



ELSEVIER

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Child Abuse & Neglect

journal homepage: www.elsevier.com/locate/chiabuneg

Adverse childhood experiences and all-cause mortality risk in adulthood

Sinéad D'Arcy-Bewick^{a,b}, Nicholas Turiano^c, Angelina R. Sutin^d, Antonio Terracciano^d, Páraic S. O'Súilleabháin^{a,b,*}

^a Department of Psychology, University of Limerick, Limerick, Ireland

^b Health Research Institute, University of Limerick, Limerick, Ireland

^c Department of Psychology, West Virginia University, WV, USA

^d College of Medicine, Florida State University, Florida, USA

ARTICLE INFO

Keywords:

Adverse childhood experiences
Mortality risk
Adulthood

ABSTRACT

Background: Adverse Childhood Experiences (ACEs) have been associated with mortality risk in adulthood. It is unclear, however, whether ACEs perpetrated beyond parents may be associated with mortality risk, if the risk is accumulative or plateaus at a certain frequency, whether associations differ dependent on ACE types, whether types interact with one another, or if observed effects differ by sex.

Objective: To examine associations between ACEs and mortality risk.

Participants and setting: 6319 participants (age range 25–74 years, mean [SD] 46.91 [12.95] years; 51.6 % female) followed from 1995/96 to 2018 as part of the survey of Midlife Development in the United States.

Methods: ACE variables were self-reported exposure to 20 ACE types from five categories: physical abuse, emotional abuse, socioeconomic disadvantage, adverse family structure, and poor health at age 16 years. Cox proportional hazards models were used to estimate mortality risk.

Results: ACEs were accumulatively associated with increased mortality risk in adjusted models (HR = 1.033; $p \leq .001$, 95 % CI, 1.014–1.053). The association was linear. Only physical abuse (HR = 1.05; $p = .024$, 95 % CI, 1.01–1.10) remained significantly predictive of increased mortality risk adjusting for other types. No interaction by sex or amongst ACE types was observed.

Conclusions: ACEs may be cumulatively associated with increased mortality risk, such that each individual ACE increases risk. Physical abuse may be an important ACE type within a mortality risk context. Individual ACE types warrant further study as each type may have their own differential impact on mortality risk.

1. Introduction

Adverse Childhood Experiences (ACEs) is a broad and evolving term that refers to a wide range of experiences that pose a threat to a child's physical or psychological well-being (Anda et al., 2010; Anderson et al., 2018; Felitti et al., 1998; Oral et al., 2016; Van Niel et al., 2014). ACEs can be viewed through the lifespan developmental perspective where exposure to adversity, particularly during

* Corresponding author at: Department of Psychology, University of Limerick, Castletroy, Galway V94T9PX, Ireland.

E-mail address: paraic.osuilleabhain@ul.ie (P.S. O'Súilleabháin).

<https://doi.org/10.1016/j.chiabu.2023.106386>

Received 10 February 2023; Received in revised form 20 July 2023; Accepted 25 July 2023

Available online 3 August 2023

0145-2134/© 2023 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

sensitive developmental periods, can lead to neurobiological and structural changes in the brain (Anda et al., 2006; Heikkinen, 2010; McLaughlin et al., 2014; Petruccelli et al., 2019). Indeed, ACEs are associated with an array of harmful outcomes in adulthood, including drug and alcohol misuse, stroke, lung diseases, cardiovascular diseases, and cancer (Bellis et al., 2015; Brown et al., 2009; Felitti et al., 1998; Godoy et al., 2021; Hu et al., 2021; Lopes et al., 2020; Petruccelli et al., 2019).

A recently published meta-analysis found that exposure to ACEs accounted for 15 % of all US deaths in one year (Grummitt et al., 2021). Consistent with lifespan and accumulation models of health and disease, cumulative adversity has been reported to be associated with mortality risk in some studies i.e., as adversity increases so too does mortality risk (Bellis et al., 2015; Brown et al., 2009; Halfon et al., 2014; Johnson et al., 2020; Kuh & Shlomo, 2004). Most studies categorize number of ACEs (e.g., 2 ACEs vs. 0; 4 ACEs vs. 0, etc.), which leads to variable reporting of mortality risk (Bellis et al., 2015; Brown et al., 2009; Johnson et al., 2020). While this approach supports the potential impact of multiple ACEs (presence of multiple different types of exposures) which frequently co-occur (Brown et al., 2009; Kelly-Irving et al., 2013), it cannot, for instance, address whether the relationship is linear (each ACE accumulatively increases mortality risk) or polynomial (a point at which the risk plateaus) (Brown et al., 2009).

With respect to mortality risk, type of adversity as well as number of ACEs varies considerably across studies. More comprehensive studies that assessed 11 or 12 ACEs have restricted outcomes by age (young adulthood or over 65 years) or have not directly measured important factors such as abuse or socioeconomic status (SES) (Bellis et al., 2015; Johnson et al., 2020; Rod et al., 2020). While adversities are related, and commonly co-occur (Dong et al., 2004), they are distinct experiences with potential differences in relation to mortality risk. Similar to broader health outcomes, efforts to understand mortality risk associated with ACEs would benefit from considering a wide range of related adverse exposures.

Research is beginning to disentangle the correlates and differential effects of different ACE types. A recent review of childhood abuse and neglect and resulting mortality risk concluded that significant variability exists across studies and effects vary considerably (D'Arcy-Bewick et al., 2022). While previous focus has largely been on parental abuse and neglect, theoretical and empirical support exists for broader inclusion of adverse conditions experienced in childhood (Anda et al., 2010). Physical abuse, sexual abuse, low SES, family conflict, parental divorce, and childhood mental illness have each been found to be significantly associated with mortality risk in individual studies (Chen et al., 2016; Kennedy et al., 2016; Larson & Halfon, 2013; Ploubidis et al., 2021; Rod et al., 2020; Rogers et al., 2021). One recommendation (D'Arcy-Bewick et al., 2022) has been to rigorously disentangle adversity experiences in future research. Even in studies that have examined a range of adversity types, there is variation in what type of specific ACE, if any, may be driving the associations. Some studies, for example, have found sexual abuse and physical abuse to be more strongly associated with mortality risk (Jackisch et al., 2019; Rogers et al., 2021), whereas other studies have found family conflict or breakdown to be the most important risk factors (Alm et al., 2019; Johnson et al., 2020; Pierce et al., 2020; Steel et al., 2020). Some evidence also exists for the differential impact of severity of ACEs (e.g., moderate vs. severe abuse) on mortality risk (Chen et al., 2016). While abuse is reported to be perpetrated predominantly by parents, most studies include parent-only abuses which excludes those who have been abused by others (Chen et al., 2016; Rogers et al., 2021). Few studies have examined whether different types of ACEs affect mortality risk in different ways and those that have, have produced varying results. Fewer still have explored how different types of ACEs may interact with each other, and with resulting mortality risk. Additionally, there appears to be sex-specific differences in the literature, but this is also unclear (Chen et al., 2016; Lee & Ryff, 2019). Female children generally appear to experience more ACEs than male children (Baglivio et al., 2014; Felitti et al., 1998). Females also appear to be at greater risk of sexual abuse, while males appear more likely to experience physical abuse (Baglivio et al., 2014; Dierkhising et al., 2019; Felitti et al., 1998). Furthermore, female adults (as compared to males) have been reported in certain studies to be at increased mortality risk following physical (Chen et al., 2016; Wang et al., 2023), emotional abuse (Chen et al., 2016), sexual abuse (Wang et al., 2023) in childhood. A review by the American Maternal Mortality Review Community found increased rates of maternal death amongst those who had experienced ACEs including emotional, physical, or sexual abuse, and household dysfunction (Kellerhals et al., 2023). Mortality risk has been reported for both sexes in further studies, with females again reported as being at greater risk following specific ACEs; serious illness, war/natural disasters, and number of events (Johnson et al., 2020). While various links between the sexes with a wide variety of mortality outcomes has been reported, much of the relations are unclear and require corroboration (Chen et al., 2016; Lee & Ryff, 2019).

In this current study, we examined the association between ACEs and all-cause mortality risk during adulthood. We addressed the above gaps by employing a comprehensive 20-item measure that incorporate ACEs (physical abuse, emotional abuse, disadvantaged SES, adverse family structure, and poor health) perpetrated by individuals beyond parents while using data from a well-characterized longitudinal cohort study to a) investigate the linear and polynomial associations on mortality risk, b) investigate individual ACE types (both separately and simultaneously), and their unique, collective, and interactive associations with all-cause mortality risk in adulthood, and c) to investigate possible sex differences in the association between ACEs and mortality risk. The rationale for investigating each of the above arises from, firstly, the varying literature about the impact of cumulative ACEs and the question about whether there is a point at which the impact plateaus. In other words, we sought to determine if there is a frequency of ACEs where the risk doesn't increase any further due to the cumulative impact of a high frequency of ACEs. Secondly, to further the literature in this area, it is important to investigate whether and how individual ACEs interact with each other and mortality risk. Finally, the inconsistencies surrounding whether there are sex differences when it comes to ACEs and mortality risk means further investigation and clarification is warranted.

2. Methods

2.1. Sample

Data was drawn from the first wave of the National Survey for Midlife Development in the United States (MIDUS) longitudinal cohort study which included 7108 non-institutionalized, English-speaking adults aged 25–74 years living in the USA. Data was collected between 1995 and 1996 from national random-digit-dialing and a subsequent self-administered questionnaire (for a detailed data collection process for MIDUS see Radler, 2014). Of the 7108 participants, 89 % provided data for the sample included in this study ($N = 6319$). At baseline, age ranged from 25 to 74 years (mean [SD] 46.38 [12.98]).

2.2. Measures

2.2.1. Adverse childhood experiences (ACEs)

Table 1 shows the items for the five categories of ACEs evaluated in this study: physical abuse, emotional abuse, disadvantaged SES, adverse family structure, and poor health at age 16. Items ($n = 20$) were identified from the baseline survey of MIDUS that had empirical and theoretical (Chen et al., 2016; Felitti et al., 1998; Morton et al., 2014; Turiano et al., 2017) relevance to the five categories of ACEs. Physical and Emotional abuse were measured using the Conflict Tactics Scale (Straus, 1979). Disadvantaged SES, adverse family structure, and poor health at age 16 were self-report measures using either continuous rated responses (e.g., physical health at age 16 ranging from 1 = poor, 5 = excellent) or dichotomous responses (parental divorce 0 = no, 1 = yes). Each item was coded as a dummy variable (1 = exposure, 0 = no exposure). Items were summed for an overall ACEs score (range = 0–20) and within each of the five categories of ACEs (see Table 1). For detailed information on how measures were handled including a table identifying the distribution of ACEs scores, see Supplementary material.

2.2.2. Confounding variables

Confounding variables (Table 2) were included because of their relevance to ACEs and mortality risk (Chen et al., 2016; Turiano et al., 2017). Age (in years), sex (female = 0, male = 1), education (highest level completed; range 1 [no school/some grade school]-12 [advanced degree]), race (white = 0, 1 = black, asian or pacific islander, multiracial or otherwise identified), marital status (married = 0, separated/divorced/widowed/never married = 1), and chronic conditions (sum of reported doctor-diagnosed chronic medical conditions, such as hypertension, cardiac disease, cancer, stroke, diabetes).

2.2.3. Mortality

Mortality data was obtained using National Death Index (NDI) reports combined with tracing/closeout phases as part of normal longitudinal sample maintenance. Survival time was defined as years from baseline assessment to date of death. Living participants (censored observations) had survival times that equaled the length of the follow-up. The most recent update for mortality data was October 31, 2018. Detailed information on the methods of processing mortality data is in supplementary materials.

Table 1
Dimensions and definitions of ACEs.

Dimension	Adversity	Definition
Physical abuse	Moderate physical abuse by mother, father, sibling, or other Severe physical abuse by mother, father, sibling, or other	How frequently someone pushed grabbed, or shoved them (moderate); slapped; threw something at; kicked, bit, or hit with a fist, hit or tried to hit with something; beat; choked; burned or scalded them (severe)
Emotional abuse	Emotional abuse by mother, father, sibling or other	How often someone insulted or swore at them; sulked or refused to talk to them; did or said something spiteful; threatened to hit; smashed or kicked something in anger
Disadvantaged SES	Family welfare, education level of head of household, being financially worse off than others	Being in receipt of welfare or assistance for dependent children for a period of 6 months or longer; head of household having less than a high school education; self-reported financially worse off than other families
Poor health	Physical health Mental health	Self-reported poor physical health at age 16 Self-reported poor mental health at age 16
Adverse family structure	Parental divorce Lack of father figure, parental death	Parents divorced in childhood; lack of father figure at home; death of parent during childhood

Table 2
Descriptive statistics of the sample.

Variable	n	Deceased		Alive		Complete sample
		(N = 1281)		(N = 5038)		
		Mean(SD)/%		Mean(SD)/%		
Sex (% female)	1281	47.9 %	5038	53.7 %	6319	51.6 %
Age (years)	1281	59.73(10.77)	5038	43.66(11.33)	6319	46.91(12.95)
Race (white)	1254	91.6 %	4495	90 %	6249	90.3 %
Education (high school or higher)	1254	6.20(2.54)	5031	7.00(2.45)	6306	6.84 (2.49)
Marital status (married)	1281	62.2 %	5035	69 %	6316	65.7 %
Chronic Conditions	1276	3.27(2.83)	5026	2.18(2.28)	6302	2.40(2.44)
Childhood Adversity	1281	3.64(3.10)/89.5 %	5038	3.53(2.99)85.7 %	6319	3.55(2.56)/87.3
Physical Abuse (PA)	1273	1.25(1.74)/48.6 %	5017	1.23(1.61)/50.6 %	6290	1.23(1.64)/48.7 %
Moderate PA	1266	0.85(1.11)/46.1 %	5007	0.87(1.06)/51.2 %	6273	0.86(1.07)/50.3 %
Severe PA	1270	0.41(0.83)/24.8 %	5009	0.36(0.76)/23.4 %	6279	0.37(0.77)/23.7 %
Emotional Abuse	1268	1.01(1.17)/52.8 %	5008	1.2(1.19)/62.7 %	6276	1.16(1.19)/60.7 %
Disadvantaged SES	1281	1.06(0.83)/73.4 %	5038	0.78(0.83)/55.4 %	3619	0.83(0.83)/59.1 %
Adverse family structure	1281	0.27(0.57)/20.3 %	5037	0.23(524)/18 %	6318	0.24(0.53)/20.1 %
Poor health at 16	1281	0.8(0.31)/7 %	5038	0.11(0.353) 9.1 %	6319	0.10(0.35)/8.7 %

2.3. Statistical analyses

Statistical analyses were conducted using RStudio (2020) and Statistical Package for Social Sciences, version 28 (IBM, 2021). Cox proportional hazards models were used to calculate hazard ratios (HRs) and 95 % confidence intervals (CIs) to estimate the risk of death to consider time-to-event, including those reported as alive (censored). Schoenfeld Residual Analysis was conducted to assess the assumption of proportionality. To assess linearity, both Martingale and Deviance Residuals were assessed. These analyses revealed a potential violation of proportionality by age ($X^2 = 19.94$, $df = 1$, $p \leq 0.001$). The relationship between age and mortality varied across time. Therefore, in accordance with the interaction method when a potential violation of the assumption occurs (Allison, 2010; O'Suilleabháin et al., 2021), all models included an interaction term for age and survival time as a confounding variable for age.

Age, and individual ACE counts were centered to aid interpretations. Examination of chronic conditions revealed several extreme outlier observations ($n = 7$). Winsorizing was employed to limit the number of chronic conditions to 13 which was deemed to represent closest observation to the frequency observations and not deemed suspect for the sample size (Dixon & Yuen, 1974). To ensure winsorization did not alter estimates significantly, main analyses were conducted with chronic conditions winsorized at both 12 and 14 (Dixon & Yuen, 1974; O'Suilleabháin et al., 2021). Results did not differ. Modification of all hypothesized associations was also investigated by sex (Chen et al., 2016; Lefevre et al., 2004).

To statistically adjust for the increased error rate due to the increased number of statistical tests associated with the individual ACE types and two-way interaction terms, False Discovery Rate analyses (FDR) was employed (Benjamini & Hochberg, 1995; Glickman et al., 2014). We performed FDR analyses with a particular view to assess significant predictor variables that were deemed close to the critical level ($p = .05$) or HRs with CIs ranging below and above 1 to account for the possibility they could be the result of Type I error. FDR controls for Type 1 error for multiple tests without significant inflation in Type II error and is particularly useful in early-stage or discovery phase research (Glickman et al., 2014). See sTable 1 in supplementary materials for FDR analyses.

A first set of Cox regression analyses were run to estimate the effects of ACEs on mortality risk. In model 1, ACE score was tested as predictor of mortality controlling for sociodemographic factors (age, sex, race, education, marital status) (Turiano et al., 2017). Model 2 added chronic conditions (O'Suilleabháin et al., 2021). Model 3 tested the polynomial association between ACEs and mortality risk. Model 4 tested whether the association varied by sex.

A second set of Cox regression analyses were estimated to examine each category of ACE. Model 5 tested each ACE category separately, controlling for the confounding variables as in Model 2. Model 6 tested all five ACE categories simultaneously. Additional analyses tested physical abuse severity (1: Moderate, 2: Severe) individually and with the other ACEs. Model 7 tested an interaction between sex and each ACE category. Exploratory analysis (termed Model 8) tested interactions between types of ACEs, with each interaction being tested individually.

3. Results

3.1. Study sample

Of the 6319 individuals included in the study, 12.7 % ($n = 805$) reported 0 ACEs, and 87.3 % reported experiencing at least 1 ACE or more ($M = 3.23$, $SD = 2.56$). The median number of reported ACEs was 3 (range = 0–17). During the follow-up that ranged from 0.8

Table 3
Cumulative ACEs and mortality risk.

Variable	Model 1	Model 2	Model 3	Model 4
	HR[95%CI]	HR[95%CI]	HR[95%CI]	HR[95%CI]
Age	97.52 [81.06–117.32]***	95.06[78.91–114.52]***	95.02[78.91–114.52]***	133.14 [109.60–161.72]***
Sex	1.25[1.11–1.40]***	1.30[1.15–1.46]***	1.30[1.09–1.55]**	1.03 [0.92–1.16]
Race	1.12[0.916–1.28]	1.14[0.93–1.40]	1.14[0.93–1.40]	1.14 [0.92–1.40]
Education	0.96[0.94–0.99]**	0.97[0.94–0.99]**	0.97[0.94–0.99]**	0.99 [0.97–1.02]
Marital status	1.16[1.03–1.31]*	1.14[1.01–1.29]*	1.14[1.01–1.29]*	0.91 [0.81–1.03]
Chronic conditions	–	1.07[1.04–1.10]***	1.07[1.05–1.10]***	1.04 [1.02–1.07]***
ACE × sex	–	–	1.00[0.96–1.04]	–
ACE (Quadratic)	–	–	–	1.00 [0.99–1.004]
Cumulative ACEs	1.04[1.02–1.06]***	1.03[1.01–1.05]***	1.03[1.01–1.06]*	1.04 [0.99–1.09]

Note. HR = Hazard Ratio, CI = Confidence Interval, *p* = significance level; *** *p* < .001; ** *p* < .01; * *p* < .05

to 23.84 years, 1281 (20.27 %) subjects died. The mean survival time for deceased individuals was 12.44 years (SD = 5.92; range = 0.08–22.97 years).

Chi-Square tests revealed that those in the deceased group were more likely to be male ($X^2_1 = 14.0, p \leq 0.001$) and unmarried ($X^2_1 = 21.2, p \leq 0.001$). Between-subjects ANOVA indicated a significant difference in mean age ($F(1,6317) = [2095.3], p \leq 0.001, R^2 = 0.25$) and education ($F(11,6294) = [15.0], p \leq 0.001, R^2 = 0.03$), such that the deceased were more likely to be older and have a lower level of education. ACE scores did not differ between those deceased or alive (*p* = .219).

3.2. ACEs and all-cause mortality

Table 3 reports the Cox regression analyses for overall ACE score and all-cause mortality. Controlling for sociodemographic factors, every additional ACE was associated with a 4 % increased risk of mortality (Model 1), which was only slightly attenuated adjusting for chronic conditions (Model 2). The association was not moderated by sex (Model 3). The polynomial (quadratic effect) was not significant, which indicated that the association between ACEs and mortality risk appears to be a linear association (Model 4).

3.3. Individual ACE type and all-cause mortality

Entered individually (Model 5), emotional abuse, physical abuse, and SES disadvantage (Table 4) were significantly associated with increased mortality risk. When treated separately, moderate physical abuse and severe physical abuse significantly predicted mortality risk. When all five types of ACEs were entered simultaneously, only disadvantaged SES and physical abuse remained significant (Model 6). Severe physical abuse (excluding moderate and overall physical abuse) also remained significant when entered into the model with the other five ACEs. FDR analyses suggested that severe physical abuse did not reach critical significance value, nor did disadvantaged SES, indicating caution around rejecting the null hypothesis. No interaction effects for sex were found for any ACE category (Model 7; sTable 2). Exploratory analyses of interaction effects between ACE type found one significant interaction (disadvantaged SES and adverse family structure) that did not reach the critical FDR threshold for statistical significance (Model 8; sTable 3).

Table 4
ACE types predicting mortality risk.

Variable	Model 5	Model 6
	HR[95 % CI]	HR[95 % CI]
Physical abuse	1.06[1.03–1.10]***	1.05[1.01–1.10]*
Moderate physical abuse	1.08[1.03–1.14]**	1.051[1.01–1.10]
Severe physical abuse	1.12[1.04–1.20]**	1.085[1.00–1.18]*
Emotional abuse	1.06[1.01–1.11]*	1.01[0.95–1.08]
SES	1.10[1.03–1.19]**	1.08[1.00–1.17]*
Family factors	1.02[0.93–1.13]	0.99[0.90–1.08]
Health at 16 years	0.90[0.75–1.08]	0.87[0.72–1.04]

Note. HR = Hazard Ratio, CI = Confidence Interval. Model 5 includes confounding age, sex, race, education, marital status and chronic conditions. Each row is a different model so that each type of adversity is tested separately from the other types of adversity. Model 6 includes the same confounding variables but also includes all the types within a single model to test the unique predictive ability of each adversity type, while controlling for all other types. Levels of physical abuse (total, moderate, severe) were added to the model separately. When both levels of physical abuse (moderate, severe) were added into the full model, neither were significant. *** *p* < .001; ** *p* < .01; * *p* < .05.

4. Discussion

4.1. Cumulative ACEs and mortality risk

We found that ACE score was associated with an increased risk of all-cause mortality in adults. This association remained after controlling for confounding variables. The results suggest that each increase of 1 ACE (in a comprehensive measure of 20) was associated with an estimated 3.3 % increase in mortality risk. We also investigated the possibility of a polynomial association to determine if mortality risk plateaus with increasing number of ACEs. The results did not support such an association. This finding adds to the broader literature suggesting the burden of ACEs on morbidity and mortality is predominantly a cumulative effect of exposure to multiple adversities (Anda et al., 2010; Bellis et al., 2015; Epel & Prather, 2018; Felitti et al., 1998; Hoffmann, 2016; Toft et al., 2018). Felitti et al.'s original ACE study indeed found a graded relationship between number of ACEs and a range of health risk behaviors and diseases such as cancer and heart disease (1998). More recent investigations into mortality risk have also suggested multiple adversities pose a greater mortality risk in adulthood (Bellis et al., 2015; Rod et al., 2020). In contrast with our findings, however, Brown et al.'s investigation into ACEs and mortality risk found no graded association in their study (Brown et al., 2009). Kelly-Irving and colleagues found a graded relationship between ACE count and mortality risk but for females only (Kelly-Irving et al., 2013), as did Chen et al. (2016) who found mortality risk increased with number of abuses experienced for females but not males. Reasons for the differing results may be that most studies have tended to categorize ACEs e.g., '5 ACEs vs 0', or 'some abuse vs none', which makes testing linear and polynomial associations more difficult. Some of these studies also restricted the sample, for example, to over 50 years of age (Kelly-Irving et al., 2013). Furthermore, given the association between sex (male/female) and mortality risk, many studies stratify analyses by sex (e.g., Kelly-Irving et al., 2013) rather than testing by way of interaction effects. This may be one reason for the differing results; we found no sex differences when we examined sex interactions with ACEs either cumulatively or individually.

4.2. Individual ACE types and mortality risk

Our study explored individual types of ACEs both simultaneously and individually. When considered individually, emotional abuse, physical abuse (both moderate and severe), and disadvantaged SES were each significantly associated with increased mortality risk. However, when all 5 categories were entered together, physical abuse (and separately, severe but not moderate physical abuse), and disadvantaged SES remained significant; however, FDR analyses suggested caution with respect to SES. We found physical abuse remained significantly associated with mortality risk, a finding that withstood FDR analysis. This finding replicates some prior studies examining physical abuse in childhood and later mortality risk (Chen et al., 2016; Rogers et al., 2021). With regards to other adversity categories, our findings did not replicate prior studies on specific adversity types and mortality risk. Nor have prior studies seemed to replicate each other. For example, some studies have identified SES (Pudrovska & Anikputa, 2014; Rod et al., 2020) as a predictor of mortality risk while others have not (Jackisch et al., 2019), and other studies have identified family relationships over other ACEs as predictive of mortality risk (Alm et al., 2019; Steel et al., 2020). Reasons for these differences may be the interplay between overlapping adversities, mediating factors that may play a role in this relationship, and the demographics of the sample used. Again, others have found differential effects based on sex (male/female) (Chen et al., 2016; Johnson et al., 2020; Lee & Ryff, 2019). Similar to our study, however, Rogers et al. (2021) found no interaction effect for sex. It is possible that the ACE measurements in previous studies, and the extent to which other ACEs were considered, explain the differences in findings. There is the possibility that the differential impact of ACEs on mortality risk does not differ between males and females.

4.3. General implications

The findings in our study have potential implications for future public policy and health care. While there is a need for replication of our findings, our study suggests that ACEs cumulatively impact individuals' mortality risk across adulthood, further adding to literature indicating the importance of preventing or reducing the impact of even one ACE. Physical abuse appeared to be particularly important when considering mortality risk. In terms of policy, evidence shows that bans on corporal (physical) punishment have been correlated with reduction in physical punishment rates (Zolotor & Puzia, 2010). Along with addressing ACEs more broadly, this study indicates that addressing physical abuse may have a long-lasting impact across the lifespan.

While some members of society are more at risk of ACEs than others, they are common and span cohorts, cultures, and social classes. This is particularly apparent considering the demographics of our study sample (predominantly white and well-educated). The considerable number of adverse outcomes arising from childhood adversities highlights the scale of the problem and underscores an urgency to address it. Organizations such as United Nations International Children's Emergency Fund (UNICEF) and the World Health Organisation (WHO) aim to implement policy tackling ACEs as well as identifying ways to address and promote successful development and aging across the lifespan (UNICEF, 2014; WHO, 2015, 2019, 2020). Prevention of ACEs can occur through enacting policy, providing appropriate supports, and engaging screening processes. This study adds further evidence to the importance of addressing ACEs, and the important role they have in mortality risk across adulthood. With replication and the uncovering of pathways explaining these links, the generation of personalized interventions could lead to a decrease to premature mortality.

4.4. Strengths and limitations

There are several strengths to this study. Taken together, there are several aspects to our study that may explain the differences

between our findings and other publications. Amongst others, our study incorporated a comprehensive measure of ACEs not previously utilized. Our study also utilized a large sample followed for over two decades, ensuring considerable power to detect effects in addition to incorporating abuse by siblings and others. Mortality data was verified via death registries. Our study included a comprehensive 20-item ACE measure and included physical abuse by those other than parents. This is particularly important given the need to expand ACEs to include abuse by others (Anda et al., 2010). There has been little previous emphasis on the examination of independent associations for ACE types. To our knowledge, three studies have investigated independent associations; Lee and Ryff (2019) who stratified analyses by gender, Rogers et al. (2021) who followed individuals up to 58 years of age, and Johnson et al. (2020) who included only those aged 65 years or above. Our study was novel in its exploration of interactions between adversity types, and across middle and later adulthood.

Limitations to our study must also be noted. Our sample was predominantly white and excluded those without a home at the time of the baseline study. This leaves the study open to healthy survivor effect (survival bias) in that those who are at highest risk of adverse childhoods as well as certain populations such as homeless, incarcerated, or at-risk marginalized or minority groups were either excluded or significantly underrepresented (D'Arcy-Bewick et al., 2022). Importantly, those already deceased are also missing from this study. In other words, possible participants who may uncover important relations would have been deceased before data collation commenced. Our study relied on retrospective self-report measures of ACEs which may be subject to recall bias. However, there is evidence that recalling certain adversities such as abuse appears relatively consistent over time and evidence exists for under-reporting rather than over-reporting of historical adversities (Maughan & Rutter, 1997). Further evidence also reports that false positive reporting is likely rare (Hardt & Rutter, 2004). In addition, although it is a limitation that the focus was on occurrence and did not include timing, recall is reported to be better for occurrence of an event rather than timing, and false positive are mostly rare (Hardt & Rutter, 2004). There are further ACEs that would also be critical to examine that were not available within the present data wave under examination, such as exposure to various violence and sexual abuse. In line with the WHO definition of children, health at age 16 in our study may have limitations without more robust assessment including health status at various points during childhood. While all-cause mortality was examined due to reliability compared to cause-specific mortality status which may be related to aging processes (Gerstorff et al., 2006), future research may benefit from examining specific causes (e.g., suicide). It would also be beneficial for future research to examine relations across specific stages during the life course, in addition to employing other important confounding factors.

5. Conclusions

Our findings suggest ACEs are cumulatively associated with increased mortality risk in adulthood. Physical abuse appears to be robustly associated with increased mortality risk. The effects of individual types of ACEs warrant further exploration, particularly in more diverse and representative samples. While ACEs can often overlap, it is important to investigate each distinct adverse experience because of potential differential impact on mortality risk, and possible resulting intervention targeting.

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Conflicts of interest and source funding

There are no conflicts of interest. MIDUS was supported by the John D. and Catherine T. MacArthur Foundation Research Network, National Institute on Aging (P01-AG020166), National Institute on Aging (U19-AG051426) funding. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability

Data is publicly available from the following url: <https://www.icpsr.umich.edu/web/NACDA/studies/2760>.

Acknowledgements

A special thanks to the participants in MIDUS, and to the MIDUS team for their work in collecting and compiling the data.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.chiabu.2023.106386>.

References

- Allison, P. D. (2010). *Survival analysis using SAS: A practical guide* (2nd ed.). SAS Institute.
- Alm, S., Brolin Låftman, S., & Bohman, H. (2019). Poor family relationships in adolescence and the risk of premature death: Findings from the Stockholm birth cohort study. *International Journal of Environmental Research and Public Health*, 16(10), 1690. <https://doi.org/10.3390/ijerph16101690>
- Anda, R. F., Felitti, V. J., Bremner, J. D., Walker, J. D., Whitfield, C., Perry, B. D., ... Giles, W. H. (2006). The enduring effects of abuse and related adverse experiences in childhood. *European Archives of Psychiatry and Clinical Neuroscience*, 256(3), 174–186. <https://doi.org/10.1007/s00406-005-0624-4>
- Anda, R. F., Butchart, A., Felitti, V. J., & Brown, D. W. (2010). Building a framework for global surveillance of the public health implications of adverse childhood experiences. *American Journal of Preventive Medicine*, 39(1), 93–98. <https://doi.org/10.1016/j.amepre.2010.03.015>
- Anderson, E. L., Fraser, A., Caleyachetty, R., Hardy, R., Lawlor, D. A., & Howe, L. D. (2018). Associations of adversity in childhood and risk factors for cardiovascular disease in mid-adulthood. *Child Abuse & Neglect*, 76, 138–148. <https://doi.org/10.1016/j.chiabu.2017.10.015>
- Baglivio, M. T., Epps, N., Swartz, K., Huq, M. S., Sheer, A., & Hardt, N. S. (2014). The prevalence of adverse childhood experiences (ACE) in the lives of juvenile offenders. *Journal of Juvenile Justice*, 3(2). <http://www.journalofjuvjustice.org/JOJJ0302/article01.htm>
- Bellis, M. A., Hughes, K., Leckenby, N., Hardcastle, K. A., Perkins, C., & Lowey, H. (2015). Measuring mortality and the burden of adult disease associated with adverse childhood experiences in England: A national survey. *Journal of Public Health*, 37(3), 445–454. <https://doi.org/10.1093/pubmed/udu065>
- Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society: Series B (Methodological)*, 57(1), 289–300. <https://doi.org/10.1111/j.2517-6161.1995.tb02031.x>
- Brown, D. W., Anda, R. F., Tiemeier, H., Felitti, V. J., Edwards, V. J., Croft, J. B., & Giles, W. H. (2009). Adverse childhood experiences and the risk of premature mortality. *American Journal of Preventive Medicine*, 37(5), 389–396. <https://doi.org/10.1016/j.amepre.2009.06.021>
- Chen, E., Turiano, N. A., Mroczek, D. K., & Miller, G. E. (2016). Association of reports of childhood abuse and all-cause mortality rates in women. *JAMA Psychiatry*, 73(9), 920. <https://doi.org/10.1001/jamapsychiatry.2016.1786>
- D'Arcy-Bewick, S., Terracciano, A., Turiano, N., Sutin, A. R., Long, R., & O'Súilleabháin, P. S. (2022). Childhood abuse and neglect, and mortality risk in adulthood: A systematic review and meta-analysis. *Child Abuse & Neglect*, 134, Article 105922. <https://doi.org/10.1016/j.chiabu.2022.105922>
- Dierkhising, C. B., Ford, J. D., Branson, C., Grasso, D. J., & Lee, R. (2019). Developmental timing of polyvictimization: Continuity, change, and association with adverse outcomes in adolescence. *Child Abuse & Neglect*, 87, 40–50. <https://doi.org/10.1016/j.chiabu.2018.07.022>
- Dixon, W. J., & Yuen, K. K. (1974). Trimming and winsorization: A review. *Statistische Hefte*, 15(2–3), 157–170. <https://doi.org/10.1007/bf02922904>
- Dong, M., Anda, R. F., Felitti, V. J., Dube, S. R., Williamson, D. F., Thompson, T. J., ... Giles, W. H. (2004). The interrelatedness of multiple forms of childhood abuse, neglect, and household dysfunction. *Child Abuse & Neglect*, 28(7), 771–784. <https://doi.org/10.1016/j.chiabu.2004.01.008>
- Epel, E. S., & Prather, A. A. (2018). Stress, telomeres, and psychopathology: Toward a deeper understanding of a triad of early aging. *Annual Review of Clinical Psychology*, 14(1), 371–397. <https://doi.org/10.1146/annurev-clinpsy-032816-045054>
- Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., ... Marks, J. S. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. *American Journal of Preventive Medicine*, 14(4), 245–258. [https://doi.org/10.1016/s0749-3797\(98\)00017-8](https://doi.org/10.1016/s0749-3797(98)00017-8)
- Gerstorf, D., Smith, J., & Baltes, P. B. (2006). A systemic-wholistic approach to differential aging: Longitudinal findings from the Berlin Aging Study. *Psychology and Aging*, 21(4), 645–663.
- Glickman, M. E., Rao, S. R., & Schultz, M. R. (2014). False discovery rate control is a recommended alternative to Bonferroni-type adjustments in health studies. *Journal of Clinical Epidemiology*, 67(8), 850–857. <https://doi.org/10.1016/j.jclinepi.2014.03.012>
- Godoy, L. C., Frankfurter, C., Cooper, M., Lay, C., Maunder, R., & Farkouh, M. E. (2021). Association of adverse childhood experiences with cardiovascular disease later in life: A review. *JAMA Cardiology*, 6(2), 228–235. <https://doi.org/10.1001/jamacardio.2020.6050>
- Grummitt, L. R., Kreski, N. T., Kim, S. G., Platt, J., Keyes, K. M., & McLaughlin, K. A. (2021). Association of childhood adversity with morbidity and mortality in US adults. *JAMA Pediatrics*. <https://doi.org/10.1001/jamapediatrics.2021.2320>
- Halfon, N., Larson, K., Lu, M., Tullis, E., & Russ, S. (2014). Lifecourse health development: Past, present and future. *Maternal and Child Health Journal*, 18(2), 344–365. <https://doi.org/10.1007/s10995-013-1346-2>
- Hardt, J., & Rutter, M. (2004). Validity of adult retrospective reports of adverse childhood experiences: Review of the evidence. *Journal of Child Psychology and Psychiatry*, 45(2), 260–273. <https://doi.org/10.1111/j.1469-7610.2004.00218.x>
- Heikkinen, E. (2010). A life course approach: Research orientations and future challenges. *European Review of Aging and Physical Activity*, 8(1), 7–12. <https://doi.org/10.1007/s11556-010-0069-2>
- Hoffmann, J. P. (2016). Cumulative stress and substance use from early adolescence to emerging adulthood. *Journal of Drug Issues*, 46(3), 267–288. <https://doi.org/10.1177/0022042616638492>
- Hu, Z., Kaminga, A. C., Yang, J., Liu, J., & Xu, H. (2021). Adverse childhood experiences and risk of cancer during adulthood: A systematic review and meta-analysis. *Child Abuse & Neglect*, 117, Article 105088. <https://doi.org/10.1016/j.chiabu.2021.105088>
- IBM Corp. (2021). *Released. IBM SPSS statistics for mac, version 28.0*. Armonk, NY: IBM Corp.
- Jackisch, J., Brännström, L., & Almqvist, Y. B. (2019). Troubled childhoods cast long shadows: Childhood adversity and premature all-cause mortality in a Swedish cohort. *SSM - Population Health*, 9, Article 100506. <https://doi.org/10.1016/j.ssmph.2019.100506>
- Johnson, J., Chaudieu, I., Ritchie, K., Scali, J., Ancelin, M.-L., & Ryan, J. (2020). The extent to which childhood adversity and recent stress influence all-cause mortality risk in older adults. *Psychoneuroendocrinology*, 111, Article 104492. <https://doi.org/10.1016/j.psyneuen.2019.104492>
- Kellerhals, S., Suh, B., Celaya, M., Ramirez, G., & Gray, K. M. (2023). Adverse childhood experiences and adverse community environments among maternal mortality cases in Arizona. *American Journal of Obstetrics & Gynecology*, 228(1), S225–S226. <https://doi.org/10.1016/j.ajog.2022.11.415>
- Kelly-Irving, M., Lepage, B., Dedieu, D., Bartley, M., Blane, D., Grosclaude, P., ... Delpierre, C. (2013). Adverse childhood experiences and premature all-cause mortality. *European Journal of Epidemiology*, 28(9), 721–734. <https://doi.org/10.1007/s10654-013-9832-9>
- Kennedy, C. C., Zubair, A., Clark, M. M., & Jowsey-Gregoire, S. (2016). Childhood abuse is associated with worse survival following lung transplantation. *Progress in Transplantation*, 26(2), 178–182. <https://doi.org/10.1177/1526924816640651>
- Kuh, D., & Shlomo, Y. B. (2004). *A life course approach to chronic disease epidemiology*. OUP Oxford: Retrieved from https://books.google.ie/books?hl=en&lr=&id=o_CFOYgHsC&oi=fnd&pg=PR17&dq=Kuh+D
- Larson, K., & Halfon, N. (2013). Parental divorce and adult longevity. *International Journal of Public Health*, 58(1), 89–97. <https://doi.org/10.1007/s00038-012-0373-x>
- Lee, C., & Ryff, C. D. (2019). Pathways linking combinations of early-life adversities to adult mortality: Tales that vary by gender. *Social Science & Medicine*, 240, Article 112566. <https://doi.org/10.1016/j.socscimed.2019.112566>
- Lefèvre, H., Jouglu, E., Pavillon, G., & Le Touleuc, A. (2004). Gender differences in premature mortality and avoidable deaths. *Revue d'Épidémiologie et de Santé Publique*, 52(4), 317–328. [https://doi.org/10.1016/s0398-7620\(04\)99061-x](https://doi.org/10.1016/s0398-7620(04)99061-x)
- Lopes, S., Hallak, J. E. C., Machado de Sousa, J. P., & Osório, F. D. L. (2020). Adverse childhood experiences and chronic lung diseases in adulthood: A systematic review and meta-analysis. *European Journal of Psychotraumatology*, 11(1), 1720336. <https://doi.org/10.1080/20008198.2020.1720336>
- Maughan, B., & Rutter, M. (1997). Retrospective reporting of childhood adversity: Issues in assessing long-term recall. *Journal of Personality Disorders*, 11(1), 19–33. <https://doi.org/10.1521/pedi.1997.11.1.19>
- McLaughlin, K. A., Sheridan, M. A., & Lambert, H. K. (2014). Childhood adversity and neural development: Deprivation and threat as distinct dimensions of early experience. *Neuroscience & Biobehavioral Reviews*, 47, 578–591. <https://doi.org/10.1016/j.neubiorev.2014.10.012>
- Morton, P. M., Mustillo, S. A., & Ferraro, K. F. (2014). Does childhood misfortune raise the risk of acute myocardial infarction in adulthood? *Social Science & Medicine*, 104, 133–141. <https://doi.org/10.1016/j.socscimed.2013.11.026>
- Oral, R., Ramirez, M., Coohey, C., Nakada, S., Walz, A., Kuntz, A., ... Peek-Asa, C. (2016). Adverse childhood experiences and trauma informed care: The future of health care. *Pediatric Research*, 79(1–2), 227–233. <https://doi.org/10.1038/pr.2015.197>

- O'Suilleabháin, P. S., Turiano, N. A., Gerstorff, D., Luchetti, M., Gallagher, S., Sesker, A. A., ... Sutin, A. R. (2021). Personality pathways to mortality: Interleukin-6 links conscientiousness to mortality risk. *Brain, Behavior, and Immunity*, 93, 238–244. <https://doi.org/10.1016/j.bbi.2021.01.032>
- Petrucelli, K., Davis, J., & Berman, T. (2019). Adverse childhood experiences and associated health outcomes: A systematic review and meta-analysis. *Child Abuse & Neglect*, 97(97), Article 104127. <https://doi.org/10.1016/j.chiabu.2019.104127>
- Pierce, J. B., Kershaw, K. N., Kiefe, C. L., Jacobs, D. R., Sidney, S., Merkin, S. S., & Feinglass, J. (2020). Association of childhood psychosocial environment with 30-year cardiovascular disease incidence and mortality in middle age. *Journal of the American Heart Association*, 9(9), Article e015326. <https://doi.org/10.1161/jaha.119.015326>
- Ploubidis, G. B., Batty, G. D., Patalay, P., Bann, D., & Goodman, A. (2021). Association of early-life mental health with biomarkers in midlife and premature mortality. *JAMA Psychiatry*, 78(1), 38–46. <https://doi.org/10.1001/jamapsychiatry.2020.2893>
- Pudrovska, T., & Anikputa, B. (2014). Early-life socioeconomic status and mortality in later life: An integration of four life-course mechanisms. *The Journals of Gerontology: Series B*, 69(3), 451–460. <https://doi.org/10.1093/geronb/gbt122>
- Radler, B. T. (2014). The midlife in the United States (MIDUS) series: A national longitudinal study of health and well-being. *Open Health Data*, 2(1). <https://doi.org/10.5334/ohd.ai>
- Rod, N. H., Bengtsson, J., Budtz-Jørgensen, E., Clipet-Jensen, C., Taylor-Robinson, D., Andersen, A.-M. N., ... Rieckmann, A. (2020). Trajectories of childhood adversity and mortality in early adulthood: A population-based cohort study. *The Lancet*, 396(10249), 489–497. [https://doi.org/10.1016/S0140-6736\(20\)30621-8](https://doi.org/10.1016/S0140-6736(20)30621-8)
- Rogers, N. T., Power, C., & Pereira, S. M. P. (2021). Child maltreatment, early life socioeconomic disadvantage and all-cause mortality in mid-adulthood: Findings from a prospective British birth cohort. *BMJ Open*, 11(9), Article e050914. <https://doi.org/10.1136/bmjopen-2021-050914>
- RStudio. (2020). Retrieved from Rstudio.com website <http://www.rstudio.com/>.
- Steel, J. L., Antoni, M., Pathak, R., Butterfield, L. H., Vodovotz, Y., Savkova, A., ... Geller, D. A. (2020). Adverse childhood experiences (ACEs), cell-mediated immunity, and survival in the context of cancer. *Brain, Behavior, and Immunity*, 88, 566–572. <https://doi.org/10.1016/j.bbi.2020.04.050>
- Straus, M. A. (1979). Measuring intrafamily conflict and violence: The conflict tactics (CT) scales. *Journal of Marriage and the Family*, 41(1), 75. <https://doi.org/10.2307/351733>
- Toft, H., Bramness, J. G., Lien, L., Abebe, D. S., Wampold, B. E., Tilden, T., ... Neupane, S. P. (2018). PTSD patients show increasing cytokine levels during treatment despite reduced psychological distress. *Neuropsychiatric Disease and Treatment*, 14, 2367–2378. <https://doi.org/10.2147/NDT.S173659>
- Turiano, N. A., Silva, N. M., McDonald, C., & Hill, P. L. (2017). Retrospective reports of childhood misfortune are associated with positive and negative affect in adulthood. *The International Journal of Aging and Human Development*, 84(3), 276–293. <https://doi.org/10.1177/0091415016688480>
- UNICEF. (2014). *Hidden in plain sight: A statistical analysis of violence against children*. New York: United Nations Children's Fund (UNICEF), Division of Data.
- Van Niel, C., Pachter, L. M., Wade, R., Felitti, V. J., & Stein, M. T. (2014). Adverse events in children. *Journal of Developmental & Behavioral Pediatrics*, 35(8), 549–551. <https://doi.org/10.1097/dbp.0000000000000102>
- Wang, Y. X., Sun, Y., Missmer, S. A., Rexrode, K. M., Roberts, A. L., Chavarro, J. E., & Rich-Edwards, J. W. (2023). Association of early life physical and sexual abuse with premature mortality among female nurses: Prospective cohort study. *bmj*, 381. <https://doi.org/10.1136/bmj-2022-073613>
- World Health Organization. (2015). *World report on ageing and health*. No. 9789241565042. World Health Organization. <https://apps.who.int/iris/handle/10665/186463>.
- World Health Organization. (2019). *WHO Guidelines for the health sector response to child maltreatment*. World Health Organization. <https://apo.who.int/publications/item/who-guidelines-for-the-health-sector-response-to-child-maltreatment>.
- World Health Organization. (2020). *Global status report on preventing violence against children 2020 (924000419X)*. World Health Organization. <https://apps.who.int/iris/bitstream/handle/10665/332394/9789240004191-eng.pdf>.
- Zolotor, A. J., & Puzia, M. E. (2010). Bans against corporal punishment: A systematic review of the laws, changes in attitudes and behaviours. *Child Abuse Review*, 19(4), 229–247. <https://doi.org/10.1002/car.1131>