BMJ Open

What is the association between adverse childhood experiences and late-life cognitive decline? Study of Healthy Aging in African Americans (STAR) Cohort Study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2023-072961
Article Type:	Original research
Date Submitted by the Author:	21-Feb-2023
Complete List of Authors:	Lor, Yi; University of California Davis, George, Kristen M; University of California Davis, Department Public Health Sciences Gilsanz, Paola; Kaiser Permanente Division of Research, Meunier, Claire; University of California Davis Peterson, Rachel; University of Montana Hayes-Larson, Eleanor; UCLA School of Public Health, Department of Epidemiology Barnes, Lisa; Rush University, Department of Neurological Sciences Mungas, Dan; University of California Davis, Department of Neurology Whitmer, Rachel; University of California Davis, Department of Public Health Sciences
Keywords:	EPIDEMIOLOGY, PUBLIC HEALTH, Risk Factors, Aging

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Journal: BMJ Open – Original Research

Title: What is the association between adverse childhood experiences and late-life cognitive decline? Study of Healthy Aging in African Americans (STAR) Cohort Study

Yi Lor (Corresponding Author), Kristen M. George, Paola Gilsanz, Claire C. Meunier, Rachel L. Peterson, Eleanor Hayes-Larson, Lisa L. Barnes, Dan M. Mungas, Rachel A. Whitmer

Author Information:

Yi Lor, MPH (**Corresponding Author**)
- Graduate Group in Epidemiology, University of California
- Email: yijlor@ucdavis.edu
- Funding: None
- Conflicts: No conflicts

Kristen M. George, PhD
- Department of Public Health Sciences, University of California Davis School of Medicine
- Email: krmgeorge@ucdavis.edu
- Funding: N/A
- Conflicts: No conflicts

Paola Gilsanz, ScD, MPH
- Division of Research, Kaiser Permanente Northern California
- Email: paola.gilsanz@kp.org
- Funding: RF1AG050782(PI: Whitmer)
- Conflicts: No Conflicts.

Claire C. Meunier, MPH
- Graduate Group in Epidemiology
- Email: Ccmeunier@ucdavis.edu
- Conflicts: None

Rachel L. Peterson, PhD, MPH, MA
- School of Public and Community Health Sciences, University of Montana
- Email: rachel.peterson@mso.umt.edu
- Funding: NIH/NIA 4R00AG073457-02
- Conflicts: No conflicts.

Elanor Hayes-Larson, PhD, MPH

- Department of Epidemiology, UCLA Fielding School of Public Health, Los Angeles, California, USA
- Email: ehayeslarson@ucla.edu
- Funding: NIA K99AG075317
- Conflicts: No conflicts

Lisa L. Barnes, PhD
- Rush Alzheimer's Disease Center and Department of Neurological Sciences, Rush University Medical Center
- Email: Lisa_L_Barnes@rush.edu
- Funding: RF1AG050782(PI: Whitmer)
- Conflicts: No conflicts.

Dan Mungas, PhD,
- Department of Neurology, University of California, Davis, Sacramento, CA, USA
- Email: dmmungas@ucdavis.edu
- Funding: N/A
- Conflicts: No conflicts

Rachel A. Whitmer, PhD
- Department of Public Health Sciences and Neurology, University of California Davis
- Email: rawhitmer@ucdavis.edu
- RF1AG050782(PI: Whitmer)
- Conflicts: No conflicts

Abstract (Word count: 290)

Objectives: Adverse childhood experiences (ACEs) are associated with higher risk of chronic disease, but little is known about the association with late life cognitive decline. We examined the longitudinal association between ACEs and late-life cognitive decline in the Study of Healthy Aging in African Americans (STAR).

Design: Linear mixed models with random intercepts and slope examined the association of individual and composite ACEs with cognitive change adjusting for years from baseline (timescale), baseline age, sex, parental education, childhood socioeconomic status, and childhood social support. Participants reported whether they had experienced 9 types of ACEs. Executive function and verbal episodic memory were measured up to 3 times over a 3-year period using the Spanish and English Neuropsychological Assessment Scales.

Settings: Kaiser Permanente Northern California members living in the Bay Area.

Participants: STAR is a cohort study of cognitive aging launched in 2018 that has enrolled 764 Black Americans ages ≥ 50 years (mean age=67.5; SD=8.5).

Results: Twenty percent of participants reported no ACEs, 23% one ACE, 20% two ACEs, 17% three ACEs, and 17% four or more ACEs. Compared to no ACEs, two ACEs (β=0.117; 95% CI 0.052-0.182), three ACEs (β=0.075; 95% CI 0.007-0.153), and 4+ ACEs (β=0.089; 95% CI 0.002-0.158), were associated with less decline in executive function. There were no significant associations between number of ACEs and baseline or longitudinal verbal episodic memory or between individual ACEs and executive function or verbal episodic memory.

Conclusion: In this cohort of older Black Americans, there was no association between ACES and baseline cognition or cognitive change in verbal episodic memory; however, experiencing ≥2 ACEs was associated with less decline in executive function. These results may indicate that

participants who survived to age 50+ and experienced ACEs may have cognitive resilience that warrants further investigation.

Strength and Limitations of this study:

- The impact of adverse childhood experience (ACEs) on late-life cognition in older Black adults is sparse with little research investigating cognitive decline.
- The Study of Healthy Aging in African-Americans (STAR) is a well-characterized cohort of older Black Americans ages 50 years or older with detailed socioeconomic lifecourse information such as education, region of birth, and childhood experiences.
- Repeated assessment of cognition in two domains across three waves (approximately 3 years) using the Spanish and English Assessment Scale (SENAS), a measurement validated in English and Spanish, and in diverse populations.
- Linear mixed models allowing for evaluation of ACEs on cognition and cognitive decline adjusting for childhood confounders such as childhood socioeconomic status and childhood support.
- ACEs assessments were limited to self-report and there were no questions asked of physical or sexual abuse.

INTRODUCTION

Childhood is a sensitive period in the lifecourse for later-life health outcomes(1,2), such that disruptions during this period can have detrimental effects on development and later life health. Adverse childhood experiences (ACEs) are traumatic events in childhood that include abuse, witnessing violence, and household dysfunction and have been associated with higher risk of cardiovascular diseases, chronic lung disease, and liver disease.(1,2) Although ACEs are associated with many of the risk factors for dementia, only a handful of studies have examined the association between ACEs and poor cognitive aging outcomes in Black Americans.(3)

Some studies indicate that ACEs have negative effects on cognitive functioning later in life.(4–7) Studies examining specific types of ACEs have reported associations between the death of a parent, physical neglect, and emotional abuse experienced during childhood with worse memory later in life.(5,6) Additionally, greater numbers of ACEs are associated with increased risk of developing Alzheimer's disease and related dementias (ADRD).(8–10) Despite findings of ACEs being associated with poorer memory and higher risk of ADRD, other studies have shown mixed results, with weak to no association of ACEs with change in cognition over time.(11,12) Furthermore, the literature is mixed on the specific impact that ACEs have on late-life cognitive functioning with some ACES being associated with slower cognitive decline in older Blacks adults but no decline in older White adults.(13,14)

Two interrelated life course theories serve as a framework for understanding how early life exposures, such as ACEs, may affect later life cognitive outcomes. The Cumulative Advantage/Disadvantage (CAD) theory posits that structural and institutional processes contribute to differential access to resources or harmful exposures that accumulate in a non-additive way over time.(15,16) Individuals who are exposed to more ACEs over time will have

an increased risk of negative health outcomes, including poor cognition, later in life. Building on this theory, the Cumulative Inequality (CI) theory incorporates life course factors that take into consideration the intergenerational, socioeconomic, and stress processes important in the environment in which a child grows up.(17,18) Both theories recognize that the trajectories established by negative childhood exposures can be altered by positive experiences throughout the life course. ACEs may be a predictor of worse outcomes in later life, but positive experiences such as social support and individual response to adversity may minimize the negative effects on cognitive outcomes. Due to the relationships between both theories, we will consider them together as the CI theory.

Compared to White Americans, Black Americans have a higher risk of ADRD and report more ACES.(19–21) However, the relationship between childhood adversity and cognition in later life among Black adults remains ambiguous.(22–24) The two studies that have examined ACEs and cognitive outcomes in Black adults have had mixed results.(11,13) One study(11) examining 427 older Blacks adults found no associations between ACEs and cognition. Another study(13) among 3700 older Black adults found that those who reported experiencing food deprivation and having thinner body size than their peers in early life had slower rates of cognitive decline compared to those who did not report food deprivation or being thinner.

The aim of this paper was to examine the association between total number of ACEs as well as the specific ACEs experienced with cognitive change in a cohort of middle-aged and older Black adults. To expand the sparse existing literature, we focus on Black individuals and their early-life experiences.(3) Based on the CI theory, we hypothesize a dose-response relationship where each additional ACE experienced is associated with faster cognitive decline, and all types of ACEs predict worse cognitive outcomes.

METHODS

Study participants and data collection

The STAR cohort consists of community-dwelling midlife to older Black adults that reside in the San Francisco Bay area of California, primarily the cities of Oakland and Richmond.(25,26) STAR aims to evaluate how lifecourse vascular and sociocultural factors influence the trajectory of cognitive aging and burden of cognitive impairment among Black Americans. Individuals eligible for STAR were long-term members of Kaiser Permanente Northern California, an integrated healthcare delivery system, who identified as Black or African American, were age 50 years or older on January 1, 2018, and had previously participated in Kaiser Permanente multiphasic health checkup (MHC) exams between 1964-1985. Stratified random sampling by age and educational attainment was used with the goal of recruiting approximately equal proportions of participants ages 50-64 and 65 and older. Exclusion criteria included electronic medical record diagnosis of dementia or other neurodegenerative diseases (frontotemporal dementia, Lewy body disease, Pick's disease, Parkinson's disease with dementia, Huntington's disease) and presence of health conditions that would impede participation in study interviews (defined by hospice activity in the past 12 months, history of severe chronic obstructive pulmonary disease in the past 6 months, congestive heart failure hospitalizations in the past 6 months, and history of end stage renal disease or dialysis in the past 12 months).

Measures

Cognition

Cognitive function was assessed at each STAR wave using the Spanish and English Neuropsychological Assessment Scales (SENAS), a battery of cognitive tests that have

undergone extensive development using item response theory methodology for valid comparisons of cognition and cognitive change across racial/ethnic and linguistically diverse groups.(27,28) Cognitive domains of executive function and verbal episodic memory were derived from the SENAS. Each domain was z-standardized using the mean and standard deviation from the full baseline sample. Details of the administration procedures, development, and psychometric characteristics can be found described in-depth elsewhere.(27,28) Cognitive trajectories were measured across three waves of data approximately 14 months apart totally over 3 years.

Adverse childhood experiences (ACEs)

During baseline interviews, participants were asked if they experienced nine separate types of ACEs during childhood from birth to age 16. ACEs included experiences of parents' divorce or separation, a parent remarrying, witnessing domestic violence, substance abuse by a family member, loss of a job by a parent, a parent going to jail, serious illness of a family member, death of mother, and death of father. ACEs were examined individually and as a composite ACE score defined as the sum of ACEs reported and recategorized as 0, 1, 2, 3, or 4 or more ACEs. Summation of ACEs models the cumulative effect that is reflective of the CI theory and cumulative ACEs score from 0 to 4 or more is one of the most commonly used methods for operationalizing ACEs. Cumulative ACEs score has been found to have a dose-response association with various health outcomes.(2,29–31) Approximately 2% of participants (n = 14) had missing ACES and were excluded from the analyses.

Covariates

We adjusted for five early-life social support factors that may confound associations between ACEs and later-life cognition. Using a five level Likert-type scale (1 = None of the

time, 2 = A little of the time, 3 = Some of the time, 4 = Most of the time, and 5 = All of the time), participants were asked: "How often was there someone in whom you could talk to, trust and confide?," "How often was there someone who showed you love and affection?," "How often was there someone who could help you with your homework?," "How often was there someone who encouraged and pushed you to succeed in school?," and "How often did you have as much contact as you would like with someone you felt close to, someone in whom you could trust and confide?" The responses were dichotomized with cutoffs between high frequency (All and most of the time) and low frequency (some, a little, and none of the time). A composite score was created for early life factor by summation of the five scores (0-20).

We additionally adjusted for early life socioeconomic status by including combined parental education (both parents with less than high school vs at least one parent with high school graduation or more), self-reported childhood family housing status (mortgage or owned home vs rental or others), and how often the participant reported going hungry as a child (Never vs ever). Parental education was reported as highest level of education completed for both maternal and paternal parent. Both parent's education was combined into one parental education and dichotomized as both parents with less than high school diploma, and either one or both parents with more than high school diploma. If both maternal and paternal education was missing, parental education was classified as less than a high school diploma, and these participants demarcated by including a missing indicator covariate in all models.

Other covariates included age at baseline interview centered at the mean baseline age, self-reported gender (male or female), and self-reported educational attainment (collapsed as less than college degree vs college graduate or more) captured during STAR baseline interviews.

Statistical analysis

The distribution of demographics, childhood social support, childhood SES indicators, and type of ACEs were estimated overall and stratified by the number of ACEs experienced. Two sets of linear mixed models were used to assess the association of cognition with: 1) composite ACE score and 2) individual ACEs, allowing for random intercept and slope to account for within-person correlation. The models were adjusted for time (as years since baseline) to estimate trajectories across three waves. We sequentially adjusted for covariates in our composite ACEs models by 1) adjusting for baseline, mean-centered age and sex, 2) adjusted for childhood SES indicators, and 3) adjusted for childhood support. For models with individual ACEs, we sequentially adjusted for covariates by 1) adjusting for baseline, mean-centered age, 2) sex, and 3) parental education. Interaction terms for time scale with exposure and covariates were added to each model to measure changes in cognition over time.

From a cohort of 764 participants, we excluded 14 participants for missing information on ACEs, 15 participants for missing early life support and SES covariates, and 16 participants for missing report of gender.

RESULTS

Our analytic sample consisted of 707 participants with a mean age of 68.6 (SD 8.7) years (range, 53-95 years) of whom 487 (68.9%) were women compared to 220 (31.1%) men (Table 1). About 21% of participants reported no ACE, 23.6% reported one ACEs, 20% reported two ACEs, 17.3% reported three ACEs, and 16.8% reported four or more ACEs. Seventy-nine percent of participants had at least one ACE. The most common ACE reported was experiencing parents' separation or divorce (38.5%), followed by serious family illness (35.4%), and witnessing domestic violence (31.5%). More than a third (35.5%) of participants had a college

degree or higher, and 38% of participants had parents with more than a high school-level education (Table 1). Participants in this cohort generally had high levels of support (average composite score of 15.8 and SD = 4.7) during childhood with majority of participants reporting someone they could trust (76%), someone to love them (86%), someone to help with homework (66%), someone to motivate or encourage in school (79%), and someone to close they could contact (77%) all or most of the time. Most participants self-reported as being well-off or above average financially during childhood (68%), and most participants never experienced childhood hunger (92%). 75% of participants had only two waves of cognitive measures, and over 83% of participants had all three waves of cognitive measures.

Composite number of ACEs

In our linear mixed models examining associations between the composite ACEs and baseline executive function (Table 2), we observed a negative non-significant associations for one ACE (β = -0.130; 95% CI -0.316 to 0.055), two ACEs (β = -0.039; 95% CI -0.231 to 0.152) and 4+ ACEs (β = -0.025; 95% CI -0.228 to 0.178), and a positive non-significant association for three ACEs (β = 0.008; 95% CI -0.193 to 0.209) compared to no ACEs. After adjusting for childhood SES, the estimates decreased for one ACE (β = -0.090; 95% CI -0.272 to 0.093), increased for three ACEs (β = 0.070; 95% CI -0.132 to 0.271), and changed direction for two ACEs (β = 0.008; 95% CI -0.181 to 0.197) and 4+ ACEs (β = 0.052; 95% CI -0.155 to 0.259) suggesting a non-significant positive association with baseline executive function. The estimates were attenuated after further adjusting for childhood support. We observed a non-significant negative association between composite ACEs and baseline verbal episodic memory for one ACE (β = -0.137; 95% CI -0.321 to 0.048), two ACEs (β = -0.041; 95% CI -0.231 to 0.149) and three ACEs (β = -0.120; 95% CI -0.320 to 0.080), but positive association for 4+ ACEs (β =

0.105; 95% CI -0.097 to 0.307). After adjusting for childhood SES, and childhood support, point estimates for the association between ACEs and baseline verbal episodic memory were attenuated.

When examined longitudinally, there was significantly slower decline in executive function among those who reported experiencing two ACEs (β=0.117; 95% CI 0.052 to 0.182), three ACEs (β=0.075; 95% CI 0.007 to 0.153), and four or more ACEs (β=0.089; 95% CI 0.002 to 0.158), but not for one ACE (β=0.053; 95% CI -0.010 to 0.116) compared to no ACEs (Table 2, Figure 1). The estimates and direction of associations remained consistent after adjusting for childhood SES and childhood social support variables (Table 2).

There were no significant associations between the composite ACEs score and verbal episodic memory over time. However, the point estimates were negative for one ACE (β=-0.017; 95% CI -0.108 to 0.075) and 4+ ACEs (β=-0.022; 95% CI -0.123 to 0.078), and point estimates were positive for two ACEs (β=0.074; 95% CI -0.021 to 0.159) and three ACEs (β=0.050; 95% CI -0.048 to 0.148) compared to no ACEs (Table 2). The longitudinal point estimates changed minimally after adjusting for parental education, childhood hunger, childhood housing, and childhood social support.

Individual ACEs

When evaluating linear mixed models for executive function and verbal episodic memory with individual ACEs as predictors, there were no significant associations with baseline cognition or change of cognition over time (Supplemental Table 1). All individual ACEs had non-significant positive associations for executive function, except for death of mother which had non-significant negative association. Longitudinal estimates for verbal episodic memory were mixed with non-significant positive associations for parent separated, parent remarried,

serious family illness, death of mother, and death of father, while non-significant negative associations were observed for witnessed violence, substance abuse, loss of job, and parent jail.

DISCUSSION

In a cohort of older Black Americans, ACEs was not significantly associated with baseline executive function or verbal episodic memory. We found that those who experienced multiple ACEs had slower decline in executive function than those who did not experience any ACEs, but we did not see this for verbal episodic memory. We observed no associations between individual ACEs and cognition at baseline or over time. Our findings did not align with our hypothesis that exposure to ACEs would be associated with lower baseline cognition and greater cognitive decline. These results are consistent with some prior work; similar results were observed in the Chicago Health and Aging Project (CHAP) cohort study of over 3700 older Black adults (average age 78 years old) where those that experienced food deprivation had slower cognitive decline later in life.(13) Our study included a younger cohort of Black Americans (average age 68 years old) compared to Barnes et al(13), on childhood adversity and cognition. In another cross sectional study, no associations were found between composite and individual ACEs across different ages of childhood with baseline cognition within Black older adults when stratified by race.(11) There is limited work on early life adversity and late-life cognition in the Black American population, and findings in our study, using an all-Black cohort, show similar results to previous work in this area.

Our study had several strengths. First, we utilized data from a well-characterized cohort of mid- to late-life Black participants. By evaluating ACEs in an all-Black cohort, we were able to identify early life experiences within this understudied group and assess relationships between

ACEs and late-life cognition using a within-group analysis, an approach that is not typically used in studies of minoritized older adults.(3,32) Second, we examined cognition using a robust psychometric battery that has specifically been validated for use in Black Americans.(27,28) By following our cohort over three waves (average 2.3 years of follow-up), we were able to examine changes in cognition over time. Lastly, our ACEs questionnaire was adapted from a robust measure used in other cohort studies with diverse participants.(11,33)

There were several limitations in our study. First, since ACEs occurred early in life, recall bias could influence responses. Older participants were asked to remember potentially traumatic events during childhood, which could lead to under- or overestimation of the prevalence of ACEs.(31,34) Social desirability bias may also prevent participants from disclosing sensitive and revealing information about their early life.(35) Experiences of abuse or neglect not captured by the ACEs questionnaire, but reflect other dimensions of childhood adversity, may have different effects on late-life cognition.(36) Finally, as a middle-age and older cohort with a short follow-up time of approximately 3 years, this study cannot examine how ACES impact long-term cognitive decline, but this will be examined with additional cognitive assessments.

ACEs were highly prevalent in our cohort with close to 80% experiencing at least one or more ACEs. We observed that experiencing ACEs was associated with slower decline in executive function, but not verbal episodic memory, indicating possible domain-specificity. A meta-analysis of ACES and late-life cognition found that the associations between ACEs and cognition varied by individual ACEs and type of cognitive outcome.(14) For example, some studies reported association of ACEs with lower cognitive scores and higher risk of neurocognitive disorder (NCD) diagnosis, while other studies found association of physical or

sexual abuse with better cognition, parental death with lower risk of NCD, and collective violence with better global cognition.(14) Our analysis did not find significant associations of individual ACEs with cognitive decline in any domain. Although ACEs could influence a child's development into adulthood through increased toxic stress pathways, these experiences may only partially contribute to cognitive functioning in late life.(3,37) Beyond cognition, other studies have shown that ACEs are associated with higher risk of cardiovascular disease, shortened telomeres, and greater functional limitations in Black adults.(38–40) Environmental, social, and behavioral factors throughout a person's life stand to mediate and even protect against the negative, long-term effects of ACEs.(6,23) In Ritchie et al(6), positive childhood environment was found to promote executive functioning. Educational attainment could also be protective for later-life cognitive function through cognitive reserve.(24) Our cohort was highly educated and reported a high prevalence of childhood support which could explain why ACES were not associated with lower baseline cognition.

The Cumulative Inequity (CI) theory provides as a meaningful framework for explaining the observed relationships in our study. One possibility for our findings is that it reflects a pattern of resiliency. Among those who experienced ACEs, many had parents who were separated or divorced (39%), had family members with serious illness (35%), or witnessed domestic violence (32%). CI theory suggests that the detrimental, cumulative impact of experiencing multiple ACEs may have been modified by other factors, such as human agency or social support.(18) Most participants reported receiving support during childhood all or most of the time and 76% reported having someone they trust or confide in, 86% having someone show them loved, 66% having someone help with homework, 79% having someone to motivate them in school, and 77% having someone close to them that they can contact. In a literature review on ACEs and

cognitive change in Black Americans, multiple studies continually found that lower SES was associated faster aging(3), which may in part explain why our cohort with relatively high childhood SES does not have significant cognitive decline due to aging despite experiencing higher ACEs. Another explanation for our findings is resiliency through selection and survival bias which may include only the healthiest individuals that chose to participate in the study. Black participants in STAR may be exceptional in that they overcame the negative effects of early childhood adversity, survived long enough, and were healthy enough to enroll in a study on cognitive aging. It is also important to consider that STAR consists of older Black individuals who's early life corresponded with de jure and de facto policies that upheld and endorsed racism in education, access to healthcare, socioeconomic status, and discrimination, which may further affirm only the most resilient individuals had the opportunity to live into old age.(41)

Our findings suggest that experiencing ACEs was not associated with worse cognition or cognitive decline in this cohort of older Black Americans. Additionally, the accumulation of ACEs may be associated with slower decline in executive function, a finding that needs to be explored further. CI theory posits that early life adversities do not fully determine cognitive trajectories in older adults and resiliency may subsequently develop through midlife and later life. Future studies are needed to understand how resiliency factors such as childhood support, education, and financial stability can be protective against ACEs as well as cognitive decline, especially among marginalized and high-risk communities.

BMJ Open

The original protocol for the study, as a supplementary file**.**

Funding: This work was supported by National Institutes of Health grant number RF1 AG050782

Competing Interests: None declared

Author Contributions: YL, KMG, PG, RLP, CCM, EHL, LLB, DMM and RAW were all involved with study design, data collection, data analysis, and reporting the results. STAR participants for providing their data for this research. All authors revised, approved final version of the manuscript, and agree to accept responsibility of all aspects of the work.

Patient Consent for Publications: Not required

Patients and Public Involvement: Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Word count: 3471 (Limit: 4000)

Ethics Approval: The Study of Healthy Aging in African Americans (STAR) was approved by Kaiser Permanente Northern California Institutional Review Board (IRB Number: 1121043)

Data availability statement: Data are available upon reasonable request. Data may be obtained from a third party and are not publicly available. Deidentified data are available to qualified investigators from the STAR Leadership Committee on approval for the purposes of replicating procedures and results.

Bibliography

1. Felitti VJ. Adverse childhood experiences and adult health. Acad Pediatr. 2009 Jun;9(3):131–2.

2. Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, et al. Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults. Am J Prev Med. 1998 May;14(4):245–58.

3. Graham KL, Paun O, Stillerman A. The Impact of Adverse Childhood Experiences on Cognition in African American Older Adults: An Integrated Literature Review. Res Gerontol Nurs. 2021 Oct;14(5):265–72.

4. Kobayashi LC, Farrell MT, Payne CF, Mall S, Montana L, Wagner RG, et al. Adverse childhood experiences and domain-specific cognitive function in a population-based study of older adults in rural South Africa. Psychol Aging. 2020 Sep;35(6):818–30.

5. Majer M, Nater UM, Lin JMS, Capuron L, Reeves WC. Association of childhood trauma with cognitive function in healthy adults: a pilot study. BMC Neurol. 2010 Jul 14;10:61.

6. Ritchie K, Jaussent I, Stewart R, Dupuy AM, Courtet P, Malafosse A, et al. Adverse childhood environment and late-life cognitive functioning. Int J Geriatr Psychiatry. 2011 May;26(5):503–10.

7. Yang L, Wang Z. Early-Life Conditions and Cognitive Function in Middle-and Old-Aged Chinese Adults: A Longitudinal Study. Int J Environ Res Public Health. 2020 May 15;17(10).

8. Donley GAR, Lönnroos E, Tuomainen TP, Kauhanen J. Association of childhood stress with late-life dementia and Alzheimer's disease: the KIHD study. Eur J Public Health. 2018 Dec 1;28(6):1069–73.

9. Radford K, Delbaere K, Draper B, Mack HA, Daylight G, Cumming R, et al. Childhood Stress and Adversity is Associated with Late-Life Dementia in Aboriginal Australians. Am J Geriatr Psychiatry Off J Am Assoc Geriatr Psychiatry. 2017 Oct;25(10):1097–106.

10. Tani Y, Fujiwara T, Kondo K. Association Between Adverse Childhood Experiences and Dementia in Older Japanese Adults. JAMA Netw Open. 2020 Feb 5;3(2):e1920740.

11. Gold AL, Meza E, Ackley SF, Mungas DM, Whitmer RA, Mayeda ER, et al. Are adverse childhood experiences associated with late-life cognitive performance across racial/ethnic groups: results from the Kaiser Healthy Aging and Diverse Life Experiences study baseline. BMJ Open. 2021 Feb 5;11(2):e042125.

12. O'Shea BQ, Demakakos P, Cadar D, Kobayashi LC. Adverse Childhood Experiences and Rate of Memory Decline From Mid to Later Life: Evidence From the English Longitudinal Study of Ageing. Am J Epidemiol. 2021 Jul 1;190(7):1294–305.

13. Barnes LL, Wilson RS, Everson-Rose SA, Hayward MD, Evans DA, Mendes de Leon CF. Effects of early-life adversity on cognitive decline in older African Americans and whites. Neurology. 2012 Dec 11;79(24):2321–7.

14. Patel P, Oremus M. The association between adverse childhood experiences and late-life cognition: A systematic review of cross-sectional and case-control studies. The Gerontologist. 2022 Mar 22;gnac041.

15. Dannefer D. Cumulative Advantage/Disadvantage and the Life Course: Cross-Fertilizing Age and Social Science Theory. J Gerontol Ser B. 2003 Nov 1;58(6):S327–37.

16. Yang MS, Hedeker D. A life-span approach to examining older vulnerable population's subjective well-being: the role of adversity and trauma. Aging Ment Health. 2020 Dec 1;24(12):2043–52.

17. Ferraro KF, Schafer MH, Wilkinson LR. Childhood Disadvantage and Health Problems in Middle and Later Life: Early Imprints on Physical Health? Am Sociol Rev. 2016 Feb 1;81(1):107–33.

18. Ferraro KF, Shippee TP. Aging and Cumulative Inequality: How Does Inequality Get Under the Skin? The Gerontologist. 2009 Jun;49(3):333–43.

19. Giano Z, Wheeler DL, Hubach RD. The frequencies and disparities of adverse childhood experiences in the U.S. BMC Public Health [Internet]. 2020 Sep 10 [cited 2021 Jan 29];20. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7488299/

20. Maguire-Jack K, Lanier P, Lombardi B. Investigating racial differences in clusters of adverse childhood experiences. Am J Orthopsychiatry. 2020;90(1):106–14.

21. Merrick MT, Ford DC, Ports KA, Guinn AS. Prevalence of Adverse Childhood Experiences From the 2011-2014 Behavioral Risk Factor Surveillance System in 23 States. JAMA Pediatr. 2018 Nov;172(11):1038–44.

22. Mayeda ER, Glymour MM, Quesenberry CP, Whitmer RA. Inequalities in dementia incidence between six racial and ethnic groups over 14 years. Alzheimers Dement J Alzheimers Assoc. 2016 Mar;12(3):216–24.

23. Peterson RL, Fain MJ, Butler EA, Ehiri JE, Carvajal SC. The role of social and behavioral risk factors in explaining racial disparities in age-related cognitive impairment: a structured narrative review. Aging Neuropsychol Cogn. 2020 Mar 3;27(2):173–96.

24. Weuve J, Barnes LL, Mendes de Leon CF, Rajan KB, Beck T, Aggarwal NT, et al. Cognitive Aging in Black and White Americans: Cognition, Cognitive Decline, and Incidence of Alzheimer Disease Dementia. Epidemiol Camb Mass. 2018 Jan;29(1):151–9.

25. George KM, Gilsanz P, Peterson RL, Barnes LL, DeCarli CS, Mayeda ER, et al. Impact of Cardiovascular Risk Factors in Adolescence, Young Adulthood, and Midlife on Late-Life

Cognition: Study of Healthy Aging in African Americans. J Gerontol Ser A. 2021 Sep 1;76(9):1692–8.

26. Whitmer RA, Barnes LL, Richards AE, Miles S, Mayeda ER, Glymour MM, et al. Introducing the Study of Healthy Aging in African Americans (STAR): Looking back to move forward. Alzheimers Dement. 2020;16(S10):e046614.

27. Mungas D, Reed BR, Crane PK, Haan MN, González H. Spanish and English Neuropsychological Assessment Scales (SENAS): further development and psychometric characteristics. Psychol Assess. 2004 Dec;16(4):347–59.

28. Mungas DM, Reed BR, Haan MN, Gonzalez H. Spanish and English Neuropsychological Assessment Scales: Relationship to demographics, language, cognition, and independent function. Neuropsychology. 2005 Jul;19(4):466–75.

29. Anda RF, Felitti VJ, Bremner JD, Walker JD, Whitfield C, Perry BD, et al. The enduring effects of abuse and related adverse experiences in childhood. Eur Arch Psychiatry Clin Neurosci. 2006 Apr;256(3):174–86.

30. Campbell TL. Screening for Adverse Childhood Experiences (ACEs) in Primary Care: A Cautionary Note. JAMA. 2020 Jun 16;323(23):2379–80.

31. Lacey RE, Minnis H. Practitioner Review: Twenty years of research with adverse childhood experience scores – Advantages, disadvantages and applications to practice. J Child Psychol Psychiatry. 2020;61(2):116–30.

32. Whitfield KE, Allaire JC, Belue R, Edwards CL. Are Comparisons the Answer to Understanding Behavioral Aspects of Aging in Racial and Ethnic Groups? J Gerontol B Psychol Sci Soc Sci. 2008 Sep;63(5):P301–8.

33. Howard VJ, McClure LA, Glymour MM, Cunningham SA, Kleindorfer DO, Crowe M, et al. Effect of duration and age at exposure to the Stroke Belt on incident stroke in adulthood. Neurology. 2013 Apr 30;80(18):1655–61.

34. Briggs EC, Amaya-Jackson L, Putnam KT, Putnam FW. All adverse childhood experiences are not equal: The contribution of synergy to adverse childhood experience scores. Am Psychol. 2021 Mar;76(2):243–52.

35. Althubaiti A. Information bias in health research: definition, pitfalls, and adjustment methods. J Multidiscip Healthc. 2016 May 4;9:211–7.

36. Krinner LM, Warren-Findlow J, Bowling J, Issel LM, Reeve CL. The dimensionality of adverse childhood experiences: A scoping review of ACE dimensions measurement. Child Abuse Negl. 2021 Nov 1;121:105270.

37. Morsy L, Rothstein R. Toxic stress and children's outcomes. Econ Policy Inst [Internet]. 2019 May 1; Available from: https://www.epi.org/publication/toxic-stress-and-childrens-

outcomes-african-american-children-growing-up-poor-are-at-greater-risk-of-disrupted-physiological-functioning-and-depressed-academic-achievement/

38. Kliewer W, Robins JL. Adverse Childhood Experiences Are Associated with Cardiometabolic Risk Indicators and Telomere Length in Low-Income African-American Adolescents. Int J Behav Med. 2022 Feb;29(1):131–5.

39. Islam SJ, Hwan Kim J, Joseph E, Topel M, Baltrus P, Liu C, et al. Association Between Early Trauma and Ideal Cardiovascular Health Among Black Americans: Results From the Morehouse-Emory Cardiovascular (MECA) Center for Health Equity. Circ Cardiovasc Qual Outcomes. 2021 Sep;14(9):e007904.

40. Sauerteig MR, Ferraro KF, Bauldry S. Life Course Stressors and Functional Limitations in Later Life Among White, Black, and Hispanic Adults: Deleterious, Hardening, or Benign? J Gerontol B Psychol Sci Soc Sci. 2022 Jan 12;77(1):249–59.

41. Glymour MM, Manly JJ. Lifecourse social conditions and racial and ethnic patterns of cognitive aging. Neuropsychol Rev. 2008 Sep;18(3):223–54.

Table 1: Baseline characteristics stratified by number of Adverse Childhood Experiences (ACEs), STAR

Characteristic	Overall Sample	0 ACEs	1 ACE	2 ACEs	3 ACEs	4+ ACEs
	N (%) or Mean (SD)					
Number of Participants	707 (100)	151 (21.4)	167 (23.6)	148 (20.0)	122 (17.3)	119 (16.8)
Baseline Age	68.6 (8.7)	69.1 (8.2)	69.0 (8.4)	68.9 (9.2)	68.8 (9.6)	66.7 (8.2)
Gender: Male	220 (31.1)	46 (30.5)	56 (33.5)	51 (34.5)	38 (31.2)	29 (24.4)
College graduate or more	252 (35.6)	51 (33.8)	60 (35.9)	54 (36.5)	44 (36.1)	43 (36.1)
Parent education: More than high school	267 (37.8)	63 (41.7)	59 (35.3)	54 (36.5)	43 (35.3)	48 (40.3)
ACEs	N (column % per variables)					
Parents were separated or divorced	272 (38.5)	0	30 (18.0)	63 (42.6)	73 (59.8)	106 (89.1)
Serious illness of a family member	250 (35.4)	0	44 (26.4)	67 (45.3)	64 (52.5)	75 (63.0)
Witnessed domestic violence	223 (31.5)	0	37 (22.2)	41 (27.7)	60 (49.2)	85 (71.4)
Substance abuse by a family member	172 (24.3)	0	18 (10.8)	35 (23.7)	41 (33.6)	78 (65.6)
Parent remarried	176 (24.9)	0	2 (1.2)	39 (26.4)	58 (47.6)	77 (64.7)
Loss of job by a parent	106 (15.0)	0	23 (13.8)	19 (12.8)	23 (18.9)	41 (34.5)
Death of your father	70 (9.9)	0	8 (4.8)	18 (12.2)	19 (15.6)	25 (21.0)
Parent had to go to jail	53 (7.5)	0	2 (1.2)	4 (2.7)	10 (8.2)	37 (31.1)
Death of your mother	42 (5.9)	0	3 (1.8)	10 (6.8)	18 (14.8)	11 (9.2)
Childhood Social Support	N (column % per variables) or Mean (SD)					
Composite childhood support	15.8 (4.7)	17.1 (4.2)	16.4 (4.3)	15.3 (4.7)	14.5 (4.8)	14.9 (5.1)
Someone to trust and confide in all to most times	537 (75.7)	125 (82.8)	136 (81.4)	104 (70.3)	87 (71.3)	83 (69.8)
Someone to love all to most times	611 (86.4)	143 (94.7)	149 (89.2)	125 (84.5)	96 (78.7)	98 (82.4)

Someone to help with homework all to most times	466 (65.9)	121 (80.1)	118 (70.6)	91 (61.49)	65 (53.3)	71 (59.1)
Someone to motivate and encourage school	559 (79.1)	135 (89.4)	145 (86.8)	107 (72.3)	87 (71.3)	85 (71.4)
Had contact with someone felt close to all or most times	547 (77.4)	126 (83.4)	138 (82.6)	112 (75.7)	87 (71.3)	84 (70.6)
Childhood Socioeconomic Status	**N (column % per variables)**					
Family financially well-off or above average	483 (68.3)	125 (82.8)	120 (71.9)	101 (68.2)	70 (57.4)	67 (56.3)
Never hungry during childhood	650 (91.9)	146 (96.7)	157 (94.0)	131 (88.5)	110 (90.2)	106 (89.1)
Family had a mortgage or owned a home during childhood	444 (62.8)	118 (78.2)	111 (66.5)	94 (63.5)	65 (53.3)	56 (47.1)

ACEs: Adverse Childhood Experiences
SD: Standard Deviation

Table 2: Linear mixed models estimate of the association of composite adverse childhood experiences (ACEs) with domain-specific cognition across 3 waves

	Executive Function			Verbal Episodic Memory		
	Model 1	**Model 2**	**Model 3**	**Model 1**	**Model 2**	**Model 3**
	β (95% CI)	**β (95% CI)**	**β (95% CI)**	**β (95% CI)**	**β (95% CI)**	**β (95% CI)**
Years from baseline	-0.071 (-0.119, -0.023)	-0.084 (-0.137, -0.03)	-0.119 (-0.222, -0.016)	-0.078 (-0.148, -0.009)	-0.108 (-0.185, -0.03)	-0.170 (-0.319, -0.02)
	Baseline					
ACEs						
0	ref	ref	ref	ref	ref	ref
1	-0.130 (-0.316, 0.055)	-0.090 (-0.272, 0.093)	-0.090 (-0.273, 0.092)	-0.137 (-0.321, 0.048)	-0.110 (-0.293, 0.073)	-0.111 (-0.294, 0.072)
2	-0.039 (-0.231, 0.152)	0.008 (-0.181, 0.197)	0.006 (-0.184, 0.196)	-0.041 (-0.231, 0.149)	-0.010 (-0.198, 0.179)	-0.014 (-0.204, 0.176)
3	0.008 (-0.193, 0.209)	0.070 (-0.132, 0.271)	0.067 (-0.136, 0.271)	-0.120 (-0.320, 0.080)	-0.085 (-0.287, 0.116)	-0.092 (-0.295, 0.111)
4+	-0.025 (-0.228, 0.178)	0.052 (-0.155, 0.259)	0.050 (-0.158, 0.258)	0.105 (-0.097, 0.307)	0.156 (-0.051, 0.363)	0.151 (-0.057, 0.359)
	Longitudinal					
ACEs						
0	ref	ref	ref	ref	ref	ref
1	0.053 (-0.010, 0.116)	0.056 (-0.007, 0.119)	0.057 (-0.006, 0.120)	-0.017 (-0.108, 0.075)	-0.020 (-0.112, 0.072)	-0.019 (-0.11, 0.073)
2	0.117 (0.052, 0.182)	0.125 (0.060, 0.191)	0.128 (0.062, 0.194)	0.074 (-0.021, 0.169)	0.077 (-0.019, 0.173)	0.082 (-0.014, 0.178)
3	0.075 (0.007, 0.143)	0.090 (0.021, 0.159)	0.094 (0.025, 0.164)	0.050 (-0.048, 0.148)	0.050 (-0.05, 0.151)	0.058 (-0.044, 0.160)
4+	0.089 (0.020, 0.158)	0.108 (0.036, 0.179)	0.111 (0.039, 0.182)	-0.022 (-0.123, 0.078)	-0.022 (-0.126, 0.082)	-0.017 (-0.121, 0.088)

Model 1: Adjusted for years from baseline, baseline age centered at mean, and sex,
Model 2: Model 1 + childhood SES
Model 3: Model 2 + composite childhood support
ACEs: Adverse Childhood Experience

CI: Confidence Interval

Figure 1: Prediction plot of linear mixed models estimate of the association of composite adverse childhood experiences (ACEs) with executive function across 3 waves

Adjusted for years from baseline, baseline age centered at mean, gender/sex, childhood SES, and composite childhood support

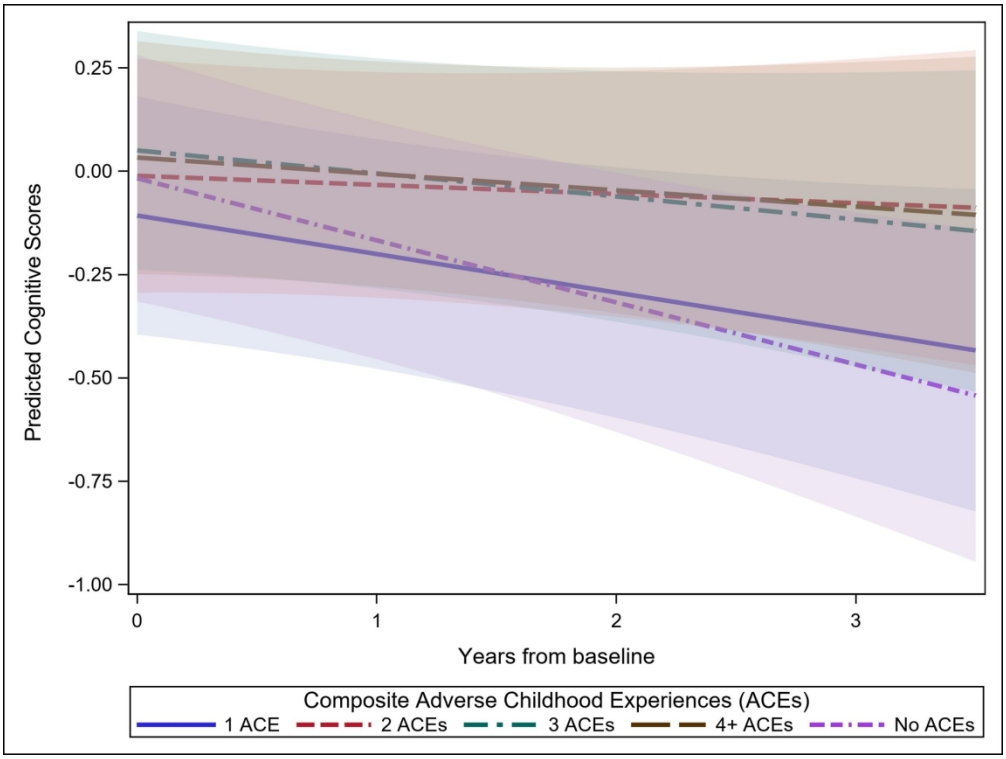
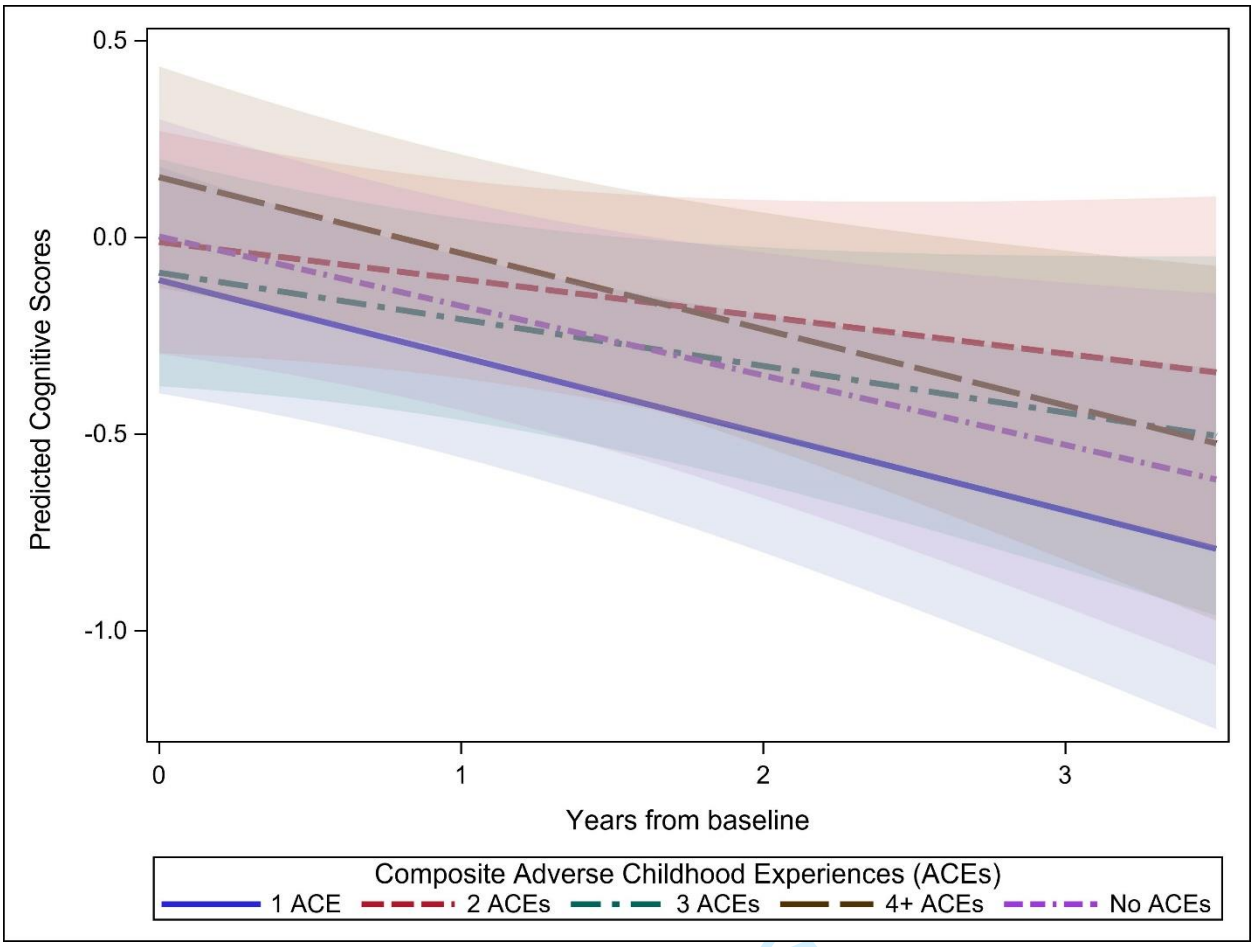


Figure 1: Prediction plot of linear mixed models estimate of the association of composite adverse childhood experiences (ACEs) with executive function across 3 waves

169x127mm (300 x 300 DPI)

Supplemental Figure 1: Prediction plot of linear mixed models estimate for the association of composite adverse childhood experiences (ACEs) with verbal episodic memory across 3 waves



Adjusted for years from baseline, baseline age centered at mean, gender/sex, childhood SES, and composite childhood support

Supplemental Table 1: Linear mixed model with random intercept and slope of the association of individual adverse childhood experiences (ACEs) with domain-specific cognition adjusted for time, gender/sex, and parental education

	Executive Function			Verbal Episodic Memory		
Cross-Sectional						
	Model 1 β (95% CI)	**Model 2** β (95% CI)	**Model 3** β (95% CI)	**Model 1** β (95% CI)	**Model 2** β (95% CI)	**Model 3** β (95% CI)
Parent Separated	-0.035 (-0.166, 0.095)	-0.040 (-0.169, 0.089)	-0.011 (-0.140, 0.118)	-0.006 (-0.140, 0.128)	-0.014 (-0.142, 0.115)	0.017 (-0.112, 0.147)
Parent Remarried	-0.007 (-0.152, 0.139)	-0.017 (-0.161, 0.127)	0.000 (-0.142, 0.142)	0.062 (-0.087, 0.212)	0.044 (-0.100, 0.188)	0.061 (-0.082, 0.203)
Witnessed Violence	0.065 (-0.071, 0.200)	0.052 (-0.082, 0.186)	0.070 (-0.062, 0.201)	0.131 (-0.009, 0.270)	0.106 (-0.028, 0.240)	0.121 (-0.012, 0.253)
Substance Abuse	0.118 (-0.029, 0.266)	0.126 (-0.02, 0.272)	0.119 (-0.025, 0.262)	0.096 (-0.056, 0.247)	0.111 (-0.035, 0.256)	0.107 (-0.037, 0.251)
Loss Job	0.014 (-0.162, 0.190)	0.007 (-0.167, 0.181)	0.034 (-0.137, 0.206)	0.029 (-0.152, 0.210)	0.016 (-0.158, 0.190)	0.033 (-0.139, 0.205)
Parent Jail	-0.120 (-0.359, 0.118)	-0.116 (-0.352, 0.12)	-0.064 (-0.298, 0.169)	-0.034 (-0.279, 0.211)	-0.022 (-0.257, 0.213)	0.020 (-0.214, 0.254)
Serious Family Illness	-0.014 (-0.146, 0.118)	-0.018 (-0.148, 0.112)	-0.011 (-0.139, 0.117)	0.032 (-0.103, 0.167)	0.025 (-0.105, 0.155)	0.029 (-0.099, 0.157)
Death Mother	-0.007 (-0.275, 0.262)	-0.033 (-0.299, 0.233)	-0.028 (-0.289, 0.233)	0.105 (-0.171, 0.381)	0.057 (-0.208, 0.322)	0.058 (-0.204, 0.320)
Death Father	-0.002 (-0.213, 0.209)	-0.006 (-0.215, 0.203)	0.025 (-0.180, 0.231)	-0.019 (-0.236, 0.199)	-0.024 (-0.233, 0.185)	-0.002 (-0.209, 0.205)
Longitudinal						
	Model 1 β (95% CI)	**Model 2** β (95% CI)	**Model 3** β (95% CI)	**Model 1** β (95% CI)	**Model 2** β (95% CI)	**Model 3** β (95% CI)
Parent Separated	-0.006 (-0.140, 0.128)	-0.014 (-0.142, 0.115)	0.017 (-0.112, 0.147)	0.018 (-0.025, 0.062)	0.018 (-0.025, 0.062)	0.018 (-0.026, 0.062)
Parent Remarried	0.062 (-0.087, 0.212)	0.044 (-0.100, 0.188)	0.061 (-0.082, 0.203)	0.045 (-0.005, 0.094)	0.045 (-0.004, 0.095)	0.045 (-0.005, 0.094)
Witnessed Violence	0.131 (-0.009, 0.270)	0.106 (-0.028, 0.240)	0.121 (-0.012, 0.253)	0.026 (-0.019, 0.072)	0.027 (-0.019, 0.072)	0.027 (-0.019, 0.072)
Substance Abuse	0.096 (-0.056, 0.247)	0.111 (-0.035, 0.256)	0.107 (-0.037, 0.251)	0.034 (-0.016, 0.083)	0.033 (-0.016, 0.083)	0.033 (-0.016, 0.083)
Loss Job	0.029 (-0.152, 0.210)	0.016 (-0.158, 0.190)	0.033 (-0.139, 0.205)	0.004 (-0.055, 0.063)	0.004 (-0.055, 0.063)	0.003 (-0.055, 0.062)
Parent Jail	-0.034 (-0.279, 0.211)	-0.022 (-0.257, 0.213)	0.020 (-0.214, 0.254)	0.067 (-0.015, 0.149)	0.066 (-0.016, 0.148)	0.067 (-0.015, 0.149)
Serious Family Illness	0.032 (-0.103, 0.167)	0.025 (-0.105, 0.155)	0.029 (-0.099, 0.157)	0.038 (-0.006, 0.082)	0.038 (-0.006, 0.082)	0.038 (-0.006, 0.083)
Death Mother	0.105 (-0.171, 0.381)	0.057 (-0.208, 0.322)	0.058 (-0.204, 0.320)	-0.005 (-0.096, 0.087)	-0.005 (-0.096, 0.086)	-0.004 (-0.095, 0.087)
Death Father	-0.019 (-0.236, 0.199)	-0.024 (-0.233, 0.185)	-0.002 (-0.209, 0.205)	0.005 (-0.067, 0.076)	0.006 (-0.066, 0.077)	0.004 (-0.067, 0.076)

Model 1: Adjusted for baseline age centered at mean,
Model 2: Model 1 + sex,
Model 3: Model 2 + parental education

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-10
Bias	9	Describe any efforts to address potential sources of bias	9-10
Study size	10	Explain how the study size was arrived at	n/a
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11
		(*b*) Describe any methods used to examine subgroups and interactions	11
		(*c*) Explain how missing data were addressed	11
		(*d*) If applicable, explain how loss to follow-up was addressed	n/a
		(*e*) Describe any sensitivity analyses	n/a
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	n/a
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11-12
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) Summarise follow-up time (eg, average and total amount)	8, 15
Outcome data	15*	Report numbers of outcome events or summary measures over time	11-12

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-13
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	16-17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

What is the association between adverse childhood experiences and late-life cognitive decline? Study of Healthy Aging in African Americans (STAR) Cohort Study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2023-072961.R1
Article Type:	Original research
Date Submitted by the Author:	12-Sep-2023
Complete List of Authors:	Lor, Yi; University of California Davis, George, Kristen M; University of California Davis, Department Public Health Sciences Gilsanz, Paola; Kaiser Permanente Division of Research, Meunier, Claire; University of California Davis Peterson, Rachel; University of Montana Hayes-Larson, Eleanor; UCLA School of Public Health, Department of Epidemiology Barnes, Lisa; Rush University, Department of Neurological Sciences Mungas, Dan; University of California Davis, Department of Neurology Whitmer, Rachel; University of California Davis, Department of Public Health Sciences
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health
Keywords:	EPIDEMIOLOGY, PUBLIC HEALTH, Risk Factors, Aging

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Journal: BMJ Open – Original Research

Title: What is the association between adverse childhood experiences and late-life cognitive decline? Study of Healthy Aging in African Americans (STAR) Cohort Study

Yi Lor (Corresponding Author), Kristen M. George, Paola Gilsanz, Claire C. Meunier, Rachel L. Peterson, Eleanor Hayes-Larson, Lisa L. Barnes, Dan M. Mungas, Rachel A. Whitmer

Author Information:

Yi Lor, MPH (**Corresponding Author**)
- Graduate Group in Epidemiology, University of California
- Email: yijlor@ucdavis.edu
- Funding: None
- Conflicts: No conflicts

Kristen M. George, PhD
- Department of Public Health Sciences, University of California Davis School of Medicine
- Email: krmgeorge@ucdavis.edu
- Funding: N/A
- Conflicts: No conflicts

Paola Gilsanz, ScD, MPH
- Division of Research, Kaiser Permanente Northern California
- Email: paola.gilsanz@kp.org
- Funding: NIH RF1AG050782 (PI: Whitmer)
- Conflicts: No conflicts.

Claire C. Meunier, MPH
- Graduate Group in Epidemiology
- Email: Ccmeunier@ucdavis.edu
- Funding: None
- Conflicts: No conflicts

Rachel L. Peterson, PhD, MPH, MA
- School of Public and Community Health Sciences, University of Montana
- Email: rachel.peterson@mso.umt.edu
- Funding: NIH/NIA 4R00AG073457-02
- Conflicts: No conflicts

Elanor Hayes-Larson, PhD, MPH

- Department of Epidemiology, UCLA Fielding School of Public Health, Los Angeles, California, USA
- Email: ehayeslarson@ucla.edu
- Funding: NIA K99AG075317
- Conflicts: No conflicts

Lisa L. Barnes, PhD
- Rush Alzheimer's Disease Center and Department of Neurological Sciences, Rush University Medical Center
- Email: Lisa_L_Barnes@rush.edu
- Funding: RF1AG050782(PI: Whitmer)
- Conflicts: No conflicts

Dan Mungas, PhD,
- Department of Neurology, University of California, Davis, Sacramento, CA, USA
- Email: dmmungas@ucdavis.edu
- Funding: N/A
- Conflicts: No conflicts

Rachel A. Whitmer, PhD
- Department of Public Health Sciences and Neurology, University of California Davis
- Email: rawhitmer@ucdavis.edu
- RF1AG050782(PI: Whitmer)
- Conflicts: No conflicts

Abstract (Word count: 290)

Objectives: Adverse childhood experiences (ACEs) are associated with higher risk of chronic disease, but little is known about the association with late life cognitive decline. We examined the longitudinal association between ACEs and late-life cognitive decline in the Study of Healthy Aging in African Americans (STAR).

Design: Linear mixed models with random intercepts and slope examined the association of individual and composite ACEs with cognitive change adjusting for years from baseline (timescale), baseline age, sex, parental education, childhood socioeconomic status, and childhood social support. Participants reported whether they had experienced 9 types of ACEs. Executive function and verbal episodic memory were measured up to 3 times over a 3-year period using the Spanish and English Neuropsychological Assessment Scales.

Settings: Kaiser Permanente Northern California members living in the Bay Area.

Participants: STAR is a cohort study of cognitive aging launched in 2018 that has enrolled 764 Black Americans ages ≥ 50 years (mean age=67.5; SD=8.5).

Results: Twenty percent of participants reported no ACEs, 23% one ACE, 20% two ACEs, 17% three ACEs, and 17% four or more ACEs. Compared to no ACEs, two ACEs (β=0.117; 95% CI 0.052-0.182), three ACEs (β=0.075; 95% CI 0.007-0.153), and 4+ ACEs (β=0.089; 95% CI 0.002-0.158), were associated with less decline in executive function. There were no significant associations between number of ACEs and baseline or longitudinal verbal episodic memory or between individual ACEs and executive function or verbal episodic memory.

Conclusion: In this cohort of older Black Americans, there was no association between ACEs and baseline cognition or cognitive change in verbal episodic memory; however, experiencing ≥2 ACEs was associated with less decline in executive function. These results may indicate that

participants who survived to age 50+ and experienced ACEs may have cognitive resilience that warrants further investigation.

Strength and Limitations of this study:

- The impact of adverse childhood experiences (ACEs) on late-life cognition in older Black adults is sparse with little research investigating cognitive decline.
- The Study of Healthy Aging in African Americans (STAR) is a well-characterized cohort of older Black Americans ages 50 years or older with detailed socioeconomic lifecourse information such as education, region of birth, and childhood experiences.
- Repeated assessment of cognition in two domains across three waves (approximately 3 years) using the Spanish and English Assessment Scale (SENAS), a measurement validated in English and Spanish, and in diverse populations.
- Linear mixed models allowing for evaluation of ACEs on cognition and cognitive decline adjusting for childhood confounders such as childhood socioeconomic status and childhood support.
- ACEs assessments were limited to self-report and there were no questions asked of physical or sexual abuse.

INTRODUCTION

Childhood is a sensitive period in the lifecourse for later-life health outcomes(1,2), such that disruptions during this period can have detrimental effects on development and later life health. Adverse childhood experiences (ACEs) are traumatic events in childhood that include abuse, witnessing violence, and household dysfunction and have been associated with higher risk of cardiovascular diseases, chronic lung disease, and liver disease(1,2). Although ACEs are associated with many of the risk factors for dementia, only a handful of studies have examined the association between ACEs and poor cognitive aging outcomes in Black Americans(3).

Cognitive decline and decreased cognitive function are early indicators of Alzheimer's disease and related dementias (ADRD)(4). Signs of these cognitive deficits often includes loss of memory and/or loss of the ability to perform high-level mental skills (executive function) such as planning, and management of thoughts and emotions. Therefore, many studies administering cognitive assessments will include some form of memory and executive function and memory assessment(5,6). Some studies indicate that ACEs have negative effects on cognitive functioning later in life(7–10). These studies examining the specific types of ACEs have reported associations of the death of a parent, parental excess alcohol and drug use, mental health problems, physical neglect, and emotional abuse experienced during childhood with worse memory later in life. Moreover, two systematic reviews found that abuse and neglect were associated with worse executive function(11,12). Additionally, greater numbers of ACEs are associated with increased risk of developing ADRD(13–15). Despite findings of ACEs being associated with poorer memory and higher risk of ADRD, other studies have shown mixed results, with weak to no association of ACEs with change in cognition over time(16,17). Furthermore, the literature is mixed on the specific impact that ACEs have on late-life cognitive

functioning with some ACEs being associated with slower cognitive decline in older Black adults but no decline in older White adults(18,19).

Two interrelated life course theories serve as a framework for understanding how early life exposures, such as ACEs, may affect later life cognitive outcomes. The Cumulative Advantage/Disadvantage theory posits that structural and institutional processes contribute to differential access to resources or harmful exposures that accumulate in a non-additive way over time(20,21). Individuals who are exposed to more ACEs over time will have an increased risk of negative health outcomes, including poor cognition, later in life. Building on this theory, the Cumulative Inequality (CI) theory incorporates life course factors that take into consideration the intergenerational, socioeconomic, and stress processes important in the environment in which a child grows up(22,23). Both theories recognize that the trajectories established by negative childhood exposures can be altered by positive experiences throughout the life course. ACEs may be a predictor of worse outcomes in later life, but positive experiences such as social support and individual response to adversity may minimize the negative effects on cognitive outcomes. Due to the relationships between both theories, we will consider them together as the CI theory.

Compared to White Americans, Black Americans have a higher risk of ADRD and report more ACEs(24–26). However, the relationship between childhood adversity and cognition in later life among Black adults remains ambiguous(27–29). The two studies that have examined ACEs and cognitive outcomes in Black adults have had mixed results(16,18). One study examining 427 older Blacks adults found no associations between ACEs and cognition(16). Another study among 3700 older Black adults found that those who reported experiencing food

deprivation and having thinner body size than their peers in early life had slower rates of cognitive decline compared to those who did not report food deprivation or being thinner(18).

The aim of this paper was to examine the association between total number of ACEs as well as the specific ACEs experienced with cognitive change in a cohort of middle-aged and older Black adults. To expand the sparse existing literature, we focus on Black individuals and their early-life experiences(3). Based on the CI theory, we hypothesize a dose-response relationship where each additional ACE experienced is associated with faster cognitive decline, and all types of ACEs predict worse cognitive outcomes.

METHODS

Study participants and data collection

The STAR cohort consists of community-dwelling midlife to older Black adults that reside in the San Francisco Bay area of California, primarily the cities of Oakland and Richmond(30,31). STAR aims to evaluate how lifecourse vascular and sociocultural factors influence the trajectory of cognitive aging and burden of cognitive impairment among Black Americans. Individuals eligible for STAR were long-term members of Kaiser Permanente Northern California, an integrated healthcare delivery system, who identified as Black or African American, were age 50 years or older on January 1, 2018, and had previously participated in Kaiser Permanente multiphasic health checkup (MHC) exams between 1964-1985. Stratified random sampling by age and educational attainment was used with the goal of recruiting approximately equal proportions of participants ages 50-64 and 65 and older. Exclusion criteria included electronic medical record diagnosis of dementia or other neurodegenerative diseases (frontotemporal dementia, Lewy body disease, Pick's disease, Parkinson's disease with dementia, Huntington's disease) and presence of health conditions that would impede

participation in study interviews (defined by hospice activity in the past 12 months, history of severe chronic obstructive pulmonary disease in the past 6 months, congestive heart failure hospitalizations in the past 6 months, and history of end stage renal disease or dialysis in the past 12 months). Although most participants of STAR resided in California by the 1960s, more than half of the participants (53%) were born outside of California, and about one-third (36%) of these participants were from the Southern states.

Patients and Public Involvement

No patients nor the public were involved in the design, conduct, reporting, or dissemination plans of our research.

Measures

Cognition

Cognitive function was assessed at each STAR wave using the Spanish and English Neuropsychological Assessment Scales (SENAS), a battery of cognitive tests that have undergone extensive development using item response theory methodology for valid comparisons of cognition and cognitive change across racial/ethnic and linguistically diverse groups(32–34). Cognitive domains of executive function and verbal episodic memory were derived from the SENAS. Executive function is a composite constructed from components of category fluency, phonemic/letter fluency, and working memory (digit span backward, and two list sorting). Verbal episodic memory was derived from two Word List Learning tests. Each domain was z-standardized using to the full baseline sample. Moreover, neither cognitive domains is limited by any ceiling or floor effect(32). Details of the administration procedures, development, and psychometric characteristics can be found described in-depth elsewhere(32–

35). Cognitive trajectories were measured across three waves of data approximately 14 months apart totally over 3 years.

Adverse childhood experiences (ACEs)

STAR fielded a modified version of the ACEs assessment from the REason for Geographic and Racial Disparities in Stroke (REGARDS) cohort(36–38). During baseline interviews, participants were asked verbally if they experienced nine separate types of ACEs during childhood from birth to age 16. ACEs included experiences of parents' divorce or separation, a parent remarrying, witnessing domestic violence, substance abuse by a family member, loss of a job by a parent, a parent going to jail, serious illness of a family member, death of mother, and death of father. ACEs were examined individually and as a composite ACE score defined as the sum of ACEs reported and recategorized as 0, 1, 2, 3, or 4 or more ACEs. Summation of ACEs models the cumulative effect that is reflective of the CI theory and cumulative ACEs score from 0 to 4 or more is one of the most commonly used methods for operationalizing ACEs. Cumulative ACEs score has been found to have a dose-response association with various health outcomes(2,39–41). Approximately 2% of participants (n = 14) had missing ACEs and were excluded from the analyses.

Covariates

As ACEs occurs early in life, we identified potential factors in early life that may cause confounding in the association of ACEs and late-life cognition and cognitive decline(7,10,16–18). We adjusted for five early-life social support factors that may confound the associations of ACEs and later-life cognition. Using a five level Likert-type scale (1 = None of the time, 2 = A little of the time, 3 = Some of the time, 4 = Most of the time, and 5 = All of the time), participants were asked: "How often was there someone in whom you could talk to, trust and

confide?," "How often was there someone who showed you love and affection?," "How often was there someone who could help you with your homework?," "How often was there someone who encouraged and pushed you to succeed in school?," and "How often did you have as much contact as you would like with someone you felt close to, someone in whom you could trust and confide?" The responses were dichotomized with cutoffs between high frequency (most and all of the time) and low frequency (none, a little, and some of the time). A composite score was created for early life factor by summation of the five scores (ranges 0-20) with higher score indicating higher levels of social support.

We additionally adjusted for early life socioeconomic status (SES) by including combined parental education (both parents with less than high school vs at least one parent with high school graduation or more), self-reported childhood family housing status (mortgage or owned home vs rental or others), and how often the participant reported going hungry as a child (never vs ever). Parental education was reported by the participants as highest level of education completed for both maternal and paternal parent. Both parent's education was combined into one parental education and dichotomized as both parents with less than high school diploma, and either one or both parents with more than high school diploma. Due to the small number of either one or both parents obtaining higher than high school diploma (38%), we operationalize parent education at the high school level cutoff. If both maternal and paternal education was missing, parental education was classified as less than a high school diploma, and these participants were demarcated by including a missing indicator covariate in all models.

Other covariates included age at baseline interview centered at the mean baseline age, sex (men or women) which was derived from self-report or participant medical records and likely reflected a mixture of sex assigned at birth and gender identity, and self-reported educational

attainment (collapsed as less than college degree, some college, and college graduate or more) captured during STAR baseline interviews.

Statistical analysis

The distribution of demographics, childhood social support, childhood SES indicators, and type of ACEs were estimated overall and stratified by the number of ACEs experienced. Two sets of linear mixed models were used to assess the association of cognition with: 1) composite ACE score and 2) individual ACEs, allowing for random intercept and slope to account for within-person correlation. The models were adjusted for time (as years since baseline) to estimate trajectories across three waves. We sequentially adjusted for covariates in our composite ACEs models by 1) adjusting for baseline mean-centered age and sex, 2) adjusted for childhood SES indicators, and 3) adjusted for childhood support. For models with individual ACEs, we sequentially adjusted for covariates by 1) adjusting for baseline mean-centered age, 2) sex, and 3) parental education. Interaction terms for time scale with exposure and covariates were added to each model to measure changes in cognition over time.

From a cohort of 764 participants, we excluded 14 participants for missing information on ACEs, 15 participants for missing early life social support and SES covariates, and 16 participants for missing report of sex.

RESULTS

Our analytic sample consisted of 707 participants with a mean age of 68.6 (SD 8.7) years (range, 53-95 years) of whom 487 (68.9%) were women compared to 220 (31.1%) men (Table 1). About 21% of participants reported no ACE, 23.6% reported one ACE, 20% reported two ACEs, 17.3% reported three ACEs, and 16.8% reported four or more ACEs. Seventy-nine percent of participants had at least one ACE. The most common ACE reported was experiencing

parents' separation or divorce (38.5%), followed by serious family illness (35.4%), and witnessing domestic violence (31.5%). More than a third (35.5%) of participants had a college degree or higher, and 38% of participants had one or both parents with more than a high school-level education (Table 1). Participants in this cohort generally had high levels of support (average composite score of 15.8 and SD = 4.7) during childhood with majority of participants reporting someone they could trust (76%), someone to love them (86%), someone to help with homework (66%), someone to motivate or encourage them in school (79%), and someone close to them they could contact (77%) all or most of the time. Most participants self-reported as being well-off or above average financially during childhood (68%), and most participants never experienced childhood hunger (92%). About 83% of our baseline cohort had two waves of cognitive measures, and over 75% of participants had all three waves of cognitive measures.

Composite number of ACEs

In our linear mixed models examining associations of the composite ACEs and baseline executive function (Table 2), we observed a negative non-significant associations for one ACE (β = -0.130; 95% CI -0.316 to 0.055), two ACEs (β = -0.039; 95% CI -0.231 to 0.152) and 4+ ACEs (β = -0.025; 95% CI -0.228 to 0.178), and a positive non-significant association for three ACEs (β = 0.008; 95% CI -0.193 to 0.209) compared to no ACEs. After adjusting for childhood SES, the estimates decreased for one ACE (β = -0.090; 95% CI -0.272 to 0.093), increased for three ACEs (β = 0.070; 95% CI -0.132 to 0.271), and changed direction for two ACEs (β = 0.008; 95% CI -0.181 to 0.197) and 4+ ACEs (β = 0.052; 95% CI -0.155 to 0.259) suggesting a non-significant positive association with baseline executive function. The estimates were attenuated after further adjusting for childhood support. We observed a non-significant negative association between composite ACEs and baseline verbal episodic memory for one ACE (β = -

0.137; 95% CI -0.321 to 0.048), two ACEs (β = -0.041; 95% CI -0.231 to 0.149) and three ACEs (β = -0.120; 95% CI -0.320 to 0.080), but positive association for 4+ ACEs (β = 0.105; 95% CI -0.097 to 0.307). After adjusting for childhood SES and childhood support, point estimates for the association between ACEs and baseline verbal episodic memory were attenuated.

When examined longitudinally, there was significantly slower decline in executive function among those who reported experiencing two ACEs (β=0.117; 95% CI 0.052 to 0.182), three ACEs (β=0.075; 95% CI 0.007 to 0.153), and four or more ACEs (β=0.089; 95% CI 0.002 to 0.158), but not for one ACE (β=0.053; 95% CI -0.010 to 0.116) compared to no ACEs (Table 2, Figure 1). The estimates and direction of associations remained consistent after adjusting for childhood SES and childhood social support variables (Table 2).

There were no significant associations between the composite ACEs score and verbal episodic memory over time (Supplemental Figure 1). However, the point estimates were negative for one ACE (β=-0.017; 95% CI -0.108 to 0.075) and 4+ ACEs (β=-0.022; 95% CI -0.123 to 0.078), and point estimates were positive for two ACEs (β=0.074; 95% CI -0.021 to 0.159) and three ACEs (β=0.050; 95% CI -0.048 to 0.148) compared to no ACEs (Table 2). The longitudinal point estimates changed minimally after adjusting for childhood SES and childhood social support.

Individual ACEs

When evaluating linear mixed models for executive function and verbal episodic memory with individual ACEs as predictors, there were no significant associations with baseline cognition or change of cognition over time (Supplemental Table 1). All individual ACEs had non-significant positive associations for executive function, except for death of mother which had non-significant negative association. Longitudinal estimates for verbal episodic memory

were mixed with non-significant positive associations for parent separated, parent remarried, serious family illness, death of mother, and death of father, while non-significant negative associations were observed for witnessed violence, substance abuse, loss of job, and parent jail.

DISCUSSION

In our cohort, ACEs was not significantly associated with baseline executive function or verbal episodic memory. We found that those who experienced multiple ACEs had slower decline in executive function than those who did not experience any ACEs, but we did not see this for verbal episodic memory. Our findings did not align with our hypothesis that exposure to ACEs would be associated with lower baseline cognition and greater cognitive decline. These results are consistent with some prior work in which similar results were observed in the Chicago Health and Aging Project (CHAP) cohort study of over 3700 older Black adults (average age 78 years) where those that experienced food deprivation had slower cognitive decline later in life(18). Our study included a younger cohort of Black Americans (average age 68 years) compared to CHAP(18) on childhood adversity and cognition. In another cross sectional study, no associations were found between composite and individual ACEs across different ages of childhood with baseline cognition within Black older adults when stratified by race(16). There is limited work on early life adversity and late-life cognition in Black Americans, and findings in our study, using an all-Black cohort, show similar results to previous work in this area.

Our estimates of the association between individual ACEs and domain-specific baseline cognition and cognitive decline were not statistically significant. The association between composite ACEs and verbal episodic memory were also not statistically significant. However, point estimates and borderline confidence intervals in our study suggests that composite ACEs

(two and three ACEs) may be associated with slower verbal episodic memory decline. These findings are consistent with other studies finding that individual household-related ACEs were not associated with cognition(7,9,10,16–19).

ACEs were highly prevalent in our cohort with close to 80% experiencing one or more ACEs. We observed that experiencing ACEs was associated with slower decline in executive function, but not verbal episodic memory, indicating possible domain-specificity. A review found that ACEs (emotional and sexual abuse) were associated with better executive function(12), while other studies found that ACEs were associated with worse memory and not executive function(7,8,10). One study examining a Chinese cohort found that experiencing at least two ACEs and three types of ACEs (childhood SES disadvantage, parental trauma, maladaptive parental trauma) were associated with decreased episodic memory(42,43), which was supported by another study that found depressive symptoms during early life to be associated with episodic memory deficit(44). A meta-analysis found that the associations between ACEs and cognition varied by individual ACEs and type of cognitive outcome(19). For example, some studies reported association of ACEs with lower cognitive scores and higher risk of neurocognitive disorder (NCD) diagnosis, while other studies found association of physical or sexual abuse with better cognition, parental death with lower risk of NCD, and collective violence with better global cognition(19). Our analysis did not find significant associations of individual ACEs with cognitive decline in any domain.

Although ACEs could influence a child's development into adulthood through increased toxic stress pathways, these experiences may only partially contribute to cognitive functioning in late life(3,45). Beyond cognition, other studies found that ACEs are associated with higher risk of cardiovascular disease, shortened telomeres, and greater functional limitations in Black

adults(46–48). Environmental, social, and behavioral factors throughout a person's life stand to mediate and even protect against the negative long-term effects of ACEs(9,28). In one study(9), positive childhood environment was found to promote executive functioning. Educational attainment could also be protective for later-life cognitive function through cognitive reserve(10,29). Our cohort was highly educated and reported a high prevalence of childhood support which could explain why ACEs were not associated with lower baseline cognition.

The Cumulative Inequity (CI) theory provides as a meaningful framework for explaining the observed relationships in our study. One possibility for our findings is that it reflects a pattern of resiliency. Among those who experienced ACEs, many had parents who were separated or divorced (39%), had family members with serious illness (35%), or witnessed domestic violence (32%). CI theory suggests that the detrimental, cumulative impact of experiencing multiple ACEs may have been modified by other factors, such as human agency or social support(23). Most participants reported receiving support during childhood most or all of the time with 76% reported having someone they trust or confide in, 86% having someone show them love, 66% having someone help with homework, 79% having someone to motivate them in school, and 77% having someone close to them that they can contact. In a literature review of Black Americans, multiple studies found that lower SES was associated with faster cellular markers of biological aging and earlier development of memory problems(3). The STAR cohort, on average, has higher SES which may mitigate the impact of ACEs on cognition. Another explanation for our findings is resiliency through selection and survival bias of only the healthiest individuals that chose to participate in the study. Black participants in STAR may be exceptional in that they overcame the negative effects of early childhood adversity, survived long enough, and were healthy enough to enroll in a study on cognitive aging. It is also important to consider that STAR

consists of older Black individuals who's early life corresponded with de jure and de facto policies that upheld and endorsed racism in education, access to healthcare, socioeconomic status, and discrimination, which may further affirm that only the most resilient individuals had the opportunity to live into old age(49).

Our study had several strengths. First, we utilized data from a well-characterized cohort of mid- to late-life Black participants. By evaluating ACEs in an all-Black cohort, we were able to identify early life experiences within this understudied group and assess relationships between ACEs and late-life cognition using a within-group analysis, an approach that is not typically used in studies of minoritized older adults(3,50). Second, we examined cognition using a robust psychometric battery that has specifically been validated for use in Black Americans(32–35). By following our cohort over three waves (average 2.3 years of follow-up), we were able to examine changes in cognition over time. Lastly, our ACEs questionnaire was adapted from a robust measure used in other cohort studies with diverse participants(16,37,38).

There were several limitations in our study. First, since ACEs occurred early in life, recall bias could influence responses. Older participants were asked to remember potentially traumatic events during childhood, which could lead to under- or overestimation of the prevalence of ACEs(41,51). Social desirability bias may also prevent participants from disclosing sensitive and revealing information about their early life(52). Experiences of abuse or neglect were not captured by the ACEs questionnaire, but may reflect other dimensions of childhood adversity with different effects on late-life cognition(53). As a middle-age and older cohort with a relatively shorter follow-up time of approximately 3 years, there could be practice effects impacting cognitive testing. Yet, when we adjusted for practice effects using a first visit indicator in the models, we found estimates to be almost identical(54). Given this short follow-

up, it is also possible that participants did not experience substantial decline, and this study cannot examine how ACEs impact long-term cognitive decline yet, but this is a future goal.

Our findings suggest that experiencing ACEs was not associated with worse cognition or cognitive decline in this cohort of older Black Americans. Additionally, the accumulation of ACEs may be associated with slower decline in executive function, a finding that needs to be explored further. CI theory posits that early life adversities do not fully determine cognitive trajectories in older adults and resiliency may subsequently develop through midlife and later life. Future studies are needed to understand how resiliency factors such as childhood support, education, and financial stability can be protective against ACEs as well as cognitive decline, especially among marginalized and high-risk communities. Specifically, mediation and moderation analyses of these protective factors will be needed to determine their effects on ACEs with late-life cognition and explain potential resiliency observed in Black Americans.

BMJ Open

The original protocol for the study, as a supplementary file**.**

Funding: This work was supported by National Institutes of Health grant number RF1 AG050782

Competing Interests: None declared

Author Contributions: YL, KMG, RLP, and RAW were involved with study design, data acquisition, data analysis, interpreting the results and drafting the work. PG, CCM, EHL, LLB, and DMM were involved in critically reviewing the contents. All authors revised, approved final version of the manuscript, and agree to accept responsibility of all aspects of the work.

Patient Consent for Publications: Not required

Word count: 3980 (Limit: 4000)

Ethics Approval: The Study of Healthy Aging in African Americans (STAR) was approved by Kaiser Permanente Northern California Institutional Review Board (IRB Number: 1121043)

Data availability statement: Data are available upon reasonable request. Data may be obtained from a third party and are not publicly available. Deidentified data are available to qualified investigators from the STAR Leadership Committee on approval for the purposes of replicating procedures and results.

Bibliography

1. Felitti VJ. Adverse childhood experiences and adult health. Acad Pediatr. 2009 Jun;9(3):131–2.

2. Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, et al. Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults. Am J Prev Med. 1998 May;14(4):245–58.

3. Graham KL, Paun O, Stillerman A. The Impact of Adverse Childhood Experiences on Cognition in African American Older Adults: An Integrated Literature Review. Res Gerontol Nurs. 2021 Oct;14(5):265–72.

4. 2021 Alzheimer's Disease Facts and Figures [Internet]. Alzheimer's Association; 2021 [cited 2021 Jun 5]. Available from: https://www.alz.org/media/documents/alzheimers-facts-and-figures.pdf

5. Cordell CB, Borson S, Boustani M, Chodosh J, Reuben D, Verghese J, et al. Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness Visit in a primary care setting. Alzheimers Dement. 2013 Mar;9(2):141–50.

6. Sheehan B. Assessment scales in dementia. Ther Adv Neurol Disord. 2012 Nov;5(6):349–58.

7. Kobayashi LC, Farrell MT, Payne CF, Mall S, Montana L, Wagner RG, et al. Adverse childhood experiences and domain-specific cognitive function in a population-based study of older adults in rural South Africa. Psychol Aging. 2020 Sep;35(6):818–30.

8. Majer M, Nater UM, Lin JMS, Capuron L, Reeves WC. Association of childhood trauma with cognitive function in healthy adults: a pilot study. BMC Neurol. 2010 Jul 14;10:61.

9. Ritchie K, Jaussent I, Stewart R, Dupuy AM, Courtet P, Malafosse A, et al. Adverse childhood environment and late-life cognitive functioning. Int J Geriatr Psychiatry. 2011 May;26(5):503–10.

10. Yang L, Wang Z. Early-Life Conditions and Cognitive Function in Middle-and Old-Aged Chinese Adults: A Longitudinal Study. Int J Environ Res Public Health. 2020 May 15;17(10).

11. Lund JI, Toombs E, Radford A, Boles K, Mushquash C. Adverse Childhood Experiences and Executive Function Difficulties in Children: A Systematic Review. Child Abuse Negl. 2020 Aug;106:104485.

12. Lund JI, Boles K, Radford A, Toombs E, Mushquash CJ. A Systematic Review of Childhood Adversity and Executive Functions Outcomes among Adults. Arch Clin Neuropsychol Off J Natl Acad Neuropsychol. 2022 Aug 23;37(6):1118–32.

13. Donley GAR, Lönnroos E, Tuomainen TP, Kauhanen J. Association of childhood stress with late-life dementia and Alzheimer's disease: the KIHD study. Eur J Public Health. 2018 Dec 1;28(6):1069–73.

14. Radford K, Delbaere K, Draper B, Mack HA, Daylight G, Cumming R, et al. Childhood Stress and Adversity is Associated with Late-Life Dementia in Aboriginal Australians. Am J Geriatr Psychiatry Off J Am Assoc Geriatr Psychiatry. 2017 Oct;25(10):1097–106.

15. Tani Y, Fujiwara T, Kondo K. Association Between Adverse Childhood Experiences and Dementia in Older Japanese Adults. JAMA Netw Open. 2020 Feb 5;3(2):e1920740.

16. Gold AL, Meza E, Ackley SF, Mungas DM, Whitmer RA, Mayeda ER, et al. Are adverse childhood experiences associated with late-life cognitive performance across racial/ethnic groups: results from the Kaiser Healthy Aging and Diverse Life Experiences study baseline. BMJ Open. 2021 Feb 5;11(2):e042125.

17. O'Shea BQ, Demakakos P, Cadar D, Kobayashi LC. Adverse Childhood Experiences and Rate of Memory Decline From Mid to Later Life: Evidence From the English Longitudinal Study of Ageing. Am J Epidemiol. 2021 Jul 1;190(7):1294–305.

18. Barnes LL, Wilson RS, Everson-Rose SA, Hayward MD, Evans DA, Mendes de Leon CF. Effects of early-life adversity on cognitive decline in older African Americans and whites. Neurology. 2012 Dec 11;79(24):2321–7.

19. Patel P, Oremus M. The association between adverse childhood experiences and late-life cognition: A systematic review of cross-sectional and case-control studies. The Gerontologist. 2022 Mar 22;gnac041.

20. Dannefer D. Cumulative Advantage/Disadvantage and the Life Course: Cross-Fertilizing Age and Social Science Theory. J Gerontol Ser B. 2003 Nov 1;58(6):S327–37.

21. Yang MS, Hedeker D. A life-span approach to examining older vulnerable population's subjective well-being: the role of adversity and trauma. Aging Ment Health. 2020 Dec 1;24(12):2043–52.

22. Ferraro KF, Schafer MH, Wilkinson LR. Childhood Disadvantage and Health Problems in Middle and Later Life: Early Imprints on Physical Health? Am Sociol Rev. 2016 Feb 1;81(1):107–33.

23. Ferraro KF, Shippee TP. Aging and Cumulative Inequality: How Does Inequality Get Under the Skin? The Gerontologist. 2009 Jun;49(3):333–43.

24. Giano Z, Wheeler DL, Hubach RD. The frequencies and disparities of adverse childhood experiences in the U.S. BMC Public Health [Internet]. 2020 Sep 10 [cited 2021 Jan 29];20. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7488299/

25. Maguire-Jack K, Lanier P, Lombardi B. Investigating racial differences in clusters of adverse childhood experiences. Am J Orthopsychiatry. 2020;90(1):106–14.

26. Merrick MT, Ford DC, Ports KA, Guinn AS. Prevalence of Adverse Childhood Experiences From the 2011-2014 Behavioral Risk Factor Surveillance System in 23 States. JAMA Pediatr. 2018 Nov;172(11):1038–44.

27. Mayeda ER, Glymour MM, Quesenberry CP, Whitmer RA. Inequalities in dementia incidence between six racial and ethnic groups over 14 years. Alzheimers Dement J Alzheimers Assoc. 2016 Mar;12(3):216–24.

28. Peterson RL, Fain MJ, Butler EA, Ehiri JE, Carvajal SC. The role of social and behavioral risk factors in explaining racial disparities in age-related cognitive impairment: a structured narrative review. Aging Neuropsychol Cogn. 2020 Mar 3;27(2):173–96.

29. Weuve J, Barnes LL, Mendes de Leon CF, Rajan KB, Beck T, Aggarwal NT, et al. Cognitive Aging in Black and White Americans: Cognition, Cognitive Decline, and Incidence of Alzheimer Disease Dementia. Epidemiol Camb Mass. 2018 Jan;29(1):151–9.

30. George KM, Gilsanz P, Peterson RL, Barnes LL, DeCarli CS, Mayeda ER, et al. Impact of Cardiovascular Risk Factors in Adolescence, Young Adulthood, and Midlife on Late-Life Cognition: Study of Healthy Aging in African Americans. J Gerontol Ser A. 2021 Sep 1;76(9):1692–8.

31. Whitmer RA, Barnes LL, Richards AE, Miles S, Mayeda ER, Glymour MM, et al. Introducing the Study of Healthy Aging in African Americans (STAR): Looking back to move forward. Alzheimers Dement. 2020;16(S10):e046614.

32. Mungas D, Reed BR, Crane PK, Haan MN, González H. Spanish and English Neuropsychological Assessment Scales (SENAS): further development and psychometric characteristics. Psychol Assess. 2004 Dec;16(4):347–59.

33. Mungas DM, Reed BR, Haan MN, Gonzalez H. Spanish and English Neuropsychological Assessment Scales: Relationship to demographics, language, cognition, and independent function. Neuropsychology. 2005 Jul;19(4):466–75.

34. Mungas D, Reed BR, Marshall SC, González HM. Development of psychometrically matched English and Spanish language neuropsychological tests for older persons. Neuropsychology. 2000 Apr;14(2):209–23.

35. Mungas D, Widaman KF, Reed BR, Farias ST. Measurement Invariance of Neuropsychological Tests in Diverse Older Persons. Neuropsychology. 2011 Mar;25(2):260–9.

36. Howard VJ, McClure LA, Glymour MM, Cunningham SA, Kleindorfer DO, Crowe M, et al. Effect of duration and age at exposure to the Stroke Belt on incident stroke in adulthood. Neurology. 2013 Apr 30;80(18):1655–61.

37. Yen IH, Bennett A, Allen S, Vable A, Long DL, Brooks M, et al. Childhood Residential Mobility and Mental and Physical Health in Later Life: Findings From the Reasons for

Geographic and Racial Differences in Stroke (REGARDS) Study. J Appl Gerontol Off J South Gerontol Soc. 2023 Aug;42(8):1859–66.

38. Howard VJ, Cushman M, Pulley L, Gomez CR, Go RC, Prineas RJ, et al. The reasons for geographic and racial differences in stroke study: objectives and design. Neuroepidemiology. 2005;25(3):135–43.

39. Anda RF, Felitti VJ, Bremner JD, Walker JD, Whitfield C, Perry BD, et al. The enduring effects of abuse and related adverse experiences in childhood. Eur Arch Psychiatry Clin Neurosci. 2006 Apr;256(3):174–86.

40. Campbell TL. Screening for Adverse Childhood Experiences (ACEs) in Primary Care: A Cautionary Note. JAMA. 2020 Jun 16;323(23):2379–80.

41. Lacey RE, Minnis H. Practitioner Review: Twenty years of research with adverse childhood experience scores – Advantages, disadvantages and applications to practice. J Child Psychol Psychiatry. 2020;61(2):116–30.

42. Lin L, Cao B, Chen W, Li J, Zhang Y, Guo VY. Association of Adverse Childhood Experiences and Social Isolation With Later-Life Cognitive Function Among Adults in China. JAMA Netw Open. 2022 Nov 11;5(11):e2241714.

43. Ding R, He P. Associations between childhood adversities and late-life cognitive function: Potential mechanisms. Soc Sci Med. 2021 Dec 1;291:114478.

44. Barch DM, Harms MP, Tillman R, Hawkey E, Luby JL. Early childhood depression, emotion regulation, episodic memory, and hippocampal development. J Abnorm Psychol. 2019 Jan;128(1):81–95.

45. Morsy L, Rothstein R. Toxic stress and children's outcomes. Econ Policy Inst [Internet]. 2019 May 1; Available from: https://www.epi.org/publication/toxic-stress-and-childrens-outcomes-african-american-children-growing-up-poor-are-at-greater-risk-of-disrupted-physiological-functioning-and-depressed-academic-achievement/

46. Kliewer W, Robins JL. Adverse Childhood Experiences Are Associated with Cardiometabolic Risk Indicators and Telomere Length in Low-Income African-American Adolescents. Int J Behav Med. 2022 Feb;29(1):131–5.

47. Islam SJ, Hwan Kim J, Joseph E, Topel M, Baltrus P, Liu C, et al. Association Between Early Trauma and Ideal Cardiovascular Health Among Black Americans: Results From the Morehouse-Emory Cardiovascular (MECA) Center for Health Equity. Circ Cardiovasc Qual Outcomes. 2021 Sep;14(9):e007904.

48. Sauerteig MR, Ferraro KF, Bauldry S. Life Course Stressors and Functional Limitations in Later Life Among White, Black, and Hispanic Adults: Deleterious, Hardening, or Benign? J Gerontol B Psychol Sci Soc Sci. 2022 Jan 12;77(1):249–59.

49. Glymour MM, Manly JJ. Lifecourse social conditions and racial and ethnic patterns of cognitive aging. Neuropsychol Rev. 2008 Sep;18(3):223–54.

50. Whitfield KE, Allaire JC, Belue R, Edwards CL. Are Comparisons the Answer to Understanding Behavioral Aspects of Aging in Racial and Ethnic Groups? J Gerontol B Psychol Sci Soc Sci. 2008 Sep;63(5):P301–8.

51. Briggs EC, Amaya-Jackson L, Putnam KT, Putnam FW. All adverse childhood experiences are not equal: The contribution of synergy to adverse childhood experience scores. Am Psychol. 2021 Mar;76(2):243–52.

52. Althubaiti A. Information bias in health research: definition, pitfalls, and adjustment methods. J Multidiscip Healthc. 2016 May 4;9:211–7.

53. Krinner LM, Warren-Findlow J, Bowling J, Issel LM, Reeve CL. The dimensionality of adverse childhood experiences: A scoping review of ACE dimensions measurement. Child Abuse Negl. 2021 Nov 1;121:105270.

54. Chen R, Calmasini C, Swinnerton K, Wang J, Haneuse S, Ackley SF, et al. Pragmatic approaches to handling practice effects in longitudinal cognitive aging research. Alzheimers Dement J Alzheimers Assoc. 2023 May 18;

Table 1: Baseline characteristics stratified by number of Adverse Childhood Experiences (ACEs), STAR

Characteristic	Overall Sample	0 ACEs	1 ACE	2 ACEs	3 ACEs	4+ ACEs
	N (%) or Mean (SD)					
Number of Participants	707 (100)	151 (21.4)	167 (23.6)	148 (20.0)	122 (17.3)	119 (16.8)
Baseline Age	68.6 (8.7)	69.1 (8.2)	69.0 (8.4)	68.9 (9.2)	68.8 (9.6)	66.7 (8.2)
Sex: Men	220 (31.1)	46 (30.5)	56 (33.5)	51 (34.5)	38 (31.2)	29 (24.4)
College graduate or more	252 (35.6)	51 (33.8)	60 (35.9)	54 (36.5)	44 (36.1)	43 (36.1)
Some college	333 (47.1)	67 (44.4)	83 (49.7)	72 (48.7)	56 (45.9)	55 (46.2)
High school or less	122 (17.3)	33 (21.9)	24 (14.4)	22 (14.9)	22 (18.0)	21 (17.7)
Parent education: More than high school	267 (37.8)	63 (41.7)	59 (35.3)	54 (36.5)	43 (35.3)	48 (40.3)
ACEs	N (column % per variables)					
Parents were separated or divorced	272 (38.5)	0	30 (18.0)	63 (42.6)	73 (59.8)	106 (89.1)
Serious illness of a family member	250 (35.4)	0	44 (26.4)	67 (45.3)	64 (52.5)	75 (63.0)
Witnessed domestic violence	223 (31.5)	0	37 (22.2)	41 (27.7)	60 (49.2)	85 (71.4)
Substance abuse by a family member	172 (24.3)	0	18 (10.8)	35 (23.7)	41 (33.6)	78 (65.6)
Parent remarried	176 (24.9)	0	2 (1.2)	39 (26.4)	58 (47.6)	77 (64.7)
Loss of job by a parent	106 (15.0)	0	23 (13.8)	19 (12.8)	23 (18.9)	41 (34.5)
Death of your father	70 (9.9)	0	8 (4.8)	18 (12.2)	19 (15.6)	25 (21.0)
Parent had to go to jail	53 (7.5)	0	2 (1.2)	4 (2.7)	10 (8.2)	37 (31.1)
Death of your mother	42 (5.9)	0	3 (1.8)	10 (6.8)	18 (14.8)	11 (9.2)
Childhood Social Support	N (column % per variables) or Mean (SD)					
Composite childhood support (range 0 – 20)	15.8 (4.7)	17.1 (4.2)	16.4 (4.3)	15.3 (4.7)	14.5 (4.8)	14.9 (5.1)
Someone to trust and confide in most to all the times	537 (75.7)	125 (82.8)	136 (81.4)	104 (70.3)	87 (71.3)	83 (69.8)

Someone to love most to all the times	611 (86.4)	143 (94.7)	149 (89.2)	125 (84.5)	96 (78.7)	98 (82.4)
Someone to help with homework most to all the times	466 (65.9)	121 (80.1)	118 (70.6)	91 (61.49)	65 (53.3)	71 (59.1)
Someone to motivate and encourage in school most to all the times	559 (79.1)	135 (89.4)	145 (86.8)	107 (72.3)	87 (71.3)	85 (71.4)
Had contact with someone felt close to most or all the times	547 (77.4)	126 (83.4)	138 (82.6)	112 (75.7)	87 (71.3)	84 (70.6)
Childhood Socioeconomic Status	**N (column % per variables)**					
Family financially above average or well-off	483 (68.3)	125 (82.8)	120 (71.9)	101 (68.2)	70 (57.4)	67 (56.3)
Never hungry during childhood	650 (91.9)	146 (96.7)	157 (94.0)	131 (88.5)	110 (90.2)	106 (89.1)
Family had a mortgage or owned a home during childhood	444 (62.8)	118 (78.2)	111 (66.5)	94 (63.5)	65 (53.3)	56 (47.1)

ACEs: Adverse Childhood Experiences
SD: Standard Deviation
Childhood Social Support: Composite childhood support derived from individual childhood social support (range 0 = no support, 20 = most support)
Individual childhood supports are on Likert scale (1 = None of the time, 2 = A little of the time, 3 = Some of the time, 4 = Most of the time, 5 = All of the time)

Table 2: Linear mixed models estimate of the association of composite adverse childhood experiences (ACEs) with domain-specific cognition across 3 waves

	Executive Function			Verbal Episodic Memory		
	Model 1	**Model 2**	**Model 3**	**Model 1**	**Model 2**	**Model 3**
	β (95% CI)	**β (95% CI)**	**β (95% CI)**	**β (95% CI)**	**β (95% CI)**	**β (95% CI)**
Years from baseline	-0.071 (-0.119, -0.023)	-0.084 (-0.137, -0.03)	-0.119 (-0.222, -0.016)	-0.078 (-0.148, -0.009)	-0.108 (-0.185, -0.03)	-0.170 (-0.319, -0.02)
	Baseline					
ACEs						
0	ref	ref	ref	ref	ref	ref
1	-0.130 (-0.316, 0.055)	-0.090 (-0.272, 0.093)	-0.090 (-0.273, 0.092)	-0.137 (-0.321, 0.048)	-0.110 (-0.293, 0.073)	-0.111 (-0.294, 0.072)
2	-0.039 (-0.231, 0.152)	0.008 (-0.181, 0.197)	0.006 (-0.184, 0.196)	-0.041 (-0.231, 0.149)	-0.010 (-0.198, 0.179)	-0.014 (-0.204, 0.176)
3	0.008 (-0.193, 0.209)	0.070 (-0.132, 0.271)	0.067 (-0.136, 0.271)	-0.120 (-0.320, 0.080)	-0.085 (-0.287, 0.116)	-0.092 (-0.295, 0.111)
4+	-0.025 (-0.228, 0.178)	0.052 (-0.155, 0.259)	0.050 (-0.158, 0.258)	0.105 (-0.097, 0.307)	0.156 (-0.051, 0.363)	0.151 (-0.057, 0.359)
	Longitudinal					
ACEs						
0	ref	ref	ref	ref	ref	ref
1	0.053 (-0.010, 0.116)	0.056 (-0.007, 0.119)	0.057 (-0.006, 0.120)	-0.017 (-0.108, 0.075)	-0.020 (-0.112, 0.072)	-0.019 (-0.11, 0.073)
2	0.117 (0.052, 0.182)	0.125 (0.060, 0.191)	0.128 (0.062, 0.194)	0.074 (-0.021, 0.169)	0.077 (-0.019, 0.173)	0.082 (-0.014, 0.178)
3	0.075 (0.007, 0.143)	0.090 (0.021, 0.159)	0.094 (0.025, 0.164)	0.050 (-0.048, 0.148)	0.050 (-0.05, 0.151)	0.058 (-0.044, 0.160)
4+	0.089 (0.020, 0.158)	0.108 (0.036, 0.179)	0.111 (0.039, 0.182)	-0.022 (-0.123, 0.078)	-0.022 (-0.126, 0.082)	-0.017 (-0.121, 0.088)

Model 1: Adjusted for years from baseline, baseline age centered at mean, and sex,
Model 2: Model 1 + childhood SES
Model 3: Model 2 + composite childhood support
ACEs: Adverse Childhood Experiences

CI: Confidence Interval

Figure 1: Prediction plot of linear mixed models estimate of the association of composite adverse childhood experiences (ACEs) with executive function across 3 waves

Adjusted for years from baseline, baseline age centered at mean, sex, childhood SES, and composite childhood support

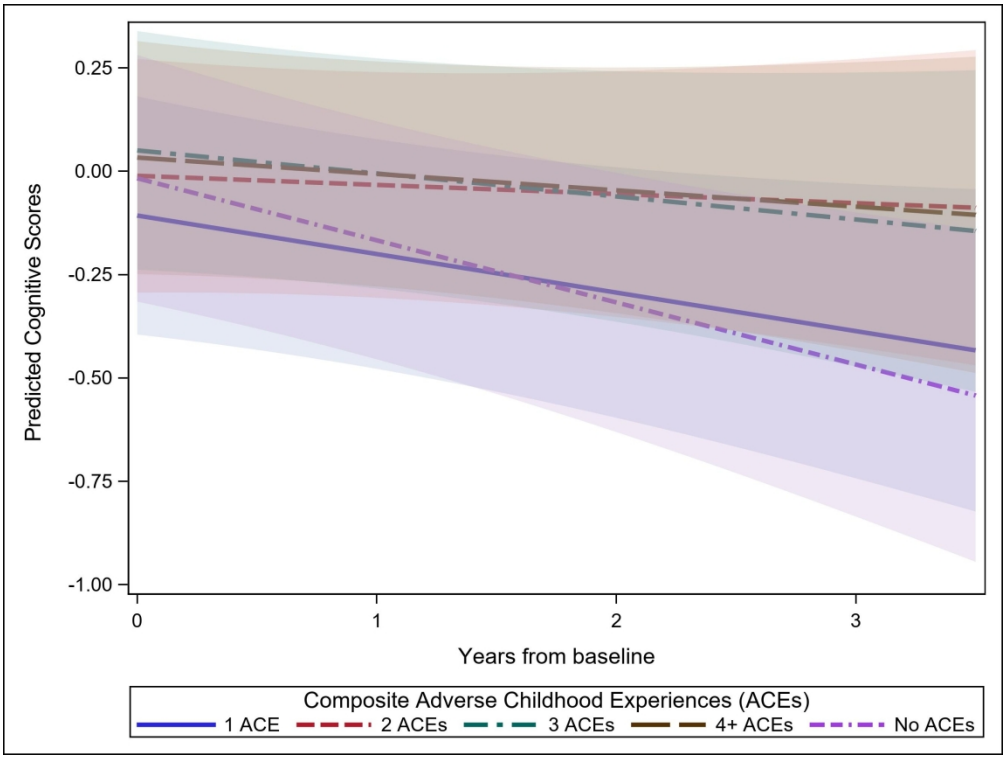
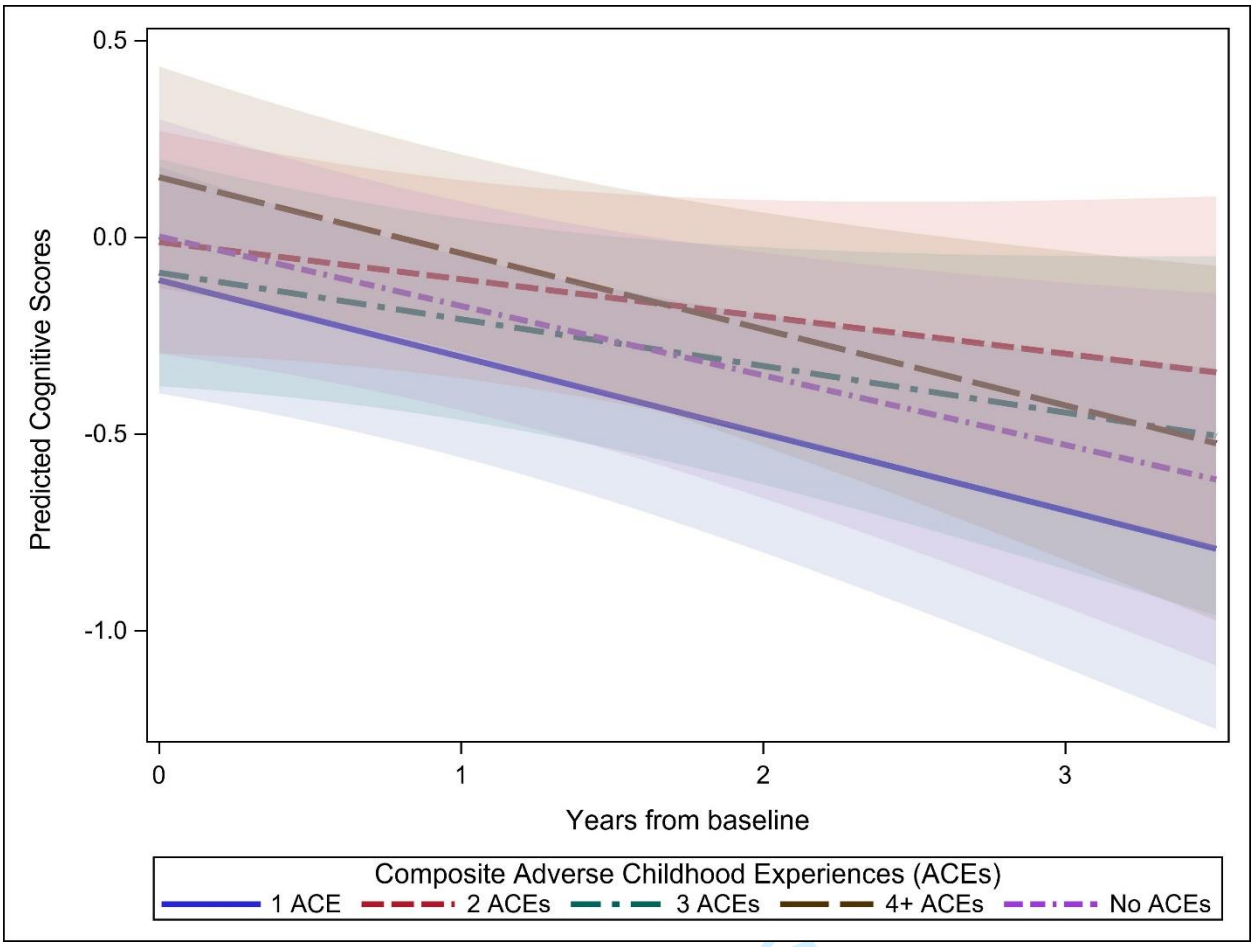


Figure 1: Prediction plot of linear mixed models estimate of the association of composite adverse childhood experiences (ACEs) with executive function across 3 waves

169x127mm (400 x 400 DPI)

Supplemental Figure 1: Prediction plot of linear mixed models estimate for the association of composite adverse childhood experiences (ACEs) with verbal episodic memory across 3 waves



Adjusted for years from baseline, baseline age centered at mean, gender/sex, childhood SES, and composite childhood support

Supplemental Table 1: Linear mixed model with random intercept and slope of the association of individual adverse childhood experiences (ACEs) with domain-specific cognition adjusted for time, gender/sex, and parental education

	Executive Function			Verbal Episodic Memory		
	Cross-Sectional					
	Model 1 β (95% CI)	**Model 2** β (95% CI)	**Model 3** β (95% CI)	**Model 1** β (95% CI)	**Model 2** β (95% CI)	**Model 3** β (95% CI)
Parent Separated	-0.035 (-0.166, 0.095)	-0.040 (-0.169, 0.089)	-0.011 (-0.140, 0.118)	-0.006 (-0.140, 0.128)	-0.014 (-0.142, 0.115)	0.017 (-0.112, 0.147)
Parent Remarried	-0.007 (-0.152, 0.139)	-0.017 (-0.161, 0.127)	0.000 (-0.142, 0.142)	0.062 (-0.087, 0.212)	0.044 (-0.100, 0.188)	0.061 (-0.082, 0.203)
Witnessed Violence	0.065 (-0.071, 0.200)	0.052 (-0.082, 0.186)	0.070 (-0.062, 0.201)	0.131 (-0.009, 0.270)	0.106 (-0.028, 0.240)	0.121 (-0.012, 0.253)
Substance Abuse	0.118 (-0.029, 0.266)	0.126 (-0.02, 0.272)	0.119 (-0.025, 0.262)	0.096 (-0.056, 0.247)	0.111 (-0.035, 0.256)	0.107 (-0.037, 0.251)
Loss Job	0.014 (-0.162, 0.190)	0.007 (-0.167, 0.181)	0.034 (-0.137, 0.206)	0.029 (-0.152, 0.210)	0.016 (-0.158, 0.190)	0.033 (-0.139, 0.205)
Parent Jail	-0.120 (-0.359, 0.118)	-0.116 (-0.352, 0.12)	-0.064 (-0.298, 0.169)	-0.034 (-0.279, 0.211)	-0.022 (-0.257, 0.213)	0.020 (-0.214, 0.254)
Serious Family Illness	-0.014 (-0.146, 0.118)	-0.018 (-0.148, 0.112)	-0.011 (-0.139, 0.117)	0.032 (-0.103, 0.167)	0.025 (-0.105, 0.155)	0.029 (-0.099, 0.157)
Death Mother	-0.007 (-0.275, 0.262)	-0.033 (-0.299, 0.233)	-0.028 (-0.289, 0.233)	0.105 (-0.171, 0.381)	0.057 (-0.208, 0.322)	0.058 (-0.204, 0.320)
Death Father	-0.002 (-0.213, 0.209)	-0.006 (-0.215, 0.203)	0.025 (-0.180, 0.231)	-0.019 (-0.236, 0.199)	-0.024 (-0.233, 0.185)	-0.002 (-0.209, 0.205)
	Longitudinal					
	Model 1 β (95% CI)	**Model 2** β (95% CI)	**Model 3** β (95% CI)	**Model 1** β (95% CI)	**Model 2** β (95% CI)	**Model 3** β (95% CI)
Parent Separated	-0.006 (-0.140, 0.128)	-0.014 (-0.142, 0.115)	0.017 (-0.112, 0.147)	0.018 (-0.025, 0.062)	0.018 (-0.025, 0.062)	0.018 (-0.026, 0.062)
Parent Remarried	0.062 (-0.087, 0.212)	0.044 (-0.100, 0.188)	0.061 (-0.082, 0.203)	0.045 (-0.005, 0.094)	0.045 (-0.004, 0.095)	0.045 (-0.005, 0.094)
Witnessed Violence	0.131 (-0.009, 0.270)	0.106 (-0.028, 0.240)	0.121 (-0.012, 0.253)	0.026 (-0.019, 0.072)	0.027 (-0.019, 0.072)	0.027 (-0.019, 0.072)
Substance Abuse	0.096 (-0.056, 0.247)	0.111 (-0.035, 0.256)	0.107 (-0.037, 0.251)	0.034 (-0.016, 0.083)	0.033 (-0.016, 0.083)	0.033 (-0.016, 0.083)
Loss Job	0.029 (-0.152, 0.210)	0.016 (-0.158, 0.190)	0.033 (-0.139, 0.205)	0.004 (-0.055, 0.063)	0.004 (-0.055, 0.063)	0.003 (-0.055, 0.062)
Parent Jail	-0.034 (-0.279, 0.211)	-0.022 (-0.257, 0.213)	0.020 (-0.214, 0.254)	0.067 (-0.015, 0.149)	0.066 (-0.016, 0.148)	0.067 (-0.015, 0.149)
Serious Family Illness	0.032 (-0.103, 0.167)	0.025 (-0.105, 0.155)	0.029 (-0.099, 0.157)	0.038 (-0.006, 0.082)	0.038 (-0.006, 0.082)	0.038 (-0.006, 0.083)
Death Mother	0.105 (-0.171, 0.381)	0.057 (-0.208, 0.322)	0.058 (-0.204, 0.320)	-0.005 (-0.096, 0.087)	-0.005 (-0.096, 0.086)	-0.004 (-0.095, 0.087)
Death Father	-0.019 (-0.236, 0.199)	-0.024 (-0.233, 0.185)	-0.002 (-0.209, 0.205)	0.005 (-0.067, 0.076)	0.006 (-0.066, 0.077)	0.004 (-0.067, 0.076)

Model 1: Adjusted for baseline age centered at mean,
Model 2: Model 1 + sex,
Model 3: Model 2 + parental education

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	7-8
Methods			
Study design	4	Present key elements of study design early in the paper	8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-11
Bias	9	Describe any efforts to address potential sources of bias	9-11
Study size	10	Explain how the study size was arrived at	n/a
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	12
		(*b*) Describe any methods used to examine subgroups and interactions	12
		(*c*) Explain how missing data were addressed	12
		(*d*) If applicable, explain how loss to follow-up was addressed	n/a
		(*e*) Describe any sensitivity analyses	n/a
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	n/a
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12-13
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) Summarise follow-up time (eg, average and total amount)	8, 15
Outcome data	15*	Report numbers of outcome events or summary measures over time	12-13

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13-15
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	17-18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	20

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.