



Loneliness Links Adverse Childhood Experiences to Mortality Risk Across 26 Years

Aisling Curtis, MSc,^{1,2} Emma M. Kirwan, MSc,^{1,2} Martina Luchetti, PhD,^{3, }
Ann-Marie Creaven, PhD,^{1,2} Nicholas Turiano, PhD,⁴ Máire McGeehan, MSc,^{1,2}
Eileen K. Graham, PhD,^{5, } and Páraic S. O'Suilleabháin, PhD^{1,2,* }

¹Department of Psychology, University of Limerick, Limerick, Ireland.

²Health Research Institute, University of Limerick, Limerick, Ireland.

³Department of Behavioral Sciences and Social Medicine, College of Medicine, Florida State University, Tallahassee, Florida, USA.

⁴Department of Psychology, West Virginia University, Morgantown, West Virginia, USA.

⁵Department of Medical Social Sciences, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, USA.

*Address correspondence to: Páraic S. O'Suilleabháin, PhD. E-mail: paraic.osuilleabhain@ul.ie

Decision Editor: Annie L. Nguyen, PhD, MPH (Psychological Sciences Section)

Abstract

Objectives: Adverse childhood experiences (ACEs) are associated with increased mortality risk. Individuals with a history of certain adversity during childhood tend to report higher levels of loneliness in later life. In our preregistered study, we examined whether loneliness mediates the ACEs to mortality risk relation.

Methods: Participants were from the Midlife in the United States Survey ($N = 4,963$; $M [SD] = 46.44 [12.52]$ years, 53.3% female). Follow-up period spanned 26 years. A comprehensive measure of ACEs was employed consisting of 20 ACEs from 5 categories: physical abuse, emotional abuse, socioeconomic disadvantage, adverse family structure, and poor health at age 16 years.

Results: ACE was a significant predictor of mortality risk. Loneliness mediated the ACEs–mortality risk relation. In other words, loneliness in adulthood accounted for the relation between ACEs and future death. These effects withstood a range of sensitivity checks and adjustments for important factors, such as social isolation.

Discussion: Loneliness appears to be a central mechanism in the long-term impact of ACEs on longevity, such that, for adversity during childhood, loneliness experienced during adulthood may be a toxic pathway to future death.

Keywords: Adversity, Isolation, Lonely, Longevity, Trauma

Adverse childhood experiences (ACEs) are a subset of childhood experiences defined as potentially traumatic events which occur at any stage in childhood. They can have detrimental and long-lasting effects on health and well-being (Felitti et al., 1998). The extent of these experiences has fast become a global issue, with almost half of all children experiencing some type of abuse (World Health Organization, 2020). The consequences of ACEs are extensive, with profound effects on physical and mental health both during childhood and across the lifespan (Hughes et al., 2017). The CDC-Kaiser ACE Study was the first to highlight the incidence and consequences of ACEs, with particular attention to abuse, neglect, and household dysfunction (Felitti et al., 1998). Since this ACE study in 1998, research on child well-being has been increasingly prevalent, and ACEs have been consistently associated with a range of long-term negative effects (Felitti et al., 1998; Nurius et al., 2019; Petrucci et al., 2019).

Evidence that links ACEs with premature mortality is also increasing. It has been reported that adults self-reporting over six ACEs (abuse, neglect, and household dysfunction)

died, on average, 20 years earlier than those reporting no ACEs (Brown et al., 2009; Felitti et al., 1998). A recent review demonstrated robust evidence for an association between childhood adversity and adult mortality risk (for review, see D'Arcy Bewick et al., 2022). Importantly, this was the first review to synthesize the unique impact of childhood abuse and neglect on the single outcome of mortality in adulthood. Studies have since reported significant associations between ACEs and mortality (O'Suilleabháin et al., 2024), and that ACEs cumulatively and individually impact mortality risk in adulthood (D'Arcy-Bewick et al., 2023). Another meta-analysis also suggested that exposure to ACEs accounted for 15% of all U.S. deaths in 1 year (Grummitt et al., 2021).

When considering prospective pathways from early life adversities to premature mortality in adulthood, the mechanisms are not fully clear. The increase in lifespan longitudinal studies, combined with methodological advances in examining indirect (mediating) pathways linking individual differences to mortality risk (for review, see Grogan et al., 2024), means research is now well-positioned

Received: September 13 2024; Editorial Decision Date: January 10 2025.

© The Author(s) 2025. Published by Oxford University Press on behalf of the Gerontological Society of America.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (<https://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.

to explore various mechanisms that may explain why ACE exposure leads to an increased risk of death. For example, self-acceptance and purpose in life have been reported to account for some of the effect of ACEs on mortality risk (O'Suilleabháin et al. 2024), but no other pathways have been tested directly. Given that much research links ACEs to health-related processes, other pathways likely exist needing to be tested. One key potential pathway is loneliness. Vast empirical literature connects loneliness to health and well-being (e.g., Luchetti et al., 2024), with the strongest evidence demonstrating associations with premature mortality risk (e.g., Deason et al., 2025; Holt-Lunstad et al., 2015; Long et al., 2023; National Academies of Sciences, Engineering, and Medicine, 2020; O'Suilleabháin et al., 2019; Wang et al., 2023). Central to loneliness is a sense of belonging and attachment, in that it is defined as a distressing feeling which coincides with one's perception that their social needs are not being met by the quality or quantity of their social relationships (Pinquart & Sorensen, 2001; Perlman & Peplau, 1998). Both accumulative and individual adversity may lead to significant challenges with forming and maintaining future relationships, leading to an increased risk of loneliness (e.g., Wols et al., 2015). Various research streams support this connection between adversity and loneliness (e.g., Lin & Chiao, 2020; Merz & Jak, 2013; Matthews et al., 2019; Nenov-Matt et al., 2020). Further, this is supported by a meta-analytic review of the literature (Curtis et al. 2025). Given the established link between loneliness during adulthood and mortality risk (e.g., Holt-Lunstad et al., 2015; Long et al., 2023), loneliness may act as a mediating factor in the relationship between adversity and mortality.

Negative effects of ACEs are often found to emerge in a cumulative fashion whereby increased exposure to ACEs is directly associated with progressively worse health and psychopathology outcomes (Hughes et al., 2017). However, this cumulative effect is not observed in all instances. For example, cumulative ACEs are not associated with increased risk-taking and sensation-seeking traits (Babad et al., 2019), or increased risk for intimate partner violence (Nikulina et al., 2021), suggesting a nuanced relationship between cumulative ACEs and adverse outcomes. Furthermore, a recent review of the literature examining the association between individual and cumulative ACEs, and loneliness demonstrated significant variability and determined that effects may also vary across type of adversity (Curtis et al. 2025).

Taken together, the aim of this preregistered study was to determine if loneliness may be an indirect (mediating) pathway linking ACEs and mortality risk. In doing so, we sought to utilize a well-established longitudinal cohort study while employing a comprehensive measure of ACEs. In keeping with making several advances within this area, in addition to examining ACEs accumulatively, we also examined individual ACE types.

Method

Preregistration

This study was preregistered on Open Science Framework (OSF), available at: <https://osf.io/35shv>. The data used within this study are publicly available through the Inter-University Consortium for Political and Social Research (ICPSR): <https://www.icpsr.umich.edu/web/ICPSR/series/203>.

Sample

The Midlife in the United States Survey (MIDUS) is a longitudinal survey-based study on over 7,000 Americans (aged 25–74) that began in 1994. The study aims were to investigate the role of behavioral, psychological, and social factors in understanding age-related differences in physical and mental health. The first wave of data (MIDUS 1) was initiated in 1995 and included 7,108 noninstitutionalized, English-speaking adults aged 25–74 years in the contiguous United States. From 2004 to 2006, the original cohort was recontacted to complete the MIDUS 2 (Ryff et al., 2017). A total of 4,963 (75%) completed follow-up interviews. Length of follow-up was 26 years.

Descriptive statistics are provided in Table 1. The current study used data from the 4,963 (mean [SD] age = 46.44 [12.52], range = 25–74) respondents who provided both ACE data at MIDUS 1 and loneliness data at MIDUS 2. Sex distribution of MIDUS participants included in this study was generally balanced including 53.3% females (data were dichotomously collected), and participants were predominantly White (92.4%). Over 70% of participants were married at MIDUS 1. Chi-squared tests revealed that those who were deceased were more likely to be male ($\chi^2 = 13.4, p < .001, \phi = -.052$) and unmarried ($\chi^2 = 5.1, p = .023, \phi = .032$). Between-subject ANOVA revealed that there was a significant difference in mean age ($t = 2031.3, p < .001, \eta^2 = 0.291$), number of chronic conditions ($t = 113.1, p < .001, \eta^2 = 0.024$), and level of education ($t = 105.2, p < .001, \eta^2 = 0.021$), indicating that those deceased were more likely to be older, have more chronic conditions, and have a lower level of education. Those deceased also had higher scores for loneliness ($t = 7.9, p = .005, \eta^2 = 0.002$). There was no significant difference between groups for social isolation ($t = 2.1, p = .152, \eta^2 = 0.001$) or number of ACEs experienced ($t = 0.1, p = .753, \eta^2 = 0.000$).

Measures

Adverse childhood experiences

Drawing from previous literature (D'Arcy-Bewick et al., 2023; O'Suilleabháin et al., 2024; Turiano et al., 2017) and available MIDUS items, 20 different ACE indicators were extracted from the MIDUS 1 survey for this study to retrospectively assess ACEs. The 20 ACE items were first coded as dummy variables, with 1 indicating exposure to that specific adversity and 0 indicating no exposure. Next, a count score was created by summing all the yes responses (0–20 range).

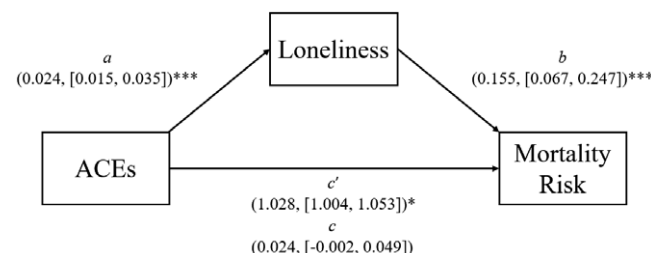


Figure 1. Path diagram. Notes: Indirect effect = 0.004, 95% CI [0.002–0.007], $p = .005$. Fully adjusted path model adjusting for sex, race, education, marital status, chronic conditions, and social isolation. ACEs to mortality risk are modeled as time-to-event (attained age). 95% CIs represent bias-corrected and bootstrapped CIs. * $p < .05$, *** $p < .001$. ACE = adverse childhood experience; CI = confidence interval.

Table 1. Descriptive Statistics of Study Sample

Variable	Deceased (<i>n</i> = 1,173)		Alive (<i>n</i> = 3,790)		Complete sample (<i>N</i> = 4,963)	
	Mean (<i>SD</i>)	%	Mean (<i>SD</i>)	%	Mean (<i>SD</i>)	%
Age at baseline	58.57 (10.46)		42.69 (10.57)		46.44 (12.52)	
Sex (female)		48.7		54.8		53.3
Race (White)		93.5		92.1		92.4
Education (college or higher)		53.9		68.4		65.0
Marital status						
Married		67.8		71.2		70.4
Separated		1.9		2.1		2.1
Divorced		13.9		11.7		12.2
Widowed		9.5		2.3		4.0
Never married		7.0		12.6		11.3
Chronic conditions	2.98 (2.59)		2.12 (2.25)		2.33 (2.36)	
Social isolation	1.66 (1.23)		1.60 (1.18)		1.61 (1.19)	
Loneliness	1.60 (0.88)		1.50 (0.82)		1.52 (0.83)	
Total ACEs	3.34 (2.98)		3.30 (2.95)		3.32 (2.96)	
Emotional abuse	1.00 (1.15)		1.19 (1.18)		1.15 (1.18)	
Physical abuse	0.85 (1.12)		0.90 (1.09)		0.88 (1.09)	
Family structure	0.24 (0.55)		0.22 (0.52)		0.23 (0.53)	
Disadvantaged SES	1.00 (0.80)		0.72 (0.66)		0.79 (0.82)	
Poor health	0.07 (0.30)		0.11 (0.36)		0.10 (0.34)	
Attained age	77.17 (10.74)		69.19 (10.53)		71.08 (11.11)	

Note: ACEs = adverse childhood experiences; SES = socioeconomic status.

The items were then divided into five categories: physical abuse, emotional abuse, disadvantaged socioeconomic status (SES), adverse family structure, and poor health at age 16. Physical and/or emotional abuse were measured using the Conflict Tactics Scale (Straus, 1979). Adverse family structure, disadvantaged SES, and poor health at age 16 were assessed by various self-report items. A full outline of the five ACE categories can be seen in [Supplementary Table 1](#).

Loneliness

Loneliness was assessed by a single item drawn from the Center for Epidemiological Studies Depression scale (CES-D; Radloff, 1977) at Wave 2—"During the past 30 days, how much of the time did you feel lonely" (5 = all the time, 4 = most of the time, 3 = some of the time, 2 = a little of the time, 1 = none of the time). A higher score was indicative of greater loneliness. Similar single-item loneliness measurements have demonstrated sensitivity in prior studies (Shiovitz-Ezra & Ayalon, 2012) and correlated well with other loneliness measures (Mund et al., 2023). The single-item direct question is a common method of assessing the subjective feeling of loneliness and has been used extensively in past and contemporary research, particularly those of large population cohorts (e.g., Graham et al., 2024).

Mortality

Mortality data were obtained using National Death Index (NDI) reports combined with tracing/closeout phases and as part of normal longitudinal sample maintenance. Survival time was defined as attained age. Attained age was utilized as it is a natural metric in observational studies while also

accounting for age (Pencina et al., 2007) from baseline assessment to date of death. Participants that were still alive at the last mortality update in December 2021 (censored observations) had an attained age equal to their calculated age at that timepoint.

Covariates

All covariates in the analysis were assessed at Wave 1. Their selection was informed by literature and their reported associations with ACEs, loneliness, and all-cause mortality (e.g., Beller & Wagner, 2018; Steptoe et al., 2013; Stokes et al., 2021). Sociodemographic controls included sex, race/ethnicity, education, and marital status. Sex was coded as either female (0) or male (1). Race was coded as either White (0) or other. Marital status was dichotomized as either married (0) or separated/divorced/widowed/never married (1). Education was coded as highest level completed by the individual (range 0–12). Number of chronic conditions was treated as a continuous variable and included the total number of doctor-diagnosed chronic medical conditions that the respondent reported experiencing or being treated for in the 12 months prior to survey (e.g., diabetes, stroke, cancer, hypertension, cardiac disease). Consistent with existing literature (Steptoe et al., 2013), an index of social isolation was derived. This index was created by assigning one point for each of the following: if the respondent was unmarried/not cohabitating, had less-than-monthly contact with each of other family members, neighbors, and/or friends, or attended religious/spiritual services or church/temple activities less than monthly. Scores ranged from 0 to 5, with a higher score indicative of greater social isolation. This social isolation index was assessed at Wave 2 to correspond with the measurement of loneliness.

Table 2. Mediation Models for ACEs as a Predictor of Mortality

Variable	Loneliness		
	Estimate	<i>p</i>	95% CI
Model 1: Cumulative ACEs			
Indirect effect	0.004	.005	0.002 to 0.007
Total effect	0.024	.065	−0.002 to 0.049
AIC	32703.082		
BIC	32858.793		
Model 2: Emotional abuse			
Indirect effect	0.007	.046	0.002 to 0.016
Total effect	0.098	.023	0.022 to 0.188
AIC	53789.896		
BIC	54194.345		

Notes: ACEs = adverse childhood experiences; AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; CI = confidence interval. All models contain all confounding factors.

Statistical Analyses

Descriptive statistics for this study were completed using SPSS (IBM, version 29.0.1). A series of Cox regression analyses were also run to estimate the effect of ACEs on mortality risk. All remaining analyses were conducted using Mplus version 8.5 (Muthén & Muthén, 2017). A series of models were employed to test whether loneliness mediated the pathway between ACEs and mortality. The cumulative ACE score was modeled first, followed by count scores for each of the five ACE subtypes examined in a second model. To estimate indirect effects, the Cox proportional hazards modeling was conducted within a structural equation modeling framework (Muthén & Muthén, 2017), with bias-corrected 1,000 bootstrapped thresholds. The use of bias correction and bootstrapping reduces the possibility of introducing skew that could bias estimates, which is particularly important when examining mediation in time-to-event data. All confidence intervals (CIs) are reported at the 95% confidence level. When examining subtypes of ACEs, tests of mediation were entered into the model simultaneously, as recommended elsewhere when working with models of this nature (e.g., Grogan et al., 2024; Turiano et al., 2015).

False discovery rate (FDR) analyses were employed to statistically adjust for the increased error rate due to the number of statistical tests completed with individual ACE subtypes. The primary goal of this procedure was to control the FDR when conducting multiple hypothesis tests simultaneously. FDR is the proportion of false positives (incorrect rejections of null hypotheses) among all the hypotheses that are rejected. After applying the procedure, each original *p*-value is adjusted to obtain a *q*-value (new critical value), which represents the FDR-adjusted significance level. Lower *q*-values indicate stronger evidence against the null hypothesis. By choosing a desired FDR level (5%), the procedure helps determine a critical threshold for significance. This threshold ensures that the expected proportion of false positives among the rejected hypotheses is controlled at or below the specified FDR level. The FDR controls Type 1 error for multiple tests without the strong inflation observed in Type 2 error, such as in Bonferroni and other error corrections (Turiano et al., 2013).

Results

Consistent with existing literature, ACEs were significant predictors of mortality risk (see [Supplementary Table 2](#)). When examining mediation, we found that loneliness was a robust indirect pathway (mediator) in the relation between ACEs and mortality risk (estimate = 0.004, *p* = .005, 95% CI [0.002–0.007], see [Figure 1](#)), even following increasing adjustment which included adjusting for social isolation (see [Table 2](#)). Despite a previously outlined direct effect for ACEs on mortality risk (hazard ratio [HR] = 1.028, *p* = .024; 95% CI [1.004–1.053]; see [Supplementary Table 2](#)), the direct effect of ACEs on mortality was no longer statistically significant when including the loneliness pathways in the model. Thus, rendering the total effect as nonsignificant (estimate = 0.024, *p* = .065, 95% CI [−0.002 to 0.049]). Utilizing sensitivity analysis, the observed significant indirect effect also withstood the removal of those who were deceased within 2 years of study commencement. The potential impact of using attained age was also assessed by testing the inclusion of age as a further covariate. The estimates remained virtually unchanged.

When examining individual subtypes of ACEs, it emerged that loneliness may partially account for the relation between emotional abuse and mortality risk (see [Table 2](#)). Specifically, loneliness appeared to account for an estimated 7.1% of the relation between emotional abuse and mortality risk. However, while this finding was initially deemed significant (i.e., below the 5% threshold), it became nonsignificant following adjustment for the FDR (see [Supplementary Table 5](#)). This indicates caution should be exercised around interpreting this mediation effect. No significant indirect or total effects were observed for physical abuse, poor health, adverse family structure or disadvantaged SES (see [Supplementary Tables 3 and 4](#)).

Discussion

The current study examined the associations between ACEs and mortality, and further tested adulthood loneliness as a possible mechanism to explain these associations. Consistent with our preregistered hypothesis, loneliness mediated the relation between ACEs and mortality risk. That is, higher ACEs were associated with higher levels of loneliness during

adulthood, which resulted in an increased mortality risk. Evidence emerged for the ACE subtype of emotional abuse, such that loneliness may partially mediate its association with mortality risk. However, FDR analyses suggested caution with interpreting this finding. We found that emotional abuse demonstrated the strongest effect on loneliness, although effects were observed for multiple types of maltreatment (Curtis et al. 2025). Consistent with existing literature (e.g., D'Arcy-Bewick et al., 2022; O'Suilleabháin et al., 2024), ACEs and certain subtypes appear to be directly related to mortality risk. These observed effects remained significant following additional adjustment. While the effect size for the ACEs and mortality risk relationship may appear small, it is worth noting that each unit change represents a single experience of adversity. Further, small statistical effects can also have large and significant impact (Carey et al., 2023).

As noted, loneliness provided an indirect (mediating) pathway between cumulative ACEs and mortality. There is evidence that ACEs are associated with a host of mortality outcomes in adulthood (Anda et al., 2009), as well as loneliness being associated with increased all-cause mortality in adulthood (e.g., Holt-Lunstad et al., 2015; Long et al., 2023; O'Suilleabháin et al., 2019). Perhaps unsurprisingly, these findings indicate that a social health determinant like loneliness appears to play a crucial role in the pathway between ACEs and mortality risk. ACEs may contribute to loneliness in adulthood due to the development of insecure attachment patterns (Thomson & Jaque, 2017), and potential challenges with socialization (Shorter et al., 2022). This may make it difficult for individuals to communicate with others and form healthy relationships (Moullin et al., 2018), resulting in increased loneliness in adulthood (Landry et al., 2022). Further, given the frequently reported consequences of ACEs, such as disadvantaged SES (Misiak et al., 2022), homelessness (Liu et al., 2021), and mental health consequences (Sahle et al., 2022), it is perhaps unsurprising that loneliness may be critically important due to societal exclusion and disadvantage. A recent meta-analytic review of the literature examining the association between ACEs and loneliness reported strong associations (for review, see Curtis et al. 2025). Given the influence of loneliness on health and well-being (O'Suilleabháin et al., 2019), patterns of loneliness during emerging (Kirwan et al., 2023; Kirwan et al. 2025) and older adulthood (Graham et al., 2024), and the enduring consequences of ACEs across the lifespan (D'Arcy-Bewick et al., 2023), it is reasonable that loneliness would act as a critical mechanism in the ACEs–mortality risk relation. This is also consistent with strengthening evidence that higher ACE scores are associated with an increased likelihood of reporting adverse outcomes in adulthood (Hashemi et al., 2021). Loneliness likely influences mortality through several downstream biobehavioral pathways, impacting underlying ongoing biological (e.g., Steptoe et al., 2004) and behavioral processes (e.g., Stickley et al., 2013). In other words, ACEs impact risk of death through greater feelings of loneliness, which trigger multiple pathways that are interwoven with health processes.

There are many strengths to this study. Firstly, the data employed were from a large population-based, prospective study with a follow-up of 26 years. Mortality data were verified via death registries and is a robust outcome measure. The study also utilized a comprehensive 20-item ACE measure. Furthermore, examination of each ACE subtype was included in this study, something which previous studies have

highlighted as warranted given that distinct ACE types may have a differential impact on mortality risk (D'Arcy-Bewick et al., 2023) and loneliness (Curtis et al. 2025). Limitations must also be noted. The sample was predominantly White and scoring higher in education. It is therefore uncertain how these findings would generalize to more vulnerable populations, such as those with lower SES or minoritized ethnic groups. This leaves the study susceptible to survival bias in that those with a significantly high risk of experiencing ACEs (e.g., homeless, marginalized or minority groups) are likely to be underrepresented, as well as those already deceased from the outset of this study (D'Arcy-Bewick et al., 2023; O'Suilleabháin et al., 2024). Despite this, this study provides strong evidence for an association for such important phenomena in a large sample followed for nearly three decades. It must be noted that differences in the identification of adversity have been reported between retrospective self-report measures compared to prospective measures (Baldwin et al., 2019; Newbury et al., 2018). Prospective measures likely identify a lower proportion of maltreated children due to them being more severe cases, whereas the higher prevalence in retrospective self-report measures likely capture true cases of maltreatment (Baldwin et al., 2019). Prospective and retrospective measures do converge on the same outcomes (Newbury et al., 2018; Reuben et al., 2016; Tajima et al., 2004; Wisdom & Morris, 1997). Retrospective reports tend to demonstrate stronger associations with psychological variables which could suggest common method bias (Baldwin et al., 2019; Podsakoff et al., 2003); however, common method bias has been reported to be absent (e.g., Rossi et al., 2024). These observations should be considered when interpreting subtypes of adversity (e.g., physical health). While the existing research would suggest the plausibility of these associations and this study provides evidence for it, it would be important for findings to be replicated using further causal mediation analyses (Rijnhar et al., 2021).

While single-item scores are reported to converge well with multi-item instruments and effects show little difference between single- and larger-scale representations of loneliness for important life outcomes (e.g., von Soest et al., 2020), it is important that future work replicates our findings with a multiple item scale to disentangle other possible mechanisms. The scaling and measurement of loneliness in the present study would suggest low levels of loneliness in the sample on average. As such, the generalizability of the findings to samples with higher loneliness levels would need to be assessed. While beyond the scope of our preregistered study, future research examining moderating effects may also be worthwhile (e.g., age, sex). While important and informative, it must be considered that ACE and loneliness measures are relatively blunt instruments for phenomena that are complex. It would be important for future research to also consider that adversity often continues throughout the lifespan and trauma has no age limit (for review, see Buckley et al., 2024). As such, observed effects may differ across the lifespan. Further, taking a count approach to ACEs inherently assumes that all ACEs are equally important. Despite being a strong indicator of accumulative adversity, each ACE might not be equally important for a given outcome. Similarly, loneliness also demonstrates change at various stages across the lifespan (Mund et al., 2020), which are consequential (Kirwan et al., 2024; Luchetti et al., 2024). Further, the effects of loneliness do not appear to be confined purely to the individual

experiencing it but can also impact those they are in close relationships with (Luchetti et al., 2022). Finally, while the current study used a comprehensive ACEs measure, certain adversities known to be important were not examined, including sexual abuse and emotional neglect, which a recent review reported to be significantly associated with loneliness (Curtis et al. 2025). Future research would benefit from examining possible associations with these ACE subtypes.

This study makes a significant contribution to the existing literature through a rigorous study on a very important topic. Loneliness appears to be an important indirect pathway linking ACEs to mortality risk across adulthood. Previous studies have identified that the examination of individual ACE subtypes warrants further exploration, and this study also contributes to existing literature by identifying the need to conduct multiple testing adjustment. With replication in further samples, prospective future interventions addressing loneliness, both individually and at a societal level, may be beneficial for individuals with a history of ACEs. Overall, this study makes a significant contribution to the literature on ACEs and related long-term consequences, particularly highlighting the potential importance of considering the relation with loneliness in the context of future risk of death.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences* online.

Funding

Funding for MIDUS stemmed from John D. and Catherine T. MacArthur Foundation, Research Network on Successful Midlife Development; United States Department of Health and Human Services; and National Institutes of Health, National Institute on Aging (5-PO1- AG20166-04; P01-AG020166). MIDUS 2, 2004–2006 (ICPSR 4652), was also funded by the United States Department of Health and Human Services, National Institutes of Health, National Institute on Aging (5-PO1-AG20166-04). M. McGeehan and E. Kirwan are both in receipt of an Irish Research Council Government of Ireland Postgraduate Scholarship (GOIPG/2023/3522; GOIPG/2021/345). E.K. Graham was supported by the National Institutes of Health, National Institute on Aging (R01-AG082954). N. Turiano was supported by the National Institute on Aging of the National Institutes of Health under award number 1R03AG081592-01. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Irish Research Council or the National Institutes of Health.

Conflict of Interest

None.

Data Availability

This study was preregistered on Open Science Framework (OSF), available at: <https://osf.io/35shv>. Study data are publicly available through the Inter-University Consortium for Political and Social Research (ICPSR): <https://www.icpsr.umich.edu/web/ICPSR/series/203>.

References

- Anda, R. F., Dong, M., Brown, D. W., Felitti, V. J., Giles, W. H., Perry, G. S., Valerie, E. J., & Dube, S. R. (2009). The relationship of adverse childhood experiences to a history of premature death of family members. *BMC Public Health*, 9, 106. <https://doi.org/10.1186/1471-2458-9-106>
- Babad, S., Zwilling, A., Carson, K. W., Fairchild, V., Razak, S., Robinson, G., & Nikulina, V. (2019). Risk-taking propensity and sensation seeking in survivors of adverse childhood experiences. *Journal of Interpersonal Violence*, 36(19-20), NP10670–NP10687. <https://doi.org/10.1177/0886260519876035>
- Baldwin, J. R., Reuben, A., Newbury, J. B., & Danese, A. (2019). Agreement between prospective and retrospective measures of childhood maltreatment: A systematic review and meta-analysis. *JAMA Psychiatry*, 76(6), 584–593. <https://doi.org/10.1001/jamapsychiatry.2019.0097>
- Beller, J., & Wagner, A. (2018). Loneliness, social isolation, their synergistic interaction, and mortality. *Health Psychology: Official Journal of the Division of Health Psychology, American Psychological Association*, 37(9), 808–813. <https://doi.org/10.1037/hea0000605>
- 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>
- Buckley, L., Turiano, N., Sesker, A., Butler, M., & O'Súilleabháin, P. S. (2024). Lifetime trauma and mortality risk: A systematic review. *Health Psychology: Official Journal of the Division of Health Psychology, American Psychological Association*, 43(4), 280–288. <https://doi.org/10.1037/hea0001343>
- Carey, E. G., Ridler, I., Ford, T. J., & Stringaris, A. (2023). Editorial perspective: When is a 'small effect' actually large and impactful? *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, 64(11), 1643–1647. <https://doi.org/10.1111/jcpp.13817>
- Curtis, A., Luchetti, M., Prendergast, C., Ahern, E., Creaven, A. M., Kirwan, E. M., Graham, E. K., & O'Súilleabháin, P. S. (2025). Adverse childhood experiences and loneliness: A systematic review and meta-analysis. *Social Science & Medicine*, 370, 117860. <https://doi.org/10.1016/j.socscimed.2025.117860>
- 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, 105922. <https://doi.org/10.1016/j.chiabu.2022.105922>
- D'Arcy-Bewick, S., Turiano, N., Sutin, A. R., Terracciano, A., & O'Súilleabháin, P. S. (2023). Adverse childhood experiences and all-cause mortality risk in adulthood. *Child Abuse & Neglect*, 144, 106386. <https://doi.org/10.1016/j.chiabu.2023.106386>
- Deason, K. G., Luchetti, M., Karakose, S., Stephan, Y., O'Súilleabháin, P. S., Hajek, A., Sutin, A. R., & Terracciano, A. (2025). Neuroticism, loneliness, all-cause and cause-specific mortality: A 17-year study of nearly 500,000 individuals. *Journal of Affective Disorders*, 368, 274–281. <https://doi.org/10.1016/j.jad.2024.09.077>
- Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., Koss, M. P., & 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)
- Graham, E. K., Beck, E. D., Jackson, K. L., Yoneda, T., McGhee, C., Pieramici, L., Atherton, O. E., Luo, J., Willroth, E. C., Steptoe, A., Mroczek, D. K., & Ong, A. D. (2024). Do we become more lonely with age? A coordinated data analysis of nine longitudinal studies. *Psychological Science*, 35(6), 579–596. <https://doi.org/10.1177/09567976241242037>
- Grogan, C. S., Turiano, N. A., Habenicht, A., McGeehan, M., & O'Súilleabháin, P. S. (2024). Personality traits and mediating pathways to mortality risk: A systematic review. *Health Psychology: Official Journal of the Division of Health Psychology, American Psychological Association*, 43(3), 214–224. <https://doi.org/10.1037/hea0001335>

- 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: A systematic review. *JAMA Pediatrics*, 175(12), 1269–1278. <https://doi.org/10.1001/jamapediatrics.2021.2320>
- Hashemi, L., Fanslow, J., Gulliver, P., & McIntosh, T. (2021). Exploring the health burden of cumulative and specific adverse childhood experiences in New Zealand: Results from a population-based study. *Child Abuse & Neglect*, 122, 105372. <https://doi.org/10.1016/j.chiabu.2021.105372>
- Holt-Lunstad, J., Smith, T. B., Baker, M., Harris, T., & Stephenson, D. (2015). Loneliness and social isolation as risk factors for mortality: A meta-analytic review. *Perspectives on Psychological Science: A Journal of the Association for Psychological Science*, 10(2), 227–237. <https://doi.org/10.1177/1745691614568352>
- Hughes, K., Bellis, M. A., Hardcastle, K. A., Sethi, D., Butchart, A., Mikton, C., Jones, L., & Dunne, M. P. (2017). The effect of multiple adverse childhood experiences on health: A systematic review and meta-analysis. *The Lancet. Public Health*, 2(8), e356–e366. [https://doi.org/10.1016/S2468-2667\(17\)30118-4](https://doi.org/10.1016/S2468-2667(17)30118-4)
- Kirwan, E. M., Burns, A., O'Suilleabháin, P. S., Summerville, S., McGeehan, M., McMahon, J., Gowda, A., & Creaven, A.-M. (2025). Loneliness in emerging adulthood: A scoping review. *Adolescent Research Review*, 10, 47–67. <https://doi.org/10.1007/s40894-024-00240-4>
- Kirwan, E. M., Luchetti, M., Burns, A., O'Suilleabháin, P. S., & Creaven, A.-M. (2024). Loneliness trajectories and psychological distress in youth: Longitudinal evidence from a population-based sample. *British Journal of Developmental Psychology*, 43, 190–204. <https://doi.org/10.1111/bjdp.12533>
- Kirwan, E. M., O'Suilleabháin, P. S., Burns, A., Ogoro, M., Allen, E., & Creaven, A.-M. (2023). Exploring loneliness in emerging adulthood: A qualitative study. *Emerging Adulthood*, 11(6), 1433–1445. <https://doi.org/10.1177/21676968231194380>
- Landry, J., Asokumar, A., Crump, C., Anisman, H., & Matheson, K. (2022). Early life adverse experiences and loneliness among young adults: The mediating role of social processes. *Frontiers in Psychology*, 13, 968383. <https://doi.org/10.3389/fpsyg.2022.968383>
- Lin, W. H., & Chiao, C. (2020). Adverse adolescence experiences, feeling lonely across life stages and loneliness in adulthood. *International Journal of Clinical and Health Psychology*, 20(3), 243–252. <https://doi.org/10.1016/j.ijchp.2020.07.006>
- Liu, M., Luong, L., Lachaud, J., Edalati, H., Reeves, A., & Hwang, S. W. (2021). Adverse childhood experiences and related outcomes among adults experiencing homelessness: A systematic review and meta-analysis. *The Lancet. Public Health*, 6(11), e836–e847. [https://doi.org/10.1016/S2468-2667\(21\)00189-4](https://doi.org/10.1016/S2468-2667(21)00189-4)
- Long, R. M., Terracciano, A., Sutin, A. R., Creaven, A. M., Gerstorf, D., D'Arcy-Bewick, S., & O'Suilleabháin, P. S. (2023). Loneliness, social isolation, and living alone associations with mortality risk in individuals living with cardiovascular disease: A systematic review, meta-analysis, and meta-regression. *Psychosomatic Medicine*, 85(1), 8–17. <https://doi.org/10.1097/PSY.0000000000001151>
- Luchetti, M., Aschwanden, D., Sesker, A. A., Zhu, X., O'Suilleabháin, P. S., Stephan, Y., Terracciano, A., & Sutin, A. R. (2024). Loneliness and risk of dementia: A meta-analysis of longitudinal data from >600,000 individuals. *Nature Mental Health*, 2, 1350–1361. <https://doi.org/10.1038/s44220-024-00328-9>
- Luchetti, M., Ledermann, T., Aschwanden, D., Nikitin, J., O'Suilleabháin, P. S., Stephan, Y., & Sutin, A. R. (2022). Actor and partner effect of loneliness on episodic memory and verbal fluency: A dyadic multilevel analysis of romantic couples across 28 countries. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences*, 77(12), 2202–2211. <https://doi.org/10.1093/geronb/gbac086>
- Matthews, T., Odgers, C. L., Danese, A., Fisher, H. L., Newbury, J. B., Caspi, A., Moffitt, T. E., & Arseneault, L. (2019). Loneliness and neighborhood characteristics: A multi-informant, nationally representative study of young adults. *Psychological Science*, 30(5), 765–775. <https://doi.org/10.1177/0956797619836102>
- Merz, E. M., & Jak, S. (2013). The long reach of childhood. Childhood experiences influence close relationships and loneliness across life. *Advances in Life Course Research*, 18(3), 212–222. <https://doi.org/10.1016/j.alcr.2013.05.002>
- Misiak, B., Stańczykiewicz, B., Pawlak, A., Szewczuk-Bogusławska, M., Samochoń, J., Samochoń, A., Tyburski, E., & Juster, R. P. (2022). Adverse childhood experiences and low socioeconomic status with respect to allostatic load in adulthood: A systematic review. *Psychoneuroendocrinology*, 136, 105602. <https://doi.org/10.1016/j.psyneuen.2021.105602>
- Moullin, S., Waldfogel, J., & Washbrook, E. (2018). Parent-child attachment as a mechanism of intergenerational (dis)advantage. *Families, Relationships and Societies*, 7(2), 265–284. <https://doi.org/10.1332/204674317x15071998786492>
- Mund, M., Freuding, M. M., Möbius, K., Horn, N., & Neyer, F. J. (2020). The stability and change of loneliness across the lifespan: A meta-analysis of longitudinal studies. *Personality and Social Psychology Review*, 24(1), 24–52. <https://doi.org/10.1177/1088868319850738>
- Mund, M., Maes, M., Drewke, P. M., Gutzeit, A., Jaki, I., & Qualter, P. (2023). Would the real loneliness please stand up? The validity of loneliness scores and the reliability of single-item scores. *Assessment*, 30(4), 1226–1248. <https://doi.org/10.1177/10731911221077227>
- Muthén, L. K., & Muthén, B. O. (2017). *Mplus: statistical analysis with latent variables: user's guide (version 8)*. Wiley.
- National Academies of Sciences, Engineering, and Medicine. (2020). *Social isolation and loneliness in older adults: Opportunities for the health care system*. National Academies Press (US).
- Newbury, J. B., Arseneault, L., Moffitt, T. E., Caspi, A., Danese, A., Baldwin, J. R., & Fisher, H. L. (2018). Measuring childhood maltreatment to predict early-adult psychopathology: Comparison of prospective informant-reports and retrospective self-reports. *Journal of Psychiatric Research*, 96, 57–64. <https://doi.org/10.1016/j.jpsychires.2017.09.020>
- Nenov-Matt, T., Barton, B. B., Dewald-Kaufmann, J., Goerigk, S., Rek, S., Zentz, K., Musil, R., Jobst, A., Padberg, F., & Reinhard, M. A. (2020). Loneliness, social isolation and their difference: A cross-diagnostic study in persistent depressive disorder and borderline personality disorder. *Frontiers in Psychiatry*, 11, 608476. <https://doi.org/10.3389/fpsy.2020.608476>
- Nikulina, V., Gelin, M., & Zwillig, A. (2021). Is there a cumulative association between adverse childhood experiences and intimate partner violence in emerging adulthood? *Journal of Interpersonal Violence*, 36(3–4), NP1205–1232NP. <https://doi.org/10.1177/0886260517741626>
- Nurius, P. S., Fleming, C. M., & Brindle, E. (2019). Life Course pathways from adverse childhood experiences to adult physical health: A structural equation model. *Journal of Aging and Health*, 31(2), 211–230. <https://doi.org/10.1177/0898264317726448>
- O'Suilleabháin, P. S., D'Arcy-Bewick, S., Fredrix, M., McGeehan, M., Kirwan, E., Willard, M., Sesker, A. A., Sutin, A. R., & Turiano, N. A. (2024). Self-acceptance and purpose in life are mechanisms linking adverse childhood experiences to mortality risk. *Psychosomatic Medicine*, 86(2), 83–88. <https://doi.org/10.1097/PSY.0000000000001266>
- O'Suilleabháin, P. S., Gallagher, S., & Steptoe, A. (2019). Loneliness, living alone, and all-cause mortality: The role of emotional and social loneliness in the elderly during 19 years of follow-up. *Psychosomatic Medicine*, 81(6), 521–526. <https://doi.org/10.1097/PSY.0000000000000710>
- Perlman, D., & Peplau, L. A. (1998). Loneliness. In H. Friedman (Ed.), *Encyclopaedia of mental health* (Vol. 2, pp. 571–581). Academic Press.
- Pencina, M. J., Larson, M. G., & D'Agostino, R. B. (2007). Choice of time scale and its effect on significance of predictors in longitudinal studies. *Statistics in Medicine*, 26(6), 1343–1359.

- Petrucelli, K., Davis, J., & Berman, T. (2019). Adverse childhood experiences and associated health outcomes: A systematic review and meta-analysis. *Child Abuse & Neglect*, 97, 104127. <https://doi.org/10.1016/j.chiabu.2019.104127>
- Pinquart, M., & Sörensen, S. (2001). Influences on loneliness in older adults: A meta-analysis. *Basic and Applied Social Psychology*, 23(4), 245–266. <https://doi.org/10.1207/153248301753225702>
- Podsakoff, P. M., MacKenzie, S. B., Lee, J. Y., & Podsakoff, N. P. (2003). Common method biases in behavioral research: A critical review of the literature and recommended remedies. *The Journal of Applied Psychology*, 88(5), 879–903. <https://doi.org/10.1037/0021-9010.88.5.879>
- Radloff, L. S. (1977). The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, 1(3), 385–401. <https://doi.org/10.1177/014662167700100306>
- Reuben, A., Moffitt, T. E., Caspi, A., Belsky, D. W., Harrington, H., Schroeder, F., Hogan, S., Ramrakha, S., Poulton, R., & Danese, A. (2016). Lest we forget: comparing retrospective and prospective assessments of adverse childhood experiences in the prediction of adult health. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, 57(10), 1103–1112. <https://doi.org/10.1111/jcpp.12621>
- Rijnhart, J. J., Lamp, S. J., Valente, M. J., MacKinnon, D. P., Twisk, J. W., & Heymans, M. W. (2021). Mediation analysis methods used in observational research: A scoping review and recommendations. *BMC Medical Research Methodology*, 21, 226. <https://doi.org/10.1186/s12874-021-01426-3>
- Rossi, A. A., Panzeri, A., Fernandez, I., Invernizzi, R., Taccini, F., & Mannarini, S. (2024). The impact of trauma core dimensions on anxiety and depression: A latent regression model through the Post-Traumatic Symptom Questionnaire (PTSQ). *Scientific Reports*, 14(1), 23036. <https://doi.org/10.1038/s41598-024-72274-6>
- Ryff, C., Almeida, D. M., Ayanian, J., Carr, D. S., Cleary, P. D., Coe, C., Davidson, R., Krueger, R. F., Lachman, M. E., Marks, N. F., Mroczek, D. K., Seeman, T., Seltzer, M. M., Singer, B. H., Sloan, R. P., Tun, P. A., Weinstein, M., & Williams, D. (2017). *Midlife in the United States (MIDUS 2), 2004–2006: Version 7*. Inter-university Consortium for Political and Social Research. <https://doi.org/10.3886/JCPSR04652.v7>
- Sahle, B. W., Reavley, N. J., Li, W., Morgan, A. J., Yap, M. B. H., Reupert, A., & Jorm, A. F. (2022). The association between adverse childhood experiences and common mental disorders and suicidality: An umbrella review of systematic reviews and meta-analyses. *European Child & Adolescent Psychiatry*, 31(10), 1489–1499. <https://doi.org/10.1007/s00787-021-01745-2>
- Shiovitz-Ezra, S., & Ayalon, L. (2012). Use of direct versus indirect approaches to measure loneliness in later life. *Research on Aging*, 34(5), 572–591. <https://doi.org/10.1177/01640275114232>
- Shorter, P., Turner, K., & Mueller-Coyne, J. (2022). Attachment Style's impact on loneliness and the motivations to use social media. *Computers in Human Behavior Reports*, 7, 100212. <https://doi.org/10.1016/j.chbr.2022.100212>
- Steptoe, A., Owen, N., Kunz-Ebrecht, S. R., & Brydon, L. (2004). Loneliness and neuroendocrine, cardiovascular, and inflammatory stress responses in middle-aged men and women. *Psychoneuroendocrinology*, 29(5), 593–611. [https://doi.org/10.1016/S0306-4530\(03\)00086-6](https://doi.org/10.1016/S0306-4530(03)00086-6)
- Steptoe, A., Shankar, A., Demakakos, P., & Wardle, J. (2013). Social isolation, loneliness, and all-cause mortality in older men and women. *Proceedings of the National Academy of Sciences of the United States of America*, 110(15), 5797–5801. <https://doi.org/10.1073/pnas.1219686110>
- Stickley, A., Koyanagi, A., Roberts, B., Richardson, E., Abbott, P., Tumanov, S., & McKee, M. (2013). Loneliness: its correlates and association with health behaviours and outcomes in nine countries of the former Soviet Union. *PLoS One*, 8(7), e67978. <https://doi.org/10.1371/journal.pone.0067978>
- Stokes, A. C., Xie, W., Lundberg, D. J., Gleib, D. A., & Weinstein, M. A. (2021). Loneliness, social isolation, and all-cause mortality in the United States. *SSM. Mental Health*, 1, 100014. <https://doi.org/10.1016/j.ssmmh.2021.100014>
- Straus, M. A. (1979). Measuring intrafamily conflict and violence: The Conflict Tactics (CT) scales. *Journal of Marriage and the Family*, 41(1), 75–88. <https://doi.org/10.2307/351733>
- Tajima, E. A., Herrenkohl, T. I., Huang, B., & Whitney, S. D. (2004). Measuring child maltreatment: A comparison of prospective parent reports and retrospective adolescent reports. *The American Journal of Orthopsychiatry*, 74(4), 424–435. <https://doi.org/10.1037/0002-9432.74.4.424>
- Thomson, P., & Jaque, S. V. (2017). Adverse childhood experiences (ACE) and adult attachment interview (AAI) in a non-clinical population. *Child Abuse & Neglect*, 70, 255–263. <https://doi.org/10.1016/j.chiabu.2017.06.001>
- Turiano, N. A., Mroczek, D. K., Moynihan, J., & Chapman, B. P. (2013). Big 5 personality traits and interleukin-6: Evidence for “healthy neuroticism” in a US population sample. *Brain, Behavior, and Immunity*, 28, 83–89. <https://doi.org/10.1016/j.bbi.2012.10.020>
- Turiano, N. A., Chapman, B. P., Gruenewald, T. L., & Mroczek, D. K. (2015). Personality and the leading behavioral contributors of mortality. *Health Psychology*, 34(1), 51–60. <https://doi.org/10.1037/hea0000038>
- 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>
- von Soest, T., Luhmann, M., Hansen, T., & Gerstorf, D. (2020). Development of loneliness in midlife and old age: Its nature and correlates. *Journal of Personality and Social Psychology*, 118(2), 388–406. <https://doi.org/10.1037/pspp0000219>
- Wang, F., Gao, Y., Han, Z., Yu, Y., Long, Z., Jiang, X., Wu, Y., Pei, B., Cao, Y., Ye, J., Wang, M., & Zhao, Y. (2023). A systematic review and meta-analysis of 90 cohort studies of social isolation, loneliness and mortality. *Nature Human Behaviour*, 7(8), 1307–1319. <https://doi.org/10.1038/s41562-023-01617-6>
- Widom, C. S., & Morris, S. (1997). Accuracy of adult recollections of childhood victimization, part 2: Childhood sexual abuse. *Psychological Assessment*, 9(1), 34–46. <https://doi.org/10.1037/1040-3590.9.1.34>
- Wols, A., Scholte, R. H. J., & Qualter, P. (2015). Prospective associations between loneliness and emotional intelligence. *Journal of Adolescence*, 39, 40–48. <https://doi.org/10.1016/j.adolescence.2014.12.007>
- World Health Organization. (2020). *Global status report on preventing violence against children 2020*. <https://apps.who.int/iris/bitstream/handle/10665/332394/9789240004191-eng.pdf>