

Adverse Childhood Experiences and Rate of Memory Decline From Mid to Later-Life: Evidence From the English Longitudinal Study of Ageing

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ABSTRACT

Evidence on the role of early-life adversity in later-life memory decline is conflicting. We investigated the relationships between adverse childhood experiences (ACEs) and memory performance and rate of decline over a ten-year follow-up among mid-to-older adults in England. Data were from biennial interviews with 5,223 participants aged 54+ in the population-representative English Longitudinal Study of Ageing from 2006/07-2016/17. We examined self-reports of nine ACEs prior to age 16, which related to abuse, household dysfunction, and separation from family. Memory was assessed at each time point as immediate and delayed recall of 10 words. Using linear mixed-effects models with person-specific random intercepts and slopes and adjusted for baseline age, age², sex, ethnicity, and childhood socioeconomic factors, we observed that most individual and cumulative ACE exposures had null-to-weakly negative associations with memory function and rate of decline over the 10-year follow-up. Having lived in residential or foster care was associated with lower baseline memory (adjusted $\beta = -0.124$ standard deviation units, 95% confidence interval: -0.273, -0.025), but not memory decline. Our findings suggest potential long-run impacts of residential or foster

care on memory, and highlight the need for accurate and detailed exposure measures when studying ACEs in relation to later-life cognitive outcomes.

Keywords: aging, adverse childhood experiences; longitudinal cohort study; cognitive aging

Abbreviations: ACEs, adverse childhood experiences; ELSA, English Longitudinal Study of Ageing; CI, confidence interval

The number of people living with dementia worldwide is expected to reach 152 million by 2050, and the estimated global cost of dementia is expected to reach \$2 trillion US dollars by 2030 (1). Dementia results in a myriad of symptoms that have a detrimental impact on quality of life, and progressively disables individuals from living with optimal functioning without assistance (2). The causes of dementia remain poorly understood, and epidemiological evidence indicates that dementia etiology could have its origins in early-life (3, 4). Episodic memory loss is a hallmark of dementia and one of its earliest symptoms, indicative of a long dementia prodrome (5–7). Little is known about the role of adverse childhood experiences (ACEs) in shaping the rate of long-term memory decline in later-life (8).

ACEs are characterized as adverse or traumatic events that occur during childhood (9–14) and have been associated with health risks across the life course. A systematic review of 37 observational studies found consistent associations between experiencing a variety of ACEs and adverse health behaviors in adulthood, such as physical inactivity, smoking, drug use, and alcohol use, as well as chronic disease outcomes including heart disease, respiratory disease, and cancer (9, 15–17). We identified only three existing longitudinal studies on ACEs and cognitive aging

outcomes, with conflicting results. The Chicago Health and Aging Project observed protective associations between not having enough food or being thin in childhood and rate of cognitive decline over 16-years in Black and African Americans, but not White Americans (18). The 1958 British Birth Cohort Study observed negative associations between abuse reported in childhood and subsequent domain-specific cognitive functions in adolescence and at age 50 (19). The Longitudinal Aging Study Amsterdam observed that ACEs were associated with rate of change in processing speed, but not memory, over 10 years, but this association was restricted to older adults who were depressed (20). Other studies are cross-sectional, some limited by small sample size, and findings are of conflicting directions and magnitudes (21–25).

The lack of consistency observed in the few longitudinal studies conducted to date is somewhat surprising, given the plausibility of direct neurobiological (26–28) and indirect social and behavioral pathways (10, 12, 29–34) between ACEs and later-life cognitive health outcomes according to life course epidemiological frameworks (35). To help resolve some of these inconsistencies and build the longitudinal evidence base on this topic, we aimed to investigate individual and cumulative relationships between nine self-reported ACEs prior to age 16, and subsequent memory function and decline over a 10-year follow-up among adults aged 54 and over in the population-representative English Longitudinal Study of Ageing. We hypothesized that older adults who reported any previous ACEs would have lower baseline memory and faster rates of aging-related memory decline. We also hypothesized that there would be a dose-response relationship between the cumulative number of reported ACEs and baseline memory

function and decline over the follow-up, consistent with evidence for other chronic disease outcomes (9, 15, 16).

METHODS

English Longitudinal Study of Ageing

The English Longitudinal Study of Ageing (ELSA) is a nationally representative cohort study of men and women ages ≥ 50 living in private households that began with Wave 1 in 2002/03 (N=12,099) (36). The ELSA study design and methodology have been well-documented elsewhere (36). Participants are followed up in biennial data collection waves consisting of in-person interviews and self-completion questionnaires (36). In 2007, after ELSA Wave 3, a Life History interview took place. The Life History Interview consisted of a computer-aided personal interview and a self-completion questionnaire that collected data on early and mid-life events including ACEs (37). The present study used Wave 3 core interview and Life History data (collected in 2006/07) as the baseline, when participants were aged ≥ 54 years, with follow-up for memory outcomes every two years through to ELSA Wave 8 (2016/17).

Study sample

Eligible participants were ELSA core sample members who completed the Wave 3 core and Life History interviews and self-completion questionnaires, who were free of Alzheimer's disease and dementia with non-proxy interviews at Wave 3 with complete covariate data, and, who had completed the ELSA cognitive assessment at any point over the follow-up (2006/07–2016/17), for a total analytical sample of 5,223 (Figure 1).

Outcome: memory

During the in-person ELSA core interviews, participants completed a series of cognitive assessments with trained interviewers (38). Memory was assessed as immediate and delayed recall of a 10-word list (one point per word recalled, for a total of 20 points) at each ELSA time point from Wave 3 (2006/07) to Wave 8 (2016/17) (38). We z-standardized the composite 20-point scores at Wave 3, such that they had a mean of 0 and standard deviation of 1. Scores at each follow-up wave were standardized to the Wave 3 distribution, to allow us to assess change relative to the study baseline distribution (39). Changes in memory function over the follow-up are thus interpreted as changes in standard deviation units of the Wave 3 (baseline) distribution over two-year intervals.

Exposure: adverse childhood experiences

The current literature lacks a standard definition of ACEs (9–12, 14, 40, 41). The landmark Kaiser ACE study focused on ACEs in the domains of child abuse (physical, psychological, and sexual abuse) and household dysfunction (substance use, mental illness, criminal behavior, violence) (9, 13, 41). The Kaiser ACE study has been used as a guide by many later studies, and, indeed, a content analysis of the ACE literature identified child abuse as the most commonly studied ACE in relation to subsequent health outcomes (40). We used the Kaiser ACE Study framework to construct our ACE measures, consistent with previous research using the ELSA data (42, 43). We thus focus on ACEs related to abuse, household dysfunction, and separation from family in childhood. These ACEs are considered as distinct exposures from family socioeconomic conditions in childhood, although family socioeconomic indicators may be important confounders of the ACE-memory aging relationships.

We derived measures of ACEs from the Wave 3 ELSA core interview and Life History interview and self-completion questionnaire. We constructed nine distinct ACE measures that are related to abuse, household dysfunction, and separation from family (all yes/no for the first instance of the ACE happening before age 16): physically abused by parents; experienced a serious physical attack or assault; was a victim of sexual assault (including rape or harassment); parents drank excessively, took drugs, or had mental health problems; parents argued or fought often; ever separated from mother for ≥ 6 months (not due to death of mother); death of mother; spent most of childhood in a single-mother family; been in residential care institution or foster family. We also included a dichotomous indicator for having experienced any ACE versus no ACEs, and a cumulative ACE exposure variable (ranging from 0 to 3+ total ACEs), to assess dose-response relationships with memory outcomes (42).

Covariates

Any confounders of the associations between ACEs and later-life memory would have to arise in early-life. We thus considered sex (male, female), baseline age (continuous), baseline age² (continuous), and ethnicity (white, non-white) as time-invariant potential early-life confounders. We also considered measures of family socioeconomic conditions in childhood as potential confounders of the ACE-memory relationships: self-reported experience of financial hardship during childhood (yes, no), self-reported father's occupation when the respondent was 14 (categorical, consisting of 4 skill level classes derived from the International Standard Classification of Occupations) (44), number of books in the household when the respondent was 10 ranging from 0 to 200+ (ordinal, coded 0-4), and total household amenities during

childhood (continuous, ranging 0-5 for identifying each of the following: fixed bath, cold running water, hot running water, inside toilet, central heating) (43). The mean VIF for these four variables was 1.00, indicating no multicollinearity. The timing of these reported childhood socioeconomic factors is not well-defined with respect to our ACE measures, which were events that occurred for the first time before age 16. Thus, while our primary interest in these variables is in their roles as potential confounders, they could possibly mediate any observed associations or, if caused by a given ACE as well as any unmeasured factors that also affect later-life memory, could potentially be colliders of the ACE-memory relationships.

Statistical analyses

We described characteristics of the sample overall and according to reported ACE exposures. We used multivariable-adjusted linear mixed-effects models with random person-specific intercepts and slopes to assess the relationships between ACEs and baseline memory function (Wave 3; 2006/07) and rate of memory decline (Waves 3 through 8; 2006/07 to 2016/17). To account for potential selection bias due to non-response to the Life History interview at Wave 3, we applied person-level non-response weights to all models (37). We ran two sets of models: Model Set 1 adjusted for baseline age, baseline age², sex, and ethnicity, and Model Set 2 additionally adjusted for the four childhood socioeconomic exposures. For each model set, ACEs were modelled individually, and then in summation to investigate dose-response relationships with the memory outcomes. We tested interactions between all covariates and time, none of which were included as they were not statistically significant. We tested for and observed no interactions between ACEs and sex in predicting memory

function and decline, therefore all analyses were conducted with both sexes combined. Finally, as the rate of memory aging is known to accelerate with increasing age, we tested for quadratic and cubic memory decline slopes, using likelihood ratio tests with maximum likelihood estimation to assess model fit (45). The final, weighted models were estimated using maximum likelihood with an unstructured correlation matrix for the random effects, allowing the correlations between the intercepts and slopes to be estimated.

Sensitivity analyses. To assess potential differential recall of ACEs based on prior memory function, we assessed whether memory score at Wave 1 of ELSA (2002/03) predicted recollection of any ACE at Wave 3 (2006/07) using a logistic regression model adjusted for age, sex, and ethnicity. We assessed the potential for attrition bias by comparing study attrition according to ACE exposure status, and ran joint models with a shared random effect linking a longitudinal sub-model for repeated episodic memory measures and a flexible parametric survival sub-model for study attrition (46). Detailed methods are shown in Web Appendix. All analyses were performed using Stata/SE 16.0 (College Station, TX).

RESULTS

Mean (standard deviation) age at baseline (2006/07) was 68 (9) years, just over half the sample was female (2,906/5,223), and 1% were non-white (74/5,223; Table 1). Overall, 38% (1,985/5,223) of participants reported experiencing at least one ACE (Table 1).

The most commonly reported ACE was having parents who argued or fought very often (18%; 933/5,223), and the least commonly reported ACE was experiencing a serious physical attack or assault (1%; 56/5,223; Web Table 1). The median follow-up time of

the analytical sample was 4.9 years (IQR = 3.5 to 5.0 years). Mean memory function declined over time, relative to the baseline, among those who remained in the study and individuals with no ACEs made up a slightly smaller share of the sample over time (Web Table 1).

Table 2 presents linear estimates and associated 95% confidence intervals (CI) for the associations between ACEs and memory function at baseline (2006/07) and change over time (2006/07 to 2016/17), with non-linear estimates visualized in Figure 2, to aid in their interpretation. Having lived in a residential care institution or foster care was associated with lower mean baseline memory score in Model Set 1 ($\beta = -0.190$; 95% CI: -0.343, -0.036; Table 2). This association was attenuated somewhat when the childhood socioeconomic variables were included in the model ($\beta = -0.124$; 95% CI: -0.273, 0.025; Table 2). Point estimates for other ACEs, including having experienced any ACE, were generally close to the null (Table 2). Non-linear memory aging slopes were of better fit for all ACEs than linear slopes, although the associations were similar in both specifications and the differences in rates of memory decline between individuals with and without ACEs were negligible (Table 2; Figure 2). We observed an imprecise dose-response relationship between cumulative number of ACEs and baseline memory function, and no relationship with rate of memory decline (Table 3; Figure 3).

Recollection of ACEs in Wave 3 (baseline of this analysis) did not vary by prior memory function at Wave 1 (OR = 1.00; 95% CI: 0.93, 1.08, for any vs. no ACEs, per standard deviation increase in memory function). Results from the unweighted joint models for longitudinal memory change and study attrition, shown in Web Table 2, were

consistent with those shown in Table 2, as well as with unweighted linear mixed-effects models shown in Web Table 3, indicating that bias due to differential attrition is negligible in this analysis.

DISCUSSION

Capturing ten years of follow-up data from a nationally representative cohort of English adults aged 54 and over, we generally observed null associations between nine ACEs and later-life memory function and decline. Having been in a residential care institution or fostered prior to the age of 16 was predictive of poorer memory at baseline, but not with change over time. This association was eight times stronger in magnitude than a one-year increase in age on baseline memory function in the fully-adjusted model. Inclusion of childhood socioeconomic circumstances attenuated this association by just over one-third, indicating that these factors have some overlap, but that living in residential or foster care as a child may have a unique role in memory aging that deserves further investigation.

Comparison with other literature

Our findings of mostly null associations between ACEs and memory outcomes are inconsistent with several cross-sectional studies that identified negative associations between various ACEs and cognitive health in mid-to-later life (19, 22–25, 47). Evidence from the few longitudinal studies on this topic is conflicting, and uses inconsistent measures of ACEs and cognitive outcomes. For example, the Longitudinal Aging Study Amsterdam defined ACEs as “any significant life events before the age of 18 years which had a lasting impact on the rest of their life” (20, p.130). The Chicago

Health and Aging Project expanded their definition of ACEs to include nutritional factors, and observed unexpected protective associations between going without food and being thin as a child with the rate of memory decline in older Black and African Americans, but not in older White Americans (18). The Kuopio Ischemic Heart Disease Risk Factor Study of Finnish men found that living in custody and experiencing a crisis or migration due to war were associated with an increased incidence of Alzheimer's disease and dementia over a 22-year follow-up (21). A longitudinal study of 17,412 older adults Japan who grew up during World War 2 found that reporting three or more ACEs related to abuse, family psychopathology, or family loss was associated with increased dementia risk over a three-year follow-up from 2013-2016 (8). While certain ACEs may be period- or population-specific (e.g. experiences of violence due to war), these inconsistencies highlight a need for a consistently applied definition and operationalization of ACE measures in order to support inference across the body of literature.

While the predominant Kaiser ACE framework excludes socioeconomic factors as ACEs, it is important to recognize that broader socioeconomic conditions may structure the risk of experiencing ACEs such as household dysfunction, and family separation. There is a large and consistent body of literature linking childhood socioeconomic factors to cognitive function, decline, and dementia risk in later-life (48–51). Some ACE studies have considered socioeconomic exposures in their ACE framework, such as the Chicago Health and Aging Project, which found that being very poor was associated with more rapid cognitive decline (18). We recommend for future studies to carefully delineate specific ACEs from socioeconomic factors, and adjust for

early-life socioeconomic factors as confounders, where appropriate. The use of ACE measures consistent with the original Kaiser ACE study may provide the greatest consistency with previous literature, in addition to standardized cognitive outcomes. However, we note there are many early-life experiential factors aside from ACEs, such as illness and nutrition, that are of substantive interest with respect to associations with adult health and should be investigated, but potentially outside of the ACEs framework.

Potential mechanisms

We hypothesized that ACEs would have negative relationships with later-life memory outcomes, which we postulated to be through direct neurobiological impacts of early life stressors as well as indirect pathways through social factors known to influence later-life memory, such as educational attainment, employment, and social networks (10, 12, 26–28, 33–35). However, either most of the ACEs assessed in this study truly have no association with memory in later-life, or another causal or artefactual mechanism is responsible for these unexpected null associations. They may also not have an impact on this population, where childhood financial hardship was rare (<5% of the sample) and 70% of the sample had secondary or post-secondary education.

Cognitive reserve is one potential causal explanation that requires further inquiry (52–54). It may be that individuals in our study who reported ACEs had obtained reserve throughout their lifetimes and were able to maintain healthy cognitive aging despite potentially having experienced neurological impacts of early-life adversity. Educational attainment, a key contributor to cognitive reserve, was similar between those who did and did not experience ACEs, which was somewhat unexpected given the “chains of risk” influences that ACEs are thought to have throughout the life course

(10, 12, 29–34). Similar to reserve, resilience is a process through which individuals can positively adapt in response to adversity (55, 56). In our study, unmeasured resilience factors may have played a role in enabling our sample to maintain memory function into later adulthood despite having experienced childhood adversity.

Limitations and strengths

Our results could alternatively be explained by methodological artefact due to study limitations. A key limitation is information bias. The ELSA assessed ACEs as binary measures of whether participants had experienced a given event or not during their childhood. We were unable to quantify variation in other aspects of the ACEs, such as the specific age(s) at which the ACE occurred, the frequency, duration, severity of the ACE, or its psychological impact at the time or afterwards. These factors have been shown to contribute to variation in the impact of early-life adversity on brain development (57, 58). We also did not have data on all possible ACEs that could be experienced, such as paternal death. While the brevity of the ACE measures in ELSA enabled their inclusion in a large, population-based study alongside rich covariate and outcome data, more detailed, precise measures of childhood adversity may be needed to obtain accurate estimates of the relationships between childhood adversity and memory decline.

ELSA sample members who had proxy interviews with a family member were excluded from this study. However, it is unlikely that the exclusion of proxies introduced bias, as only 82/5,223 sample members transitioned into having a proxy interview with proxy-reported cognitive impairment (defined as scoring >3.38 on the Informant Questionnaire on Cognitive Decline in the Elderly; IQCODE). Despite the use of a life

history calendar to aid with recall, our results may have been biased by recall error in a direction that is difficult to predict. We may also have underestimated the relationships between ACEs and memory outcomes if individuals who experienced the most severe ACEs differentially died prior to the time of this study or not participated, if they had worse memory, on average, than those who did not experience ACEs. There is a chance that type I error may explain the observed association between having been in a residential care institution and baseline memory function, given that we estimated 18 associations for the ACEs in Table 2. This association requires investigation in other studies for confirmation.

Strengths of this study include the large, population-representative nature of the ELSA, with 10 years of follow-up data using reliable measures of episodic memory (59). These features allowed us to conduct one of the first longitudinal studies on the relationships between individual and cumulative ACEs and the rate of memory aging over an entire decade in an older study sample. By applying non-response weights to our analysis, we were able to account for differential response to the Life History interview that captured our exposure measures. Our use of linear mixed-effects models allowed us to retain all available outcome data on individuals in estimating the memory intercepts and slopes, even if they dropped out of the study. We do not expect our findings to be affected by learning effects in cognitive testing, as the Wave 3 interview was the third cognitive assessment for the study sample.

Conclusion

In this longitudinal study of adults aged 54 years and older in England, we observed that individual and cumulative ACEs had null-to-weakly negative associations

with memory function and decline over a 10-year period during aging. We found that having lived in residential or foster care as a child was associated with lower baseline memory with a magnitude equivalent to approximately eight years of increased age. Overall, this study illustrates the potentially complex nature of early-life predictors of memory aging and suggests that the neurobiological and social impacts of most standard ACEs may not strongly apply to memory aging in the older English population. Future studies should obtain comprehensive and consistent measures of childhood adversity and triangulate relationships observed across different populations and study designs.

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ORIGINAL UNEDITED MANUSCRIPT

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Table 1. Sample characteristics by ACE exposure status, English Longitudinal Study of Ageing, 2006/07 – 2016/17

Characteristic	Overall (5,223)		No ACEs (3,238)		Any ACEs (1,985)	
	N	%	N	%	N	%
Female	2,906	55.6	1,772	54.7	1,134	57.1
Baseline age ^a	67.7 (9.0)		67.9 (9.1)		67.4 (8.7)	
Non-White	74	1.4	39	1.2	35	1.8
Married or living as married	3,621	69.3	2,262	69.9	1,359	68.5
Experienced financial hardship during childhood	138	2.6	50	1.5	88	4.4
Number of childhood household amenities ^a	2.7 (1.5)		2.8 (1.5)		2.7 (1.6)	
Highest educational qualification						
No qualification	1,556	29.8	929	28.7	627	31.6
Secondary education (e.g. graduate certificate of secondary education or equivalent)	2,506	48.0	1,570	48.5	936	47.2
Post-secondary education (e.g. university or higher)	1,161	22.2	739	22.8	422	21.3
Father's occupation at age 14						
Skill level 1 (casual jobs/armed forces)	196	3.8	105	3.2	91	4.6
Skill level 2 (administrative/clerical/skilled trade/plant operator)	2,453	47.0	1,551	47.9	902	45.4
Skill level 3 (professional/technical)	638	12.2	414	12.8	224	11.3
Skill level 4 (manager/owner)	639	12.2	450	13.9	189	9.5
Other job	1,142	21.9	660	20.4	482	24.3
Retired or unemployed	155	3.0	58	1.8	97	4.9
Number of books in household at age 10						
0-10 books	1,394	26.7	767	23.7	627	31.6
11-25 books	1,255	24.0	807	24.9	448	22.6
26-100 books	1,494	28.6	997	30.8	497	25.0
101-200 books	450	8.6	294	9.1	156	7.9
More than 200 books	381	7.3	254	7.8	127	6.4
Don't know/not applicable	249	4.8	119	3.7	130	6.5
Health characteristics						
Cancer	471	9.0	288	8.9	183	9.3
Diabetes	511	9.8	318	9.8	193	9.7
Lung disease	376	7.2	192	5.9	184	9.3
Heart disease	1,694	32.4	1,030	31.8	664	33.5
Depression	256	4.9	125	3.9	131	6.6
Number of mobility impairments	2 (2.5) ^a		1.8 (2.4) ^a		2.1 (2.6) ^a	

ACE = adverse childhood experience

^a Values are expressed as mean (standard deviation).

^b The possible value range for number of childhood household amenities was 0-5.

Table 2. Results from linear mixed-effects models for the associations between ACEs and memory function and decline, English Longitudinal Study of Ageing, 2006/07-2016/17 (N =5,223)

ACEs	Model Set 1 ^a (without childhood SES)		Model Set 2 ^b (with childhood SES)	
	β	95% CI	β	95% CI
Physically abused by parents				
Intercept (baseline memory without ACE) ^c	2.136	0.884, 3.388	0.918	-0.312, 2.149
Mean difference for those who were physically abused by parents	-0.064	-0.203, 0.075	-0.076	-0.214, 0.061
Time ^d	-0.069	-0.075, -0.063	-0.070	-0.076, -0.063
Time x physically abused by parents ^d	-0.011	-0.052, 0.029	-0.011	-0.051, 0.029
Serious physical attack/assault				
Intercept (baseline memory without ACE) ^c	2.165	0.911, 3.419	0.947	-0.284, 2.178
Mean difference for those who experienced physical attack/assault	-0.204	-0.443, 0.035	-0.217	-0.454, 0.020
Time ^d	-0.070	-0.076, -0.064	-0.071	-0.077, -0.064
Time x serious physical attack/assault ^d	0.056	-0.007, 0.118	0.056	-0.006, 0.119
Sexual assault				
Intercept (baseline memory without ACE) ^c	2.094	0.842, 3.346	0.873	-0.356, 2.102
Mean difference for those sexually assaulted	0.068	-0.066, 0.202	0.064	-0.068, 0.197
Time ^d	-0.070	-0.076, -0.064	-0.070	-0.077, -0.064
Time x sexual assault ^d	0.020	-0.015, 0.055	0.019	-0.016, 0.054
Parental drinking/drug use/mental health				
Intercept (baseline memory without ACE) ^c	2.148	0.896, 3.401	0.908	-0.324, 2.140
Mean difference for those who experienced parental drinking/drug use/mental health problems	-0.041	-0.143, 0.062	0.007	-0.093, 0.108
Time ^d	-0.069	-0.075, -0.063	-0.070	-0.076, -0.063
Time x parental drinking/drug use/mental health ^d	-0.006	-0.034, 0.022	-0.006	-0.034, 0.022
Parents argue or fight very often				
Intercept (baseline memory without ACE) ^c	2.109	0.855, 3.362	0.857	-0.374, 2.09
Mean difference for those whose parents argued or fought very often	-0.003	-0.062, 0.056	0.028	-0.030, 0.085
Time ^d	-0.072	-0.079, -0.065	-0.072	-0.079, -0.066
Time x parents argue or fight very often ^d	0.012	-0.003, 0.028	0.012	-0.003, 0.028
Separated from mother for 6 months or more				
Intercept (baseline memory without ACE) ^c	2.066	0.808, 3.324	0.879	-0.357, 2.115
Mean difference for those separated from mother for 6 months or more	-0.010	-0.080, 0.061	0.011	-0.057, 0.079
Time ^d	-0.068	-0.074, -0.061	-0.068	-0.075, -0.062
Time x separated from mother for 6 months or more ^d	-0.013	-0.030, 0.005	-0.013	-0.030, 0.005
Maternal death				
Intercept (baseline memory without ACE) ^c	2.126	0.874, 3.378	0.906	-0.325, 2.136
Mean difference for those whose mother died before age 16	-0.137	-0.288, 0.015	-0.068	-0.218, 0.083
Time ^d	-0.069	-0.075, -0.063	-0.070	-0.076, -0.063
Time x maternal death ^d	-0.015	-0.058, 0.028	-0.015	-0.057, 0.028

Most of childhood in a single-mother family

Intercept (baseline memory without ACE) ^c	2.113	0.861, 3.365	0.911	-0.319, 2.142
Mean difference for those who spent most of childhood in a single mother family	-0.048	-0.145, 0.048	0.035	-0.059, 0.129
Time ^d	-0.069	-0.076, -0.063	-0.070	-0.076, -0.064
Time x most of childhood in single-mother family ^d	-0.000	-0.029, 0.028	0.000	-0.028, 0.029

Been in residential care institution/fostered

Intercept (baseline memory without ACE) ^c	2.122	0.870, 3.374	0.903	-0.328, 2.134
Mean difference for those who have been in residential care institution or were fostered	-0.190	-0.343, -0.036	-0.124	-0.273, 0.025
Time ^d	-0.069	-0.076, -0.063	-0.070	-0.076, -0.064
Time x been in residential care institution/fostered ^d	0.003	-0.036, 0.042	0.003	-0.036, 0.042

Any adverse childhood experience

Intercept (baseline memory without any ACE) ^c	2.123	0.872, 3.374	0.902	-0.329, 2.133
Mean difference for those with any ACE	-0.021	-0.068, 0.027	0.021	-0.025, 0.068
Time ^d	-0.069	-0.077, -0.061	-0.070	-0.077, -0.062
Time x any adverse childhood experience ^d	-0.001	-0.013, 0.012	-0.001	-0.013, 0.012

ACE = adverse childhood experience; CI = confidence interval; SES = socioeconomic status

^a Models adjust for baseline age, baseline age², sex, ethnicity, time, and are weighted for non-response to the Life History interview.

^b Models adjust for baseline age, baseline age², sex, ethnicity, time, childhood financial hardship, number of childhood household amenities, number of books in home at age 10, and father's occupation at age 14, and are weighted for non-response to the Life History interview.

^c Intercepts represent mean baseline memory function for individuals in the reference categories of covariates, without the ACE.

^d Coefficients are expressed as changes in standard deviation units of the baseline distribution of memory scores over 2-year intervals.

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Table 3. The association between total number of ACEs and memory function and decline, English Longitudinal Study of Ageing, 2006/07 to 2016/17

Cumulative ACEs	β^a	95% CI
Intercept (baseline memory without any ACEs) ^b	0.906	-0.325, 2.137
Total number of ACEs		
0	0	Referent
1	0.027	-0.025, 0.079
2	0.024	-0.063, 0.110
3+	-0.031	-0.157, 0.096
<i>P-value for linear trend</i>	0.716	
Total number of ACEs x Time		
0	0	Referent
1	-0.000	-0.014, 0.014
2	-0.005	-0.028, 0.019
3+	0.009	-0.025, 0.043
<i>P-value for slope</i>	0.935	

ACE = adverse childhood experience; CI = confidence interval

^a Models adjust for baseline age, baseline age², sex, ethnicity, time, childhood financial hardship, number of childhood household amenities, number of books in home at age 10, and father's occupation at age 14, and are weighted for non-response to the Life History interview. Coefficients are expressed as changes in standard deviation units of the baseline distribution of memory scores over 2-year intervals.

^b The intercept represents mean baseline memory function for individuals in the reference categories of covariates, without any ACEs.

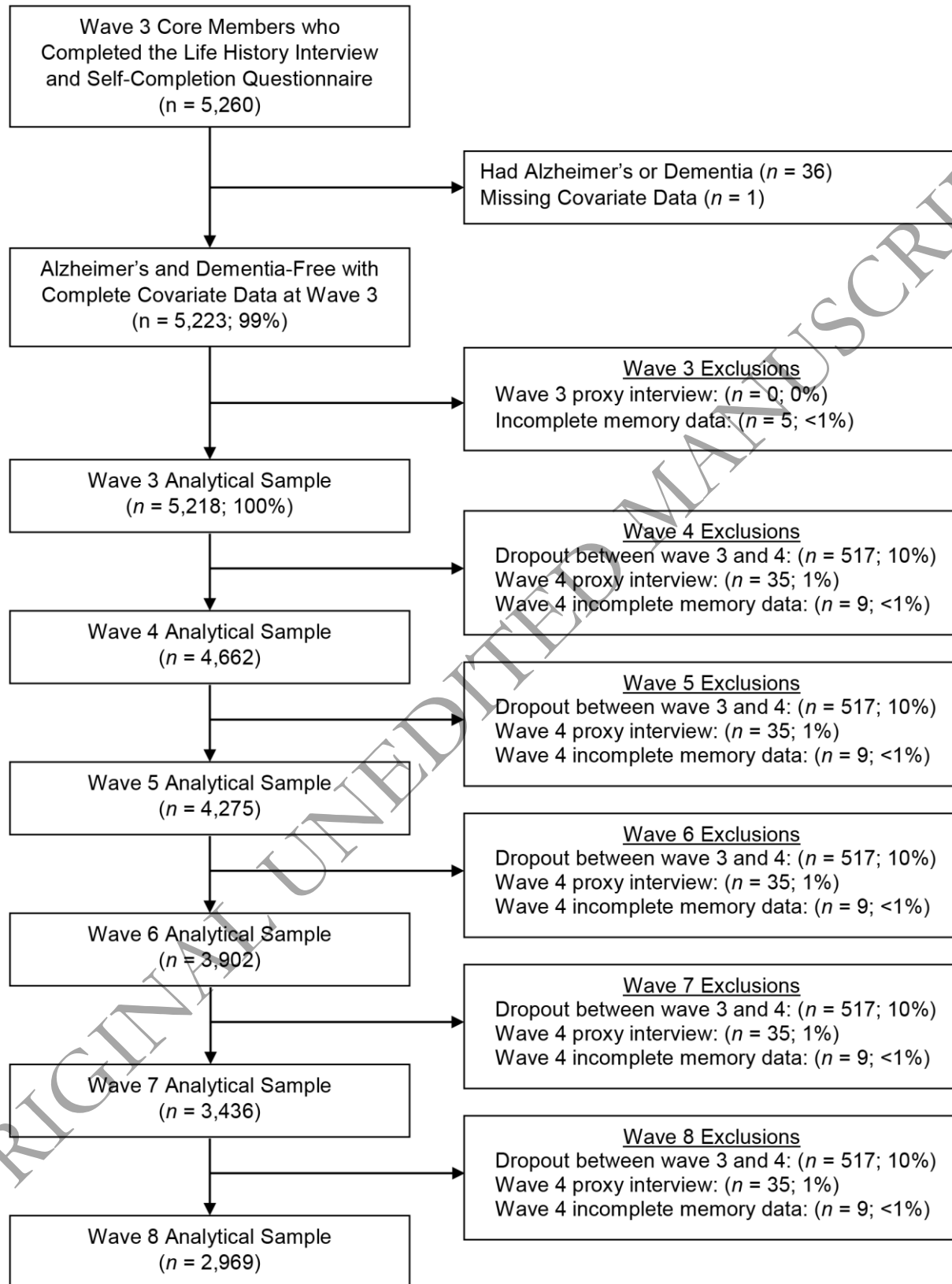
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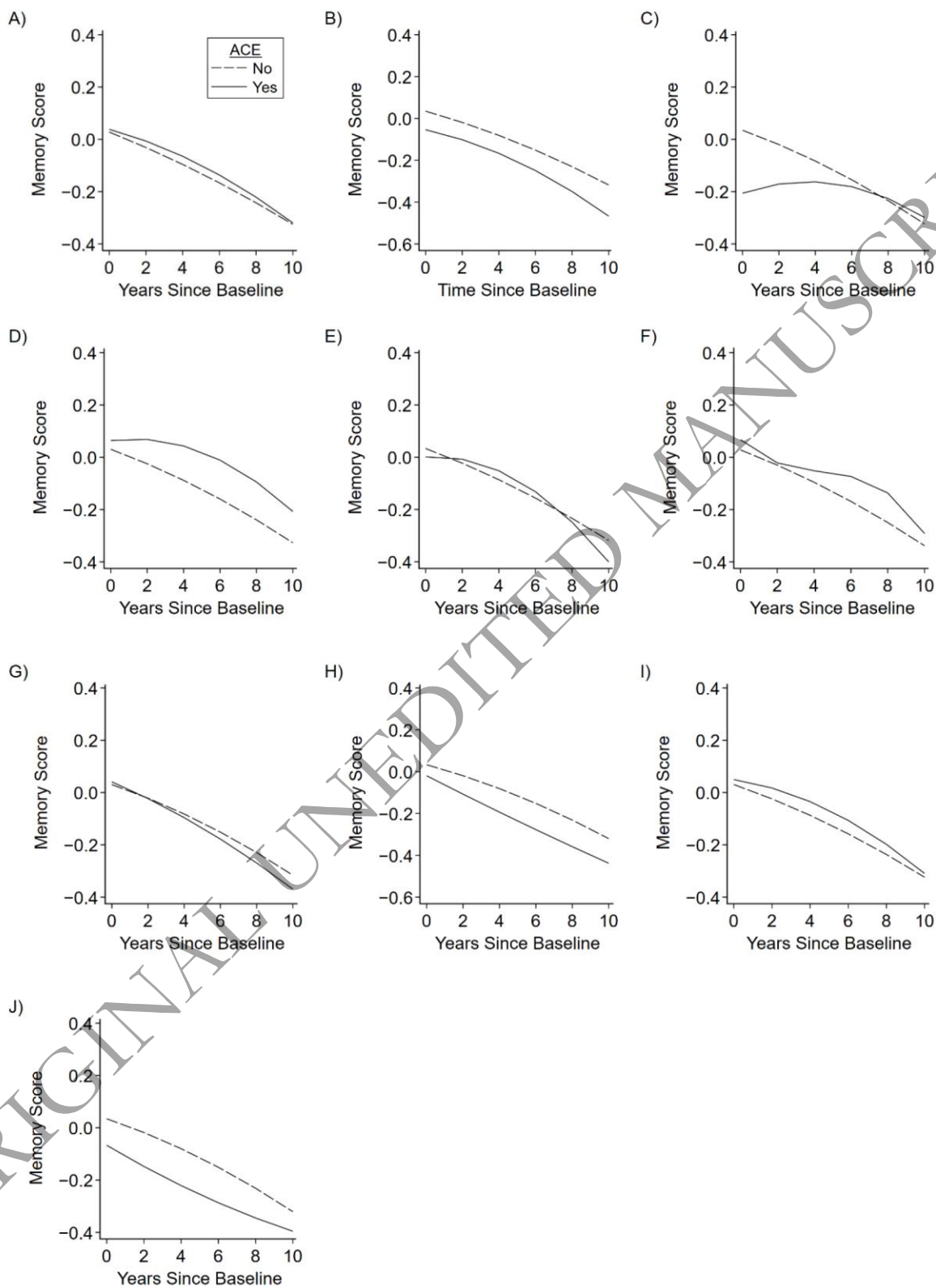
Figure 1. Study flow diagram of the participants' selection into the study, English Longitudinal Study of Ageing, 2006/07 to 2016/17. Figure title: Study Flow Diagram

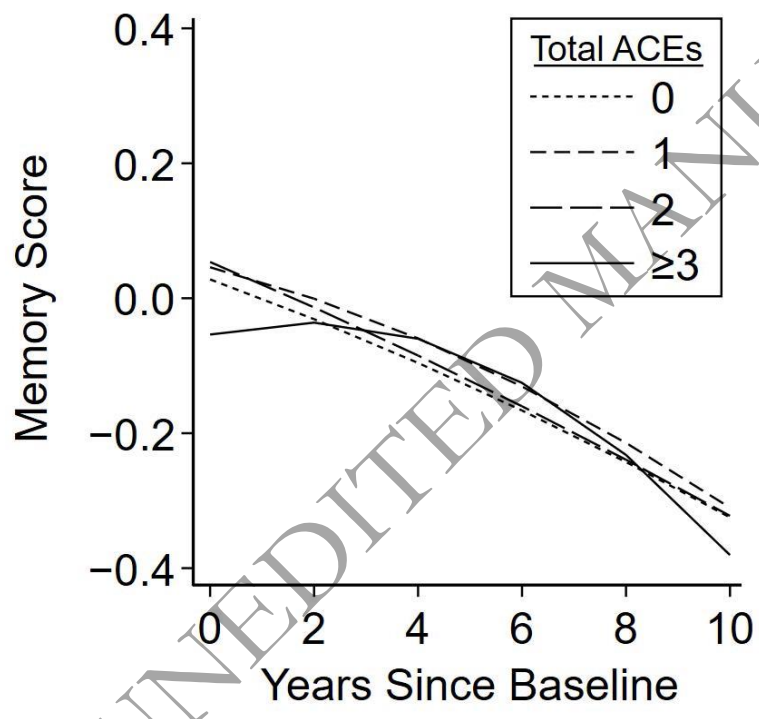
Figure 2. Predicted memory scores over the follow-up by ACE, English Longitudinal Study of Ageing, 2006/07 to 2016/17. Predicted memory scores are expressed at each time point in standard deviation units of the baseline distribution and are adjusted for baseline age, baseline age², sex, ethnicity, time, childhood financial hardship, number of childhood household amenities, number of books in home at age 10, and father's occupation at age 14, and weighted for non-response to the Life History interview. A) Any ACE; B) Physical abuse by parents; C) Physical attack or assault; D) Sexual assault; E) Parental drinking/drug use/mental health; F) Parents argue/fight often; G) Separated from mother; H) Maternal death; I) Single-mother family; J) Residential care institution/fostered. ACE = adverse childhood experience. Figure title: Individual ACEs

Figure 3. Predicted memory scores over the follow-up by total number of ACEs, English Longitudinal Study of Ageing 2006-2017. Predicted memory scores at each time point are expressed in standard deviation units of the baseline distribution and are adjusted for baseline age, baseline age², sex, ethnicity, time, childhood financial hardship, number of childhood household amenities, number of books in home at age 10, and father's occupation at age 14, and weighted for non-response to the Life History interview. ACE = adverse childhood experience. Figure title: Total ACEs

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