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Childhood Adversity and Midlife Health: Shining a Light on the Black Box of Psychosocial Mechanisms

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Abstract

Adverse childhood experiences (ACEs) are associated with poorer health, which has spurred public health efforts to reduce the number of adverse events children experience. Unfortunately, it is unlikely that all ACEs can be prevented. For adults who already experienced ACEs in childhood, what psychological, social, and behavioral intervention targets might reduce risk for negative health outcomes? To provide insight into the "black box" of psychosocial mechanisms linking ACEs to poor health, our study used data from the Dunedin Study, a longitudinal cohort assessed from birth to age 45. Mediation models ($N = 859$) were used to examine whether candidate psychosocial variables in adulthood explained the association between childhood ACEs and health in midlife. Potential psychosocial mediators included stressful life events, perceived stress, negative emotionality, and health behaviors. Children who experienced more ACEs had poorer health in midlife. They also had significantly more stressful life events, more perceived stress, more negative emotionality, and unhealthier behaviors as adults. These mediators were each independently associated with poorer health in midlife and statistically mediated the association between ACEs and midlife health. Health behaviors evidenced the strongest indirect effect from ACEs to midlife health. Together, these psychosocial mediators accounted for the association between ACEs in childhood and health three decades later. Public health efforts to mitigate the health consequences of ACEs could aim to reduce the stressful life events people experience, reduce negative emotionality, reduce perceived stress, or improve health behaviors among adults who experienced childhood adversity.

Keywords Adverse childhood experiences · Stressful life events · Health behaviors · Personality · Health · Perceived stress

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Introduction

In the late 1990s, the Center for Disease Control (CDC) initiated the CDC-Kaiser ACE Study in conjunction with Kaiser Permanente to investigate childhood experiences and later health among almost 17,000 Americans (Centers for Disease Control and Prevention, 2016). The study focused on the prevalence of childhood adversity, as well as the adult health outcomes associated with adversity. The results highlighted two critical findings. First, adverse childhood experiences (ACEs) were far more common than previously recognized (Felitti, 2002)—60% of Americans had experienced a childhood ACE in the form of abuse, neglect, or family instability. Second, ACEs were associated with a host of negative adult health outcomes (Felitti et al., 1998). These central findings have been replicated numerous times. ACEs remain common—both in the USA and worldwide (Carlson et al., 2019; Merrick et al., 2018)—and are associated with

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poorer adult health (Baldwin et al., 2021; Bellis et al., 2015; Brown et al., 2009; Deschênes et al., 2021; Kelly-Irving et al., 2013a, b; Pierce et al., 2020; Reuben et al., 2016).

The association between ACEs and poorer health decades later is a stark reminder of how early experiences influence the life course. Such findings raise a critical question—how is it that childhood adversity translates to poorer health in adulthood? A growing body of literature has sought to explain the epidemiological findings from the original CDC-Kaiser study and subsequent replications by testing how ACEs might become biologically embedded to influence health (Kelly-Irving et al., 2013a, b; Solis et al., 2015; Su et al., 2015). Shining a light on the black box of plausible biopsychosocial mechanisms explaining this association could help identify future intervention targets that might improve health among the millions of who have experienced childhood adversity.

Prior empirical research linking ACEs and ill health has focused on both physiological and psychosocial mechanisms of action. Physiological mechanisms have included general "wear-and-tear" in the form of allostatic load (Solis et al., 2015), as well more specific pathways, such as earlier onset hypertension, chronic activation of the hypothalamic–pituitary–adrenal (HPA) axis, and epigenetic changes to DNA methylation (Kelly-Irving et al., 2013a, b; Su et al., 2015). Studies examining physiological pathways consistently highlight psychosocial mechanisms that might, in turn, influence physiology as an important link in the casual chain from ACEs to ill health. It is unlikely that poor health outcomes associated with ACEs are biologically embedded in the moment they are experienced, particularly given the wide-range of health outcomes. Instead, early adversity likely alters psychosocial functioning that then translates into physiological deterioration and eventual ill health, likely over years and decades.

What are the potential psychological, social, and behavioral mechanisms that might explain how ACEs are linked to poor health in adulthood? Prior research provides several plausible candidate mediators. First, adverse experiences like divorce have been linked to poorer health behaviors (Bourassa et al., 2019). Higher levels of smoking, lower levels of physical activity, or poorer diet are health-relevant behaviors that could be associated with ACEs (Bellis et al., 2014). Second, ACEs may influence people's personality as they age into adulthood (Ramsawh et al., 2011). Someone who experiences adversity might be more likely to develop a stress-reactive style of responding to their environment, which could translate to poorer health given links between neuroticism and ill health (Lahey, 2009). Third, it is possible that people who grow up in challenging, chaotic environments are more likely to experience similarly challenging, chaotic environments in adulthood, and experience a disproportionate number of stressful life events in adulthood as a result. Fourth, experiencing childhood adversity could make people more likely to experience their lives as more stressful, increasing their perceived stress in adulthood (Hong et al., 2018). Alterations in these candidate mechanisms could, in turn, lead to poorer downstream health.

Why is it important to identify the psychosocial and behavioral mechanisms linking ACEs and health? Recent public efforts, such as the California ACEs Aware campaign (ACEsaware.org), have sought to reduce the number of children experiencing ACEs and increase screening for ACEs. However, millions of people have already experienced childhood adversity, and unfortunately, millions more are likely to in the future. Preventing ACEs could reduce the health consequences associated with childhood adversity, but targeting health-relevant psychosocial sequelae of ACEs is another promising avenue. If we can identify modifiable intervention targets among adults who experienced ACEs, we may be able to reduce negative health outcomes through behavioral intervention. Testing potential mechanisms using longitudinal studies that assess ACEs and health later in life is an essential step in identifying the best targets for interventions that could improve the health of adults who experienced ACEs.

Present Study

The current study examined ACEs and midlife health using the Dunedin Longitudinal Study, a cohort assessed from birth until age 45. The investigation aimed to untangle which psychosocial mechanisms might explain poor health outcomes associated with ACEs. Figure 1 outlines the conceptual model guiding the study. Candidate mechanisms included stressful life events, perceived stress, negative emotionality, and health behaviors. Midlife health was assessed using a factor derived from self-rated health, other-rated health, and biomarker health at age 45. We hypothesized that children who experienced more ACEs would have poorer midlife health and that the psychosocial mechanisms would mediate this association.

Children with more ACEs are more likely to be raised in socioeconomically disadvantaged circumstances (Walsh et al., 2019), which raises the question whether ACEs contribute to health beyond low childhood SES. To address this possibility, we conducted sensitivity analyses in which we tested our primary models adjusting for childhood socioeconomic status (SES), as well models that included childhood SES as an additional form of childhood adversity.

Method

Participants and Study Design

Participants are members of the Dunedin Study, a longitudinal investigation of a population-representative birth cohort. The 1037 participants (91% of eligible births; 52% male)

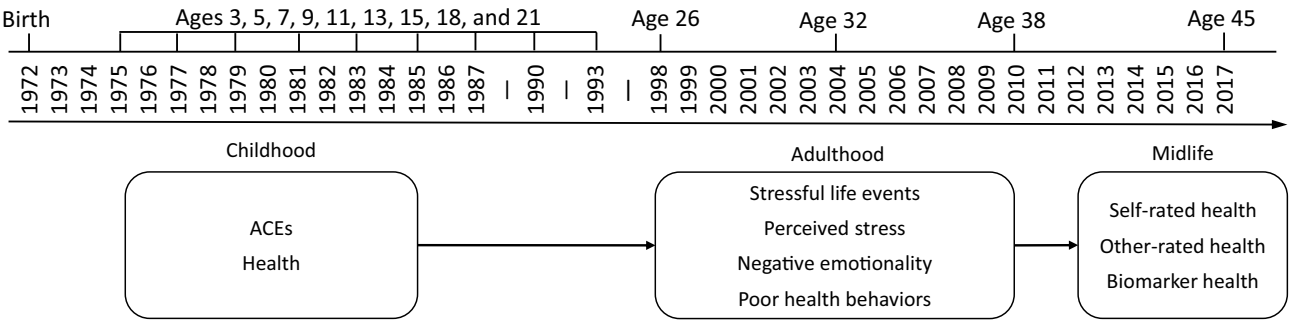

Fig. 1 Conceptual model of the study's measurement space and primary variables of interest

were all individuals born between April 1972 and March 1973 in Dunedin, New Zealand, who were eligible based on residence in the province and who participated in the first assessment at age 3 (Poulton et al., 2015). The cohort represented the full range of socioeconomic status (SES) in the general population of New Zealand's South Island. As adults, the cohort matches the results from the New Zealand National Health and Nutrition Survey on key adult health indicators (Poulton et al., 2015). It matches the distribution of educational attainment among citizens of the same age from the New Zealand Census (Richmond-Rakerd et al., 2020). The cohort is predominantly white (93%), matching South Island demographics (Poulton et al., 2015). Assessments were performed at birth; at ages 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, 38 and, most recently at age 45 years (completed April 2019), when 938 of the 997 participants (94.1%) still alive participated. The primary analysis sample included participants who had prospective data on ACEs, the four candidate mediators, and health during childhood and adulthood ($N = 859$, 86.2% of living cohort members, 49.8% women). Supplemental Fig. 1 shows the current study sample did not significantly differ from the Dunedin cohort in terms of childhood SES or ACEs.

Measures

Adverse Childhood Experiences (ACEs)

As previously described (Reuben et al., 2016), records from the first 15 years of participants' lives were reviewed by four independent raters from the Dunedin Study team to yield a prospective measure comprising 10 ACEs identified in the CDC ACE study (CDC, 2016). The ratings included five types of child harm (physical abuse, emotional abuse, physical neglect, emotional neglect, and sexual abuse) and five types of household dysfunction (incarceration of a family member, household substance abuse, household mental illness, loss of a parent, and household partner violence). Inter-rater agreement across all ACEs averaged a kappa of 0.79 (range = 0.76–0.82; Reuben et al., 2016). In line with the CDC study (Felitti et al., 1998), counts greater than four were recoded to four (mean = 1.0, $SD = 1.2$, range 0 to 4).

Candidate Psychosocial Mechanisms

Four candidate mechanisms were assessed in adulthood.

Stressful Life Events in Adulthood

The number of stressful life events that participants experienced from age 32 to 44 was assessed using a life history calendar (Caspi et al., 1996), as previously described (Bourassa et al., 2021). Participants reported events occurring over the past 5–6 years between study assessments at age 38 and 45, such that there were two assessments that included events spanning age 32 to 37 and age 38 to 44). Events were coded to provide a count of (1) each breakup; (2) whether someone moved frequently (10 or more moves, see Caspi et al., 2003); (3) homelessness during the assessment period; (4) incarceration during the assessment period; (5) the death of a friend or family member; (6) a job loss; (7) experiencing a medical illness, mental illness, injury, or accident; (8) a friend or family member experiencing a medical illness, mental illness, injury, or accident; (9) legal problems; (10) a physical or sexual assault; (11) serious financial problems; and (12) a natural or human-made disaster (e.g., fires, earthquakes). The events in were summed within each study period, averaged across periods, then truncated to a maximum of 30 events (mean = 11.3, $SD = 7.7$, range = 0 to 30). The measure evidenced strong inter-rater reliability—percent agreement = 92.2%, kappa = 0.91 (Bourassa et al., 2021).

Negative Emotionality

We assessed negative emotionality using two measures of personality, the Multidimensional Personality Questionnaire (MPQ; Patrick et al., 2002), and the Big 5 Neuroticism (Benet-Martinez & John, 1998). Participants completed the

MPQ at age 18 and 26 and we used the MPQ Stress Reactivity subscale scores in the current study, which assesses a low threshold for the experience of negative emotions such as fear, anxiety, and anger. Big 5 personality dimensions were assessed via informants nominated by the study participant as people who know them well (e.g., close friends, family) at ages 26 and 32. Each participant nominated up to three informants who then reported on five items assessing the participant's neuroticism. Items were asked on a three-point scale from "No" to "Yes – Certainly applies" and were averaged to create the subscale. MPQ stress reactivity at age 18 and 26 and Big 5 Neuroticism at age 26 and 32 were z-scored and averaged to create an index of negative emotionality in adulthood (mean = 0, *SD* = 1.0, range = −1.6 to 2.1).

Perceived Stress

Participants completed the Perceived Stress Scale, a validated measure of subjective stress (Cohen et al., 1983), at age 32. The 10-item measure assessed the degree to which people appraised their life as stressful. Higher scores represented relatively greater perceived stress (mean = 5.7, *SD* = 3.8, range = 0 to 20).

Health Behaviors

Health behaviors were assessed at age 32 and 38 using a published index of health behaviors (Lourida et al., 2019). The measure included the presence or absence of four health behaviors as reported by participants: smoking, physical activity, unhealthy diet, and alcohol consumption. Participants received one point for each unhealthy behavior—current smoking, not meeting physical activity guidelines, an unhealthy diet, and no/heavy alcohol consumption (see Lourida et al., 2019). Higher scores corresponded to poorer health behaviors (mean = 1.7, *SD* = 1.0, range 0 to 4).

Midlife Health

Midlife health was assessed using three indicators of health at age 45. The measures were z-scored and recoded such that higher scores represented relatively better health. We then created a single factor representing midlife health using principal component analysis. Self-rated health correlated with both other-rated ($r = 0.54$, $p < 0.001$) and biomarker-assessed health ($r = 0.36$, $p < 0.001$). Other-rated health was also correlated with biomarker-assessed health ($r = 0.43$, $p < 0.001$). Exported factor scores indexed participants' midlife health.

Self-rated Health

Self-reported health was assessed using an item that asked participants, "In general, would you say your health is?" Responses were on a 5-point scale (mean = 3.67, *SD* = 0.89) ranging from 1 ("poor") to 5 ("excellent").

Other-Rated Health

Other-rated health was assessed using informant and study interviewer reports using the item from the self-reported health question that participants answered. For informants, participants nominated three people who knew them well who were mailed a questionnaire. Study interviewers made ratings based on their perceptions of participants' health during the Study visit. At least one report was received for 97% of participants. Agreement among informants was moderately high (two-way random effects ICC = 0.71, 95% CI 0.67 to 0.75). For interviewers, four members of the study team involved in the participants' study age 45 assessment provided ratings. Agreement among interviewers was high (ICC = 0.80, 95% CI 0.78 to 0.82). Mean informant and interviewer ratings were moderately correlated ($r = 0.53$, $p < 0.001$) and were averaged to create the index of other-rated health (mean = 3.5, *SD* = 0.7, range = 1.0 to 4.9).

Biomarker Health

Biomarker health was assessed using the sum of nine biomarkers of physical health at age 45, as previously described (Israel et al., 2014; Reuben et al., 2016). This measure represents the number clinical cutoffs met for each measure assessing better or poorer health among participants. The measures included waist circumference (greater than 88 cm for women or greater than 102 cm for men), high-density lipoprotein levels (40 mg/dL or lower for men and 50 mg/dL or less for women), triglyceride levels (2.26 mmol/L or greater), blood pressure (systolic reading 130 mmHg or higher or diastolic reading 85 mmHg or higher), glycated hemoglobin concentration (greater than 5.7% percentage of total hemoglobin), cardiorespiratory fitness (membership in the lowest sex-specific quintile for maximum oxygen consumption adjusted for body weight, pulmonary function (forced expiratory volume in 1 s (FEV_1) and FEV_1/forced vital capacity (FVC); FEV1/FVC ratio below 0.70), periodontal disease (defined as 1 + site(s) with 5 or more mm of combined attachment loss), and systemic inflammation (CRP level greater than 3 mg/L). Higher scores denoted poorer health (mean = 2.5, *SD* = 1.9, range = 0 to 9).

Childhood Covariates

The study also included two potentially relevant childhood covariates.

Childhood Health

Participants' childhood health was assessed using a panel of biomarkers and clinical ratings taken at study phases spanning birth to age 11. As previously described (Belsky et al., 2015), two study staff members rated children's overall health at ages 3, 5, 7, 9, and 11 years based on review of birth records and assessment dossiers. These reports included a pediatric clinician's assessments and mothers' reports of infections, diseases, injuries, hospitalizations, and other health problems during standardized interviews. Clinical tests of motor development and measures of body mass, triceps and subscapular skinfold thickness, resting blood pressure, FEV1, and FEV1/FVC were also included. Scores were standardized (mean = 0, $SD = 1$, range −2.5 to 2.5) such that higher scores represented poorer health.

Childhood Socioeconomic Status (SES)

Childhood SES was measured using the 6-point Elley-Irving Socioeconomic Index for New Zealand (Elley & Irving, 1976). Childhood SES represented the average of the highest SES level of either parent from participants' birth through age 15 (mean = 3.8, $SD = 1.1$, range = 1 (unskilled laborer) to 6 (professional)). Children growing up in households whose average SES was lower than 3 (e.g., office cashier, floor finisher, cleaner, fish filleter) were grouped as growing up in low-SES households (Elley & Irving, 1976).

Data Analysis

The current study used path analysis (Muthén & Muthén, 2012) to test whether psychosocial mediators explained the association between ACEs and midlife health. We first tested the bivariate association between ACEs and the midlife health factor, then while accounting for childhood health and sex. We next tested the full mediation model, which included the association between ACEs, the psychosocial mediators, and midlife health. We also tested this mediation model for each midlife health indicator independently. Finally, we conducted sensitivity analyses to investigate whether accounting for childhood SES might explain the association between ACEs and health. Models were run in MPLUS version 8.3 (Muthén & Muthén, 2012) using full maximum likelihood estimation and bootstrapping ($N = 1{,}000$). All mediators were allowed to freely covary with other mediators in the models. We report standardized regression coefficients (βs) with 95% confidence intervals (CIs). Fit statistics were not reported, as all models were fully saturated. Analyses reported here were checked and confirmed by an independent data analyst for reproducibility creating new code from the manuscript and applying it to a copy of the original data.

Results

Do ACEs Predict Poorer Health in Midlife?

Children who experienced more ACEs had poorer midlife health, $\beta = -0.19$, 95% CI [−0.25, −0.13], $p < 0.001$. This association remained when controlling for childhood health and sex, $\beta = -0.18$, 95% CI [−0.24, −0.11], $p < 0.001$. The association between ACEs and health was similar to that for childhood health, $\beta = 0.23$, 95% CI [0.16, 0.29], $p < 0.001$.

Do the Candidate Mediators Explain the Association Between ACEs and Midlife Health?

We next tested whether the candidate psychosocial variables statistically mediated the association of ACEs and midlife health. Children who experienced more ACEs had significantly more stressful life events, more perceived stress, more negative emotionality, and poorer health behaviors in adulthood (Table 1). In turn, more stressful life events, more perceived stress, more negative emotionality, and poorer health behaviors were each associated with poorer midlife health (Table 1). When compared to the association between childhood health and midlife health ($\beta = 0.20$, 95% CI [0.14, 0.26], $p < 0.001$), the associations for perceived stress and negative emotionality were half as large, the association for stressful life events was similar, and the association for health behaviors was approximately 1.5 times larger. There was a significant indirect effect of ACEs on midlife health via all four of the mediators, and the size of the indirect effect for health behaviors was approximately three times the size of the other mediators. The association between ACEs and the midlife health was reduced to non-significance when accounting for the candidate mediators, $\beta = -0.04$, 95% CI [−0.11, 0.01], $p = .102$, indicating that the four psychosocial constructs mediated the association between ACEs and midlife health (Fig. 2).

Do Results Vary Across the Three Midlife Health Indicators?

Self-rated Health

As with the primary results, children who experienced more ACEs had poorer midlife self-rated health and this association was explained by more stressful life events, more

Table 1 Associations between ACEs, psychosocial mediators, and midlife health

$N = 859$	β	95% CI	p
ACEs predicting psychosocial mediators			
ACEs → stressful life events	0.11	[0.04, 0.18]	.002
ACEs → perceived stress	0.17	[0.10, 0.24]	< .001
ACEs → negative emotionality	0.21	[0.14, 0.27]	< .001
ACEs → poorer health behaviors	0.23	[0.16, 0.29]	< .001
Psychosocial mediators predicting midlife health			
Stressful life events → midlife health	−0.19	[−0.25, −0.12]	< .001
Perceived stress → midlife health	−0.10	[−0.17, −0.03]	.005
Negative emotionality → midlife health	−0.10	[−0.17, −0.03]	.005
Poorer health behaviors → midlife health	−0.31	[−0.36, −0.25]	< .001
Indirect effects from ACEs to midlife health			
Via stressful life events	−0.02	[−0.04, −0.01]	.006
Via perceived stress	−0.02	[−0.03, −0.00]	.018
Via negative emotionality	−0.02	[−0.04, −0.00]	.013
Via poorer health behaviors	−0.07	[−0.09, −0.05]	< .001
Covariances among mediators			
Stressful life events with perceived stress	0.30	[0.23, 0.37]	< .001
Stressful life events with negative emotionality	0.24	[0.17, 0.31]	< .001
Stressful life events with poorer health behaviors	0.10	[0.03, 0.16]	.004
Perceived stress with negative emotionality	0.42	[0.36, 0.47]	.002
Perceived stress with poorer health behaviors	0.12	[0.06, 0.19]	< .001
Negative emotionality with poorer health behaviors	0.15	[0.08, 0.21]	< .001

β statistics represent standardized regression coefficients.

All models were adjusted for sex and childhood health

ACEs adverse childhood experiences, *CI* confidence interval

negative emotionality, and poorer health behaviors in adulthood. In contrast to the primary findings, greater perceived stress was not associated with poorer self-rated midlife health (Table 2) nor did perceived stress mediated the association between ACEs and midlife self-rated health.

Other-rated Health

Results for other-rated health matched the main study results—children who experienced more ACEs had poorer midlife other-rated health and this association was explained by more stressful life events, more perceived stress, more negative emotionality, and poorer health behaviors in adulthood.

Biomarker-assessed Health

Similar to the primary findings, children who experienced more ACEs had poorer biomarker-assessed midlife health and this association was explained by poorer health behavior. In contrast to the main study findings, however, stressful life events, negative emotionality, and perceived stress were not associated with biomarker-assessed health nor did they mediate the association between ACEs and biomarker-assessed heath.

Sensitivity Analysis: the Role of Childhood SES

We next conducted sensitivity analyses to examine the role of childhood SES when assessing the association between ACEs and midlife health. For example, it was possible that the association between ACEs and health was better explained by childhood SES. Alternatively, low childhood SES could be considered an additional ACE and contribute to the current study's findings. To address these possibilities, we conducted two sensitivity analyses. First, we included childhood SES as a covariate in the primary models. Second, we included low childhood SES as an additional possible ACE in the primary models. The results of these two sensitivity analyses are presented in Table 3. The substantive findings remained similar when controlling for childhood SES and including low SES as an additional ACE, though some effect sizes were slightly altered in absolute size in each case. In short, the health relevance of childhood ACEs appears distinct from the effect of childhood SES.

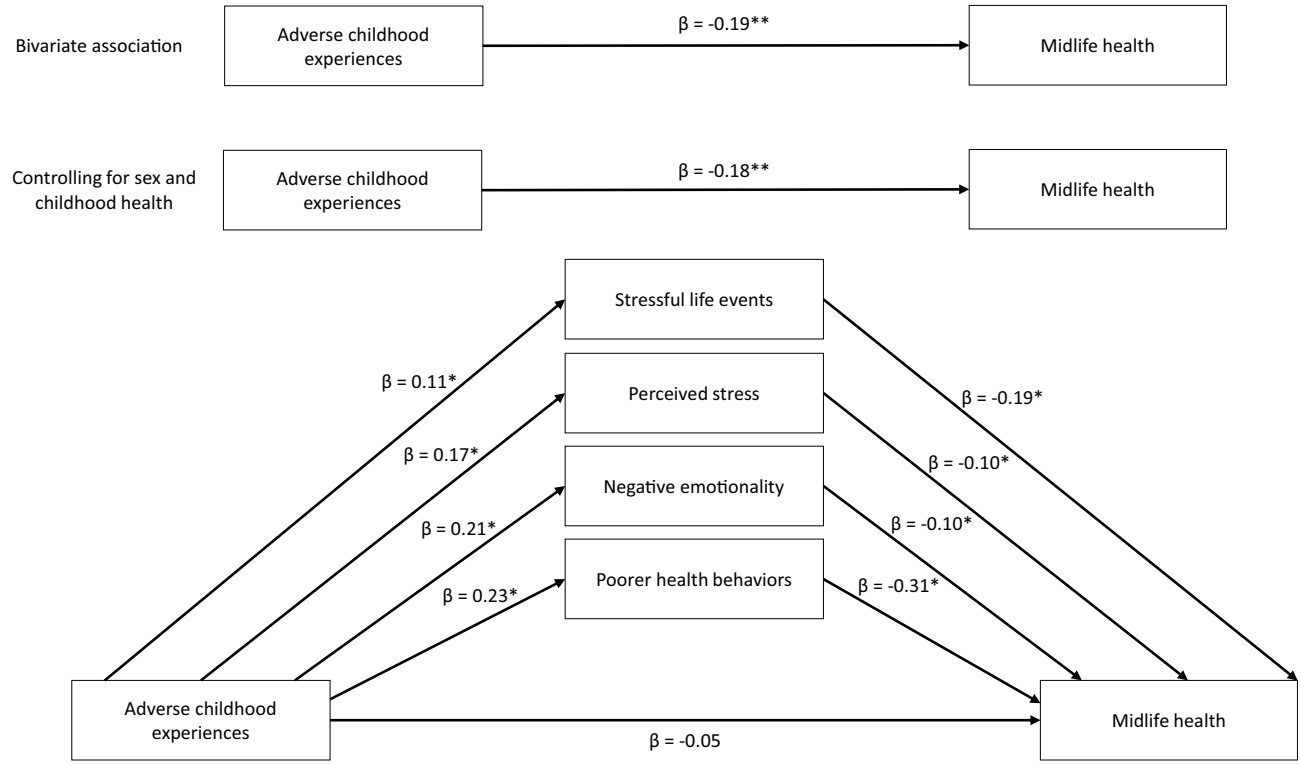

Fig. 2 Model results for associations among ACEs, proposed mechanisms, and health. All endogenous variables were regressed on sex and childhood health as covariates. *$p < .05$

Discussion

This study used data from 859 participants in the Dunedin Study to help shine a light on the "black box" of potential psychosocial mechanisms that might link ACEs and midlife health. The results showed that children who experienced more ACEs went on to have poorer health in midlife, whether health was measured by self-report, other-report, or a suite of biomarkers. Children who experienced ACEs had more stressful life events, more perceived stress, more negative emotionality, and poorer health behaviors in adulthood, and these psychosocial mechanisms in turn statistically mediated the association between ACEs and poorer midlife health. When compared to the size of the association between childhood health and midlife health, the magnitudes of the associations of stressful life events and health behaviors with midlife health were similar, suggesting the associations are comparable to an established predictor of future health. Health behaviors evidenced the strongest indirect effect from ACEs to midlife health. The study results remained when controlling for childhood SES, as well as when considering low childhood SES as an additional childhood adversity.

The study findings were relatively consistent across the three health outcomes when compared to the overall results, with some relevant differences. Both self-rated and other-rated health findings matched well with the overall pattern of indirect associations linking ACEs to the midlife health factor, whereas the biomarker-assessed health outcome showed significant associations for only health behavior. The other candidate psychosocial mediators were not associated with biomarker-assessed health at age 45 and did not evidence a significant indirect effect. These results suggest that health behaviors are the most consistent link between ACEs and both subjective and clinical indicators of midlife health. These findings might reflect the strong direct pathways from health behaviors, such as smoking and diet, to physiological health, particularly when compared to other psychosocial pathways that might operate indirectly. However, it is also possible that changes in health observable to participants at age 45 were not yet reflected in the clinical assessments, but might become evident at older ages. Regardless, these results suggest that changes in adult health behaviors could be a promising avenue to improve the health for those who experienced ACEs in childhood.

These results have theoretical and clinical implications. Theoretically, these results suggest ACEs could affect health through differences in adult psychosocial characteristics. These results align well with prior research finding that stressful life events can alter people's health behavior and

Table 2 Associations between the psychosocial mediators and each midlife health outcome

$N = 859$	β	95% CI	p
Main effect			
ACEs → self-rated health	−0.13	[−0.20, −0.07]	< .001
Direct effects on self-rated health			
Stressful life events → self-rated health	−0.16	[−0.22, −0.09]	< .001
Perceived stress → self-rated health	−0.06	[-0.13, 0.02]	.152
Negative emotionality → self-rated health	−0.11	[−0.19, −0.03]	.004
Poorer health behaviors → self-rated health	−0.24	[−0.30, −0.19]	< .001
Indirect effects of ACEs on self-rated health			
Via stressful life events	−0.02	[−0.03, −0.00]	.012
Via perceived stress	−0.01	[−0.02, 0.00]	.172
Via negative emotionality	−0.02	[−0.04, -0.01]	.013
Via poorer health behaviors	−0.06	[−0.08, −0.04]	< .001
Main effect			
ACEs → other-rated health	−0.18	[−0.25, −0.12]	< .001
Direct effects on other-rated health			
Stressful life events → other-rated health	−0.28	[−0.34, −0.21]	< .001
Perceived stress → other-rated health	−0.11	[−0.17, −0.05]	.001
Negative emotionality → other -rated health	−0.11	[−0.18, −0.04]	.001
Poorer health behaviors → other-rated health	−0.29	[−0.34, −0.23]	< .001
Indirect effects of ACEs on other-rated health			
Via stressful life events	−0.03	[−0.05, −0.01]	.004
Via perceived stress	−0.02	[−0.03, −0.01]	.009
Via negative emotionality	−0.02	[−0.04, −0.01]	.004
Via poorer health behaviors	−0.07	[−0.09, −0.04]	< .001
Main effect			
ACEs → biomarker-assessed health	−0.11	[−0.18, −0.05]	< .001
Direct effects on biomarker-assessed health			
Stressful life events → biomarker-assessed health	0.00	[−0.07, 0.08]	.959
Perceived stress → biomarker-assessed health	−0.07	[−0.14, 0.01]	.082
Negative emotionality → biomarker-assessed health	−0.00	[−0.08, 0.07]	.928
Poorer health behaviors → biomarker-assessed health	−0.19	[−0.26, −0.13]	< .001
Indirect effects of ACEs on biomarker-assessed health			
Via stressful life events	0.00	[−0.01, 0.01]	.961
Via perceived stress	−0.01	[−0.02, 0.01]	.106
Via negative emotionality	0.00	[−0.01, 0.01]	.929
Via poorer health behaviors	−0.04	[−0.06, −0.02]	< .001

β statistics represent standardized regression coefficients.

All direct effects of ACEs on the psychosocial mediators remained the same as reported in Table 1. All models were adjusted for sex and childhood health

ACEs adverse childhood experiences, *CI* confidence interval

personality (Bourassa et al., 2019; Lahey, 2009) and suggest an indirect route through which ACEs affect later health via differences in adult stressful life events, perceived stress, negative emotionality, and health behaviors. It is possible that the ways in which early life stressors impact later outcomes reflects changes in behavior that have been found to accompany poverty (Shah et al., 2012). People who experience adversity or unstable environments in childhood could direct their focus and behaviors differently than those who do not experience such adversity, translating to different downstream health outcomes. Although these variables mediated the association between ACEs and health in this sample, these results do not preclude other potential direct or indirect routes through which ACEs might be linked to later health. For example, it is possible that ACEs might also affect later health by sensitizing people to the experience of stressful life events (Bourassa et al., 2021) or directly changing physiological functioning (Kelly-Irving et al., 2013a,

Table 3 Associations between ACEs, psychosocial mediators, and midlife health: assessing the role of childhood SES

	Adjusting for childhood SES	Low childhood SES as an ACE
$N = 859$	β 95% CI	β 95% CI
Main effect		
ACEs → midlife health	−0.12** [−0.19, −0.05]	−0.19** [−0.26, −0.12]
ACEs predicting psychosocial mediators		
ACEs → stressful life events	0.11** [0.04, 0.18]	0.11** [0.04, 0.18]
ACEs → perceived stress	0.15** [0.08, 0.23]	0.18** [0.11, 0.25]
ACEs → negative emotionality	0.20** [0.13, 0.26]	0.20** [0.14, 0.26]
ACEs → poorer health behaviors	0.18** [0.11, 0.25]	0.24** [0.18, 0.31]
Psychosocial mediators predicting midlife health		
Stressful life events → midlife health	−0.19** [−0.26, −0.13]	−0.19** [−0.25, −0.13]
Perceived stress → midlife health	−0.10** [−0.16, −0.03]	−0.10** [−0.16, −0.03]
Negative emotionality → midlife health	−0.10** [−0.17, −0.03]	−0.10** [−0.16, −0.03]
Poorer health behaviors → midlife health	−0.29** [−0.34, −0.23]	−0.30** [−0.36, −0.24]
Indirect effects from ACEs to midlife health		
Via stressful life events	−0.02** [−0.04, −0.01]	−0.02** [−0.04, −0.01]
Via perceived stress	−0.01* [−0.03, 0.00]	−0.02* [−0.03, −0.00]
Via negative emotionality	−0.02* [−0.04, 0.00]	−0.02* [−0.03, −0.00]
Via poorer health behaviors	−0.05** [−0.07, −0.03]	−0.07** [−0.10, −0.05]

β statistics represent standardized regression coefficients.

All models were adjusted for sex and childhood health

ACEs adverse childhood experiences, *CI* confidence interval

*$p < .05$, **$p < .01$

2013b; Solis et al., 2015; Su et al., 2015). Regardless, given that the health burden of ACEs is disproportionately borne by marginalized and vulnerable populations—including racial and ethnic minorities, LGBT + communities, and those raised in socioeconomic disadvantage (McBride & Williams, 2013; Walsh et al., 2019)—these findings help provide insight into how ACEs could contribute to existing health disparities.

Clinically, the results of this study point to psychosocial targets in adulthood that might reduce the negative health outcomes associated with ACEs. With millions of people having experienced multiple ACEs in the past (Felitti et al., 1998; Merrick et al., 2018), there is a need for interventions that could improve the health of adults with a history of ACEs. These results suggest that intervening to reduce negative emotionality, stressful life events, perceived stress, and improving health behaviors in particular could address this need (Baldwin et al., 2021; Bellis et al., 2015; Brown et al., 2009; Kelly-Irving et al., 2013a, 2013b; Pierce et al., 2020). Notably, these intervention targets are largely modifiable and have established, efficacious behavioral treatments (Armstrong & Rimes, 2016; Jayawardene et al., 2017; Maglione et al., 2017; Martins & McNeil, 2009; Rogers et al., 2017; Sauer-Zavala et al., 2020). For example, mindfulness-based interventions and motivational interviewing have shown efficacy in promoting healthy behavior change for smoking, weight loss, and physical activity level (Maglione et al., 2017; Martins & McNeil, 2009; Rogers et al., 2017). Similarly, mindfulness-based cognitive therapy and the unified protocol have both been shown to reduce levels of negative emotionality in the form of neuroticism (Armstrong & Rimes, 2016; Sauer-Zavala et al., 2020). Higher levels of stress can also be addressed through the use of mindfulness and cognitive-behavioral therapy (Jayawardene et al., 2017; Svärdman et al., 2022). To the extent that stressful life events might lead to increased stress, such interventions might also address the pathways of ACEs on health via stressful life events, though future studies would be needed to confirm this empirically.

These findings are particularly important given the developmental context of ACEs, these candidate psychosocial mediators and midlife health. ACEs occurring in childhood are not preventable after the fact. Even if laudable efforts such as the ACEs aware campaign (ACEsaware.org) might reduce the number of ACEs in the future, they will not prevent all ACEs from occurring nor will they address health consequences for people over age 15 who have already experienced ACEs. By linking ACEs to health-relevant psychosocial mediators in adulthood, this study outlines potential avenues to reduce the negative health consequences of ACEs among adults who already experienced adversity, potentially at a period in their life where they might be better equipped to engage with therapies like mindfulness or CBT. In short, adults who have experienced multiple ACEs in childhood

comprise a group at risk for poor health who might benefit from efficacious interventions to address these psychosocial mediators. Given the higher prevalence of ACEs among groups facing long-standing health disparities (McBride & Williams, 2013; Walsh et al., 2019), interventions addressing the psychosocial sequelae of childhood adversity, particularly health behaviors, might also reduce existing health disparities.

This study has notable strengths. First, by using a deeply phenotyped longitudinal birth cohort studied over five decades, we were able to assess ACEs, psychosocial variables in adulthood, and midlife health prospectively. The longitudinal assessment provides temporal precedence and some assurance that the observed associations were not influenced by difficulties with retrospective reports of ACEs or psychosocial mediators. Second, the study used multiple methods of assessing health. Combining self-report, other-report, and biomarker-assessed health helps ensure that the associations observed in the study were not due to shared method variance among the relevant measures. Third, the cohort is intact and an age 52 follow-up will be completed over the next several years. This follow-up and planned future waves will provide the opportunity to continue to study ACEs, psychosocial mechanisms, and health outcomes during older ages, when clinical endpoints like the development of chronic diseases and premature mortality become more common. This future work would provide development scope from childhood to older age. Finally, the size of the sample was an additional strength. The 859 participants provided the mediation models greater statistical power than might be the case for smaller cohorts.

The results of the current study should be understood within the context of its limitations. First, the current findings used data from a longitudinal cohort study. Experimental studies or intervention trials will be needed to test whether altering these psychosocial variables might improve the health of adults who experienced ACEs. Second, although we selected four candidate mechanisms that might link ACEs and health from the existing scientific literature, other biobehavioral mechanisms might play a part in this association, such as social support or changes to stress-response physiology. Third, the birth cohort was composed of New Zealanders born in a single year 5 decades ago, and the composition of the sample was predominantly white. As a result, it is possible that different patterns of associations could be observed in different countries, different subpopulations within different countries, or among different age cohorts. The results of this study would benefit from replication in samples from other countries, in diverse populations, and among other age cohorts. Fourth, the timing of the psychosocial mediators was not identical across the ages of the data collection due to changes in the assessments between waves. It is possible that the timing of the measurement occasions influenced the pattern of results. Fifth, it is not possible to draw causal conclusions from these data, as they are observational. There are a number of alternative predictors that could account for the observed associations and there are alternative model specifications that are possible. Future intervention studies could provide causal evidence among the associations observed in this study. Finally, the current study examined health outcomes in midlife using three indicators: self-rated health, other-rated health, and biomarker health. Although these are validated health outcomes and appropriate given the age of the sample, future studies would benefit from examining clinical outcomes, such as the development and progression of chronic disease and mortality.

Conclusions

Participants with more ACEs reported more stressful life events, had greater negative emotionality, higher levels of perceived stress, and poorer health behaviors as adults, and these constructs predicted poorer health in midlife in turn. These psychosocial variables statistically mediated the association between ACEs and midlife health. These results suggest four modifiable mechanisms that future interventions could target to address the negative health outcomes associated with ACEs.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11121-022-01431-y.

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Declarations

Ethics Approval The authors certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments. Study protocols were approved by the Southern Health and Disability Ethics Committee at the New Zealand Ministry of Health and The Duke University Health System Institutional Review Board for Clinical Investigations. We thank the Dunedin Multidisciplinary Health and Development Study members, Unit research staff, and Study founder Phil Silva, PhD, University of Otago.

Consent to Participate Written informed consent was obtained from study participants.

Conflict of Interest The authors declare no competing interests.

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