | 0.53 (0.30 to 0.76)*** | 0.45 (0.22 to 0.67)*** |
| 6 | 1 091 | 0.69 (0.45 to 0.93)*** | 0.45 (0.21 to 0.69)*** | 0.39 (0.16 to 0.63)** |
| 7 | 740 | 0.84 (0.58 to 1.09)*** | 0.56 (0.30 to 0.82)*** | 0.45 (0.19 to 0.70)** |
| Per CSD score | 8 716 | 0.11 (0.09 to 0.14)*** | 0.07 (0.05 to 0.10)*** | 0.06 (0.03 to 0.08)*** |
| P for trend | | <0.001 | <0.001 | <0.001 |
| **Number of adverse childhood experience (ACE) items (score)** | | | | |
| 0 | 4 822 | Ref. (0) | Ref. (0) | Ref. (0) |
| 1 | 2 592 | 0.40 (0.29 to 0.51)*** | 0.40 (0.29 to 0.50)*** | 0.38 (0.28 to 0.49)*** |
| 2 | 1 040 | 0.70 (0.55 to 0.85)*** | 0.66 (0.51 to 0.81)*** | 0.64 (0.49 to 0.79)*** |
| 3 | 235 | 1.26 (0.97 to 1.56)*** | 1.15 (0.86 to 1.44)*** | 1.11 (0.82 to 1.40)*** |
| 4 | 26 | 2.74 (1.88 to 3.60)*** | 2.61 (1.76 to 3.45)*** | 2.56 (1.72 to 3.40)*** |
| 5 | 1 | 11.70 (7.33 to 16.08)*** | 11.62 (7.33 to 15.91)*** | 11.50 (7.22 to 15.78)*** |
| Per ACE score | 8 716 | 0.41 (0.35 to 0.47)*** | 0.38 (0.33 to 0.44)*** | 0.37 (0.31 to 0.43)*** |
| P for trend | | <0.001 | <0.001 | <0.001 |

716 CI, confidence interval; GDS, Geriatric Depression Scale: higher scores indicating more negative



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symptoms; N, number; Ref, reference.
Model 1: adjusting for sex, and age.
Model 2: additionally adjusting for education, occupation, marital status, household income, smoking, alcohol drinking, physical activity, body mass index, and stressful life events in adulthood.
Model 3: additionally adjusting for adverse childhood experiences (ACE score) or childhood socioeconomic disadvantages (CSD score).
$^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.



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726 Table 3. Associations of childhood socioeconomic disadvantages and adverse childhood
727 experiences with GDS score in adulthood by sex.

| | *N* | Adjusted mean differences β (95% CI) in GDS score | | |
|---|---|---|---|---|
| | | Model 1 | Model 2 | Model 3 |
| | | **Men** | | |
| **Number of childhood socioeconomic disadvantage (CSD) items (score)** | | | | |
| 0 | 97 | Ref. (0) | Ref. (0) | Ref. (0) |
| 1 | 220 | 0.23 (-0.27 to 0.74) | 0.11 (-0.38 to 0.61) | 0.14 (-0.35 to 0.63) |
| 2 | 167 | 0.73 (0.20 to 1.26)** | 0.65 (0.14 to 1.17)* | 0.67 (0.15 to 1.18)* |
| 3 | 196 | 0.14 (-0.38 to 0.65) | -0.02 (-0.53 to 0.48) | 0.01 (-0.49 to 0.51) |
| 4 | 513 | 0.29 (-0.17 to 0.75) | 0.16 (-0.29 to 0.62) | 0.15 (-0.30 to 0.60) |
| 5 | 440 | 0.44 (-0.03 to 0.91) | 0.24 (-0.23 to 0.70) | 0.20 (-0.26 to 0.66) |
| 6 | 339 | 0.30 (-0.18 to 0.78) | 0.13 (-0.35 to 0.61) | 0.11 (-0.37 to 0.58) |
| 7 | 236 | 0.56 (0.06 to 1.07)* | 0.35 (-0.15 to 0.85) | 0.24 (-0.25 to 0.74) |
| Per CSD score | 2 208 | 0.04 (-0.01 to 0.08) | 0.01 (-0.03 to 0.06) | -0.003 (-0.05 to 0.04) |
| P for trend | | 0.14 | 0.58 | 0.90 |
| | | **Women** | | |
| **Number of childhood socioeconomic disadvantage (CSD) items (score)** | | | | |
| 0 | 420 | Ref. (0) | Ref. (0) | Ref. (0) |
| 1 | 995 | 0.15 (-0.11 to 0.42) | 0.11 (-0.15 to 0.37) | 0.10 (-0.15 to 0.36) |
| 2 | 584 | 0.32 (0.03 to 0.61)* | 0.23 (-0.05 to 0.51) | 0.18 (-0.10 to 0.46) |
| 3 | 652 | 0.43 (0.15 to 0.71)** | 0.33 (0.05 to 0.61)* | 0.29 (0.01 to 0.56)* |
| 4 | 1 572 | 0.40 (0.15 to 0.65)** | 0.24 (-0.003 to 0.49) | 0.20 (-0.05 to 0.44) |
| 5 | 1 029 | 0.85 (0.59 to 1.11)*** | 0.63 (0.36 to 0.89)*** | 0.52 (0.26 to 0.79)*** |
| 6 | 753 | 0.82 (0.54 to 1.10)*** | 0.55 (0.27 to 0.83)*** | 0.49 (0.21 to 0.77)** |
| 7 | 504 | 0.92 (0.61 to | 0.61 (0.31 to | 0.51 (0.20 to |



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| | | | | |
|---|---|---|---|---|
| | | 1.22)*** | 0.92)*** | 0.81)** |
| Per CSD score | 6 508 | 0.14 (0.11 to 0.17)*** | 0.09 (0.06 to 0.12)*** | 0.08 (0.05 to 0.11)*** |
| P for trend | | <0.001 | <0.001 | <0.001 |
| P for sex interaction | | <0.001 | 0.004 | 0.002 |
| | | | **Men** | |
| **Number of adverse childhood experience (ACE) items (score)** | | | | |
| 0 | 1 080 | Ref. (0) | Ref. (0) | Ref. (0) |
| 1 | 710 | 0.24 (0.04 to 0.44)* | 0.24 (0.04 to 0.43)* | 0.22 (0.03 to 0.42)* |
| 2 | 334 | 0.60 (0.34 to 0.86)*** | 0.60 (0.34 to 0.86)*** | 0.59 (0.33 to 0.84)*** |
| 3 | 77 | 1.26 (0.77 to 1.75)*** | 1.14 (0.66 to 1.62)*** | 1.15 (0.67 to 1.63)*** |
| 4 | 7 | 2.21 (0.65 to 3.77)** | 2.18 (0.66 to 3.71)** | 2.17 (0.64 to 3.69)** |
| 5 | 0 | - | - | - |
| Per ACE score | 2 208 | 0.35 (0.24 to 0.45)*** | 0.33 (0.23 to 0.43)*** | 0.33 (0.22 to 0.43)*** |
| P for trend | | <0.001 | <0.001 | <0.001 |
| | | | **Women** | |
| **Number of adverse childhood experience (ACE) items (score)** | | | | |
| 0 | 3 742 | Ref. (0) | Ref. (0) | Ref. (0) |
| 1 | 1 882 | 0.46 (0.33 to 0.58)*** | 0.46 (0.34 to 0.59)*** | 0.44 (0.31 to 0.56)*** |
| 2 | 706 | 0.74 (0.56 to 0.93)*** | 0.70 (0.51 to 0.88)*** | 0.66 (0.48 to 0.84)*** |
| 3 | 158 | 1.27 (0.91 to 1.63)*** | 1.15 (0.79 to 1.51)*** | 1.10 (0.74 to 1.45)*** |
| 4 | 19 | 2.93 (1.90 to 3.95)*** | 2.77 (1.77 to 3.78)*** | 2.73 (1.73 to 3.74)*** |
| 5 | 1 | 11.69 (7.23 to 16.14)*** | 11.61 (7.24 to 15.98)*** | 11.45 (7.09 to 15.81)*** |
| Per ACE score | 6 508 | 0.43 (0.36 to 0.50)*** | 0.41 (0.34 to 0.48)*** | 0.39 (0.32 to 0.46)*** |
| P for trend | | <0.001 | <0.001 | <0.001 |
| P for sex interaction | | 0.22 | 0.34 | 0.33 |

728 CI: confidence interval; GDS, Geriatric Depression Scale: higher scores indicating more negative
729 symptoms; N, number; Ref, reference.



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Model 1: adjusting for age.
Model 2: additionally adjusting for education, occupation, marital status, household income, smoking, alcohol drinking, physical activity, body mass index, and stressful life events in adulthood.
Model 3: additionally adjusting for adverse childhood experiences (ACE score) or childhood socioeconomic disadvantages (CSD score).
$^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.



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738 Table 4. Associations of childhood socioeconomic disadvantages and adverse childhood
739 experiences with GDS score in adulthood by social deprivation index.

| | *N* | Adjusted mean differences β (95% CI) in GDS score | | |
|---|---|---|---|---|
| | | Model 1 | Model 2 | Model 3 |
| | | **Low social deprivation index (SDI) in adulthood (0-1)** | | |
| **Number of childhood socioeconomic disadvantage (CSD) items (score)** | | | | |
| 0 | 437 | Ref. (0) | Ref. (0) | Ref. (0) |
| 1 | 1044 | 0.24 (0.009 to 0.48)* | 0.20 (-0.03 to 0.43) | 0.19 (-0.04 to 0.42) |
| 2 | 587 | 0.48 (0.23 to 0.74)*** | 0.44 (0.18 to 0.69)** | 0.40 (0.14 to 0.65)** |
| 3 | 654 | 0.40 (0.14 to 0.65)** | 0.32 (0.07 to 0.57)* | 0.29 (0.04 to 0.54)* |
| 4 | 1451 | 0.33 (0.10 to 0.55)** | 0.24 (0.01 to 0.46)* | 0.19 (-0.04 to 0.41) |
| 5 | 889 | 0.61 (0.37 to 0.85)*** | 0.49 (0.25 to 0.73)*** | 0.42 (0.17 to 0.66)** |
| 6 | 587 | 0.51 (0.25 to 0.77)*** | 0.39 (0.13 to 0.66)** | 0.34 (0.08 to 0.60)* |
| 7 | 342 | 0.57 (0.27 to 0.87)*** | 0.45 (0.15 to 0.75)** | 0.32 (0.01 to 0.62)* |
| Per CSD score | 5991 | 0.07 (0.04 to 0.09)*** | 0.05 (0.02 to 0.08)** | 0.03 (0.01 to 0.06)* |
| P for trend | | <0.001 | 0.001 | 0.02 |
| | | **High social deprivation index (SDI) in adulthood (2-4)** | | |
| **Number of childhood socioeconomic disadvantage (CSD) items (score)** | | | | |
| 0 | 29 | Ref. (0) | Ref. (0) | Ref. (0) |
| 1 | 68 | -0.09 (-1.23 to 1.06) | -0.40 (-1.54 to 0.73) | -0.25 (-1.36 to 0.86) |
| 2 | 73 | 0.07 (-1.06 to 1.20) | -0.19 (-1.31 to 0.93) | -0.11 (-1.20 to 0.98) |
| 3 | 97 | 0.21 (-0.88 to 1.30) | 0.16 (-0.92 to 1.25) | 0.19 (-0.87 to 1.25) |
| 4 | 317 | 0.41 (-0.59 to 1.41) | 0.26 (-0.74 to 1.26) | 0.32 (-0.65 to 1.30) |
| 5 | 303 | 0.91 (-0.10 to 1.91) | 0.68 (-0.32 to 1.69) | 0.58 (-0.40 to 1.57) |
| 6 | 243 | 0.65 (-0.36 to 1.66) | 0.50 (-0.52 to 1.52) | 0.47 (-0.53 to 1.46) |



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| | | | | |
|---|---|---|---|---|
| 7 | 195 | 0.84 (-0.19 to 1.87) | 0.70 (-0.34 to 1.73) | 0.65 (-0.36 to 1.65) |
| Per CSD score | 1325 | 0.15 (0.07 to 0.24)*** | 0.16 (0.07 to 0.24)*** | 0.13 (0.04 to 0.21)** |
| P for trend | | <0.001 | <0.001 | 0.003 |
| P for SDI interaction | | 0.30 | 0.12 | 0.16 |
| | **Low social deprivation index (SDI) in adulthood (0-1)** | | | |
| **Number of adverse childhood experience (ACE) items (score)** | | | | |
| 0 | 3428 | Ref. (0) | Ref. (0) | Ref. (0) |
| 1 | 1749 | 0.39 (0.27 to 0.51)*** | 0.39 (0.27 to 0.51)*** | 0.37 (0.26 to 0.49)*** |
| 2 | 656 | 0.66 (0.49 to 0.84)*** | 0.64 (0.47 to 0.82)*** | 0.63 (0.45 to 0.80)*** |
| 3 | 141 | 1.11 (0.76 to 1.46)*** | 1.02 (0.67 to 1.37)*** | 0.99 (0.65 to 1.34)*** |
| 4 | 17 | 1.89 (0.90 to 2.88)*** | 1.70 (0.72 to 2.68)** | 1.69 (0.71 to 2.67)** |
| 5 | 0 | - | - | - |
| Per ACE score | 5991 | 0.36 (0.29 to 0.43)*** | 0.35 (0.28 to 0.41)*** | 0.34 (0.27 to 0.40)*** |
| P for trend | | <0.001 | <0.001 | <0.001 |
| | **High social deprivation index (SDI) in adulthood (2-4)** | | | |
| **Number of adverse childhood experience (ACE) items (score)** | | | | |
| 0 | 639 | Ref. (0) | Ref. (0) | Ref. (0) |
| 1 | 415 | 0.47 (0.15 to 0.80)** | 0.50 (0.19 to 0.82)** | 0.47 (0.15 to 0.79)** |
| 2 | 216 | 1.04 (0.64 to 1.44)*** | 1.00 (0.60 to 1.40)*** | 0.95 (0.55 to 1.35)*** |
| 3 | 49 | 2.08 (1.34 to 2.83)*** | 1.97 (1.24 to 2.71)*** | 1.88 (1.14 to 2.61)*** |
| 4 | 5 | 4.20 (1.93 to 6.46)*** | 4.23 (2.01 to 6.46)*** | 4.13 (1.91 to 6.35)*** |
| 5 | 1 | 11.38 (6.34 to 16.41)*** | 11.89 (6.94 to 16.84)*** | 11.69 (6.74 to 16.64)*** |
| Per ACE score | 1325 | 0.64 (0.48 to 0.80)*** | 0.63 (0.47 to 0.79)*** | 0.60 (0.44 to 0.76)*** |
| P for trend | | <0.001 | <0.001 | <0.001 |
| P for SDI interaction | | 0.01 | 0.008 | 0.008 |

740 CI: confidence interval; GDS, Geriatric Depression Scale: higher scores indicating more negative
741 symptoms; N, number; Ref, reference.



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Model 1: adjusting for sex, and age.
Model 2: additionally adjusting for education, occupation, marital status, household income, smoking, alcohol drinking, physical activity, body mass index, and stressful life events in adulthood.
Model 3: additionally adjusting for adverse childhood experiences (ACE score) or childhood socioeconomic disadvantages (CSD score).
$^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$.



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750 Table 5. Associations of childhood socioeconomic disadvantages and adverse childhood
751 experiences with GDS score in adulthood with mediation by potential mediators.

| Mediators | Indirect effect (ACME) Estimate (95% CI)[a] | Direct effect (ADE) Estimate (95% CI)[a] | Total effect Estimate (95% CI)[a] | Proportion via mediation % (95% CI)[a] |
|---|---|---|---|---|
| **Childhood socioeconomic disadvantages** | | | | |
| Education (secondary or above vs primary or below) | 0.0208 (0.0157 to 0.0264)* | 0.0832 (0.0592 to 0.1110)* | 0.1040 (0.0802 to 0.1311)* | 20.11 (15.88 to 25.93)* |
| Occupation (unemployment vs employment) | -0.0001 (-0.0008 to 0.0005) | 0.1123 (0.0891 to 0.1391)* | 0.1122 (0.0890 to 0.1389)* | -0.08 (-0.09 to -0.06) |
| Marital status[b] (never married vs married) | -0.0011 (-0.0035 to 0.0002) | 0.1129 (0.0884 to 0.1412)* | 0.1118 (0.0878 to 0.1403)* | -0.99 (-1.25 to -0.79) |
| Household income[c] (≥ 30,000 CNY/year vs < 30,000 CNY/year) | 0.0116 (0.0084 to 0.0146)* | 0.0843 (0.0593 to 0.1131)* | 0.0959 (0.0712 to 0.1248)* | 12.19 (9.32 to 16.32)* |
| Smoking (ever vs never) | 0.0025 (0.0004 to 0.0049)* | 0.1111 (0.0879 to 0.1379)* | 0.1136 (0.0904 to 0.1403)* | 2.17 (1.75 to 2.72)* |
| Alcohol drinking (ever vs never) | 0.0007 (-0.0013 to 0.0029) | 0.1119 (0.8873 to 0.1386)* | 0.1125 (0.0891 to 0.1389)* | 0.58 (0.47 to 0.74) |
| Physical activity (moderate or above vs inactive) | 0.0016 (-0.0014 to 0.0045) | 0.1128 (0.0897 to 0.1395)* | 0.1144 (0.0908 to 0.1408)* | 1.42 (1.15 to 1.79) |
| Body mass index | -0.00004 (-0.0013 to 0.0012) | 0.1124 (0.0892 to 0.1391)* | 0.1123 (0.0890 to 0.1392)* | -0.04 (-0.05 to -0.03) |
| SLE in adulthood (yes vs no) | -0.0014 (-0.0033 to 0.0001) | 0.1131 (0.0900 to 0.1398)* | 0.1117 (0.0887 to 0.1387)* | -1.29 (-1.62 to -1.04) |
| **Adverse childhood experiences** | | | | |
| Education (secondary or above vs primary or below) | 0.0093 (0.0034 to 0.0157)* | 0.3981 (0.3444 to 0.4603)* | 0.4074 (0.3522 to 0.4689)* | 2.28 (1.98 to 2.63)* |
| Occupation (unemployment vs employment) | -0.0005 (-0.0026 to 0.0012) | 0.4076 (0.3535 to 0.4700)* | 0.4071 (0.3531 to 0.4691)* | -0.12 (-0.14 to -0.011) |
| Marital status[b] (never married vs married) | 0.00004 (-0.0017 to 0.0019) | 0.3838 (0.3254 to 0.4512)* | 0.3838 (0.3261 to 0.4506)* | 0.01 (0.01 to 0.01) |



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| | | | | |
|---|---|---|---|---|
| Household income[c] (≥ 30,000 CNY/year vs < 30,000 CNY/year) | 0.0051 (-0.0032 to 0.0131) | 0.4249 (0.3674 to 0.4913)* | 0.4300 (0.3715 to 0.4984)* | 1.18 (1.02 to 1.37) |
| Smoking (ever vs never) | 0.0005 (-0.0019 to 0.0030) | 0.4067 (0.3527 to 0.4690)* | 0.4072 (0.3540 to 0.4695)* | 0.12 (0.10 to 0.13) |
| Alcohol drinking (ever vs never) | -0.0046 (-0.0097 to -0.0003)* | 0.4120 (0.3581 to 0.4743)* | 0.4074 (0.3526 to 0.4692)* | -1.14 (-1.31 to -0.99)* |
| Physical activity (moderate or above vs inactive) | 0.0053 (0.0010 to 0.0101)* | 0.4039 (0.3500 to 0.4661)* | 0.4092 (0.3544 to 0.4721)* | 1.29 (1.12 to 1.49)* |
| Body mass index | 0.0023 (-0.0003 to 0.0056) | 0.4049 (0.3509 to 0.4672)* | 0.4072 (0.3526 to 0.4701)* | 0.57 (0.50 to 0.67) |
| SLE in adulthood (yes vs no) | 0.0070 (0.0030 to 0.0115)* | 0.3990 (0.3450 to 0.4613)* | 0.4059 (0.3525 to 0.4686)* | 1.72 (1.48 to 1.97)* |

ACME, average causal mediated effect; ADE, average direct effect; CI, confidence interval; GDS, Geriatric Depression Scale; SLE, stressful life events

[a] Adjusting for sex and age

[b] Sample size = 7 328

[c] Sample size = 7 316

*P < 0.05



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