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Title: Adverse Childhood Experiences and the Risk of Premature Mortality

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Abstract: Background. Strong, graded relationships between exposure to childhood traumatic stressors and numerous negative health behaviours and outcomes, healthcare utilization and overall health status inspired the question whether these adverse childhood experiences (ACEs) are associated with premature death during adulthood.

Methods. Baseline survey data on health behaviours, health status and exposure to ACEs were collected from 17,337 adults aged >18 years during 1995-1997. ACEs included abuse (emotional, physical, sexual), witnessing domestic violence, parental separation or divorce, or growing up in a household where members with mentally ill, substance abusers, or sent to prison. We used the ACE Score (an integer count of the 8 categories of ACEs) as a measure of cumulative exposure to traumatic stress during childhood. We identified deaths during follow-up (between baseline appointment date and 31 December 2006) using mortality records obtained from a search of the National Death Index. We computed expected years of life lost (YLL) and years of potential life lost (YPLL) using standard methods. We estimated the relative risk of death from all causes at age ≤ 65 years and at age ≤ 75 years across the number of categories of ACEs using multivariable-adjusted Cox proportional hazards regression. Analysis conducted January-February 2009.

Results. Overall, 1539 persons died during follow-up; the crude death rate was 91.0 per 1000 population; the age-adjusted rate was 54.7 per 1000 population. Persons with ≥ 6 ACEs died nearly 20 years earlier on average than those without ACEs (60.6 years, 95%CI=56.2-65.1 v. 79.1 years, 95%CI=78.4-79.9). Average YLL per death was nearly three times greater among persons with ≥ 6 ACEs (25.2 years) than those without ACEs (9.2 years). Roughly a third (n=526) of those who died during follow-up were aged ≤ 75 years at the time of death accounting for 4792 years of potential life lost (YPLL75). After multivariable-adjustment, adults with ≥ 6 ACEs were 1.7 (95%CI=1.06-2.83) times more likely to die at ages ≤ 75 years and 2.4 (95%CI=1.30-4.39) times more likely to die at ages ≤ 65 years.

Conclusions. ACEs are associated with an increased risk of premature death although we did not observe a graded increase in the risk of premature death across the number of categories of ACEs. The increase in risk was only partly explained by documented ACE-related health and social problems suggesting other possible mechanisms by which ACEs may contribute to premature death.

Adverse Childhood Experiences and the Risk of Premature Mortality

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Abstract

Background. Strong, graded relationships between exposure to childhood traumatic stressors and numerous negative health behaviours and outcomes, healthcare utilization and overall health status inspired the question whether these adverse childhood experiences (ACEs) are associated with premature death during adulthood.

Purpose: To determine whether ACEs are associated with an increased risk of premature death during adulthood.

Methods. Baseline survey data on health behaviours, health status and exposure to ACEs were collected from 17,337 adults aged >18 years during 1995–1997. ACEs included abuse (emotional, physical, sexual), witnessing domestic violence, parental separation or divorce, or growing up in a household where members with mentally ill, substance abusers, or sent to prison. The ACE Score (an integer count of the 8 categories of ACEs) was used as a measure of cumulative exposure to traumatic stress during childhood. Deaths were identified during follow-up assessments (between baseline appointment date and 31 December 2006) using mortality records obtained from a search of the National Death Index. Expected years of life lost (YLL) and years of potential life lost (YPLL) were computed using standard methods. The relative risk of death from all causes at age ≤ 65 years and at age ≤ 75 years was estimated across the number of categories of ACEs using multivariable-adjusted Cox proportional hazards regression. Analysis conducted January–February 2009.

Results. Overall, 1539 people died during follow-up; the crude death rate was 91.0 per 1000 population; the age-adjusted rate was 54.7 per 1000 population. People with ≥ 6 ACEs died nearly 20 years earlier on average than those without ACEs (60.6 years, 95% CI=56.2–65.1 vs 79.1 years, 95% CI=78.4–79.9). Average YLL per death was nearly three times greater among people with ≥ 6 ACEs (25.2 years) than those without ACEs (9.2 years). Roughly a third (n=526) of those who died during follow-up were aged ≤ 75 years at the time of death

accounting for 4792 years of potential life lost (YPLL₇₅). After multivariable adjustment, adults with ≥ 6 ACEs were 1.7 (95% CI=1.06–2.83) times more likely to die when aged ≤ 75 years and 2.4 (95% CI=1.30–4.39) times more likely to die when aged ≤ 65 years.

Conclusions. ACEs are associated with an increased risk of premature death although a graded increase in the risk of premature death was not observed across the number of categories of ACEs. The increase in risk was only partly explained by documented ACE-related health and social problems suggesting other possible mechanisms by which ACEs may contribute to premature death.

Introduction

The Adverse Childhood Experiences (ACE) Study, a collaborative effort between Kaiser Permanente (San Diego, CA), and the CDC (Atlanta, GA), was designed to examine the long-term relationship between adverse childhood experiences (ACEs) and a variety of health behaviors and health outcomes in adulthood.¹ The ACE Study proposes that stressful or traumatic childhood experiences have negative neurodevelopmental impacts that lead through life pathways and increase the risk of a variety of behavioral, health and social problems. The ACE pyramid is used to depict this concept (see www.cdc.gov/nccdphp/ace/pyramid). The seminal paper of the ACE Study¹ described associations between the number of categories of ACEs and prevalent cases of disease that underlie many of the leading causes of death in the U.S. Relationships have since been reported between ACEs and numerous health risk behaviours, health outcomes, healthcare utilization and health status.² A case-control study³ conducted in Washington State described an increased risk of death prior to age 18 years among substantiated cases of child abuse relative to a comparison population, while a study of substantiated cases of abuse and matched neighborhood controls reported no association between abuse and mortality in young adulthood.⁴ On the basis of this evidence, a prospective cohort study of 16,908 adults was initiated to assess the relationship between the cumulative effects of ACEs and premature mortality.

Methods

The ACE Study is based at Kaiser Permanente's San Diego Health Appraisal Clinic, a primary care clinic where more than 50,000 adult members of the Kaiser Permanente HMO receive an annual, standardized, biopsychosocial medical examination.⁵ Each member who visits the Health Appraisal Clinic completes a standardized medical questionnaire.¹ The medical history is completed by a healthcare provider who also performs a general physical

exam and reviews laboratory test results with the patient.¹ Appointments for most members are obtained by self-referral with 20% referred by their healthcare provider.¹ A review of continuously enrolled (between 1992 and 1995) Kaiser Permanente members aged ≥ 25 years in San Diego revealed that 81% of those members had been evaluated at the Health Appraisal Clinic.¹

All health plan members who completed standardized medical exams at the clinic between August and November of 1995, between January and March of 1996 (Wave I: $n=13,494$), and between April and October of 1997 (Wave II: $n=13,330$) were eligible to participate in the baseline ACE Study.⁶ Within 2 weeks after a member's visit to the clinic, a study questionnaire was mailed asking questions about health behaviors and ACEs. The overall response rate to the mailed questionnaire was 68% (18,175/26,824).⁶ ACE questionnaire nonrespondents were generally younger and more often men, nonwhite, and of lower education level than those who responded.⁷

Definition of ACEs

ACEs include childhood emotional, physical, or sexual abuse and household dysfunction during childhood. The categories are verbal abuse, physical abuse, contact sexual abuse, a battered mother, household substance abuse, household mental illness, incarcerated household members, parental separation or divorce (Table 1). The experiences chosen for study were based on prior research that has shown to them to have significant negative health or social implications, and for which substantial efforts are being made in the public and private sector to reduce their frequency of occurrence. A complete description of ACEs is provided elsewhere.^{5,8}

Exposure to ACEs is captured in the ACE Score. The ACE Score is a simple summation (integer count) of exposure to each of eight categories of adverse experiences during the

respondents' first 18 years of life. Exposure to any ACE category counts as one "point" on the score. The statistical characteristics and validity of the ACE Score and test-retest reliability of the questions have been published elsewhere.^{9,10} Analyses were completed using both a continuous ACE Score variable and a six-level categorical ACE Score variable (0, 1, 2, 3, 4 or 5, and 6 or more ACEs) with 0 ACEs serving as the ref category.

Follow-Up Data

To ascertain the vital status of cohort members through 31 December 2006, ACE Study baseline data were merged with mortality data from the National Death Index (NDI), shown to capture 93%–98% of all deaths in the U.S.^{11–13} Linkage of ACE Study participants with NDI records followed standardized procedures used by the National Center for Health Statistics.^{14–16} Briefly, 6795 study participants were matched to the NDI by Social Security number, first and last names, middle initial, gender, birth date, and state of residence. Eligible participants with a "true" NDI record match were assumed to be dead ($n=1539$), and those with no NDI record match or an NDI record match considered to be a "false" match were assumed to be alive.^{14–16} A description of the merging process is provided in Appendix A, available online at www.ajpm-online.net.

Follow-up time was calculated as the difference between the ACE Study baseline interview date and the last known date alive for study participants listed as decedents in the NDI and as the difference between the interview date and 31 December 2006 for those assumed to be alive ($n=15,369$). A total of 429 observations were excluded from follow-up because the baseline appointment date occurred outside of a period of enrollment in the Kaiser health plan or within 120 days of a period of enrollment; therefore these people were not enrolled in the Kaiser health plan at baseline and thus were not eligible for study follow-up. The 120-day

rule was incorporated to account for possible coverage by the health insurance plan under coverage continuation provided by the Consolidated Omnibus Budget Reconciliation Act of 1985 (COBRA). There were no deaths identified among these observations. People excluded from follow-up were slightly younger and more likely to be nonwhite, unmarried, or report financial problems than those who constituted the follow-up cohort. Small differences were observed by gender or education level. No meaningful difference was observed in the ACE Score distribution between the two groups.

Measures of Premature Mortality

Crude and age-adjusted death rates are dominated by the underlying disease processes of older adults and thus do not reflect the burden of deaths occurring at younger ages, which are often preventable and have the potential to affect the available work force. Thus, measures of premature mortality attempt to give more importance to the death of younger adults than to older adults. Relationships between the number of categories of ACEs and several measures of premature mortality were studied.

Standard expected Years of Life Lost (YLL). The YLL measure, developed by the Global Burden of Disease (GBD) Study,¹⁷ is based on comparing the average age of death to an external standard life expectancy curve. For groups with life expectancies that exceed these standards, a health gap for each death remains since the model life table is used to define the loss function and thus captures lost years of life for a death at each age.¹⁸ Thus, the YLL measures lost life years for every death. This is in contrast to approaches based on normative population survival which do not measure deaths after a designated cut-off age. In keeping with the methods used by the GBD Study, YLL, average YLL and age-standardized YLL (ASYLL) were computed using established methods.¹⁹ The Coale and Demeny²⁰ model life

tables were used with life expectancy at birth assumed to be 82.5 years for women (West, Level 26) and 80 years for men (West, Level 25).

Years of Potential Life Lost (YPLL). YPLL measures the number of years lost for an individual who fails to live an expected number of years based on a specified life expectancy.²¹ YPLL is calculated by subtracting age-at-death from a specified standard death age (e.g., 65, 75 years) for each decedent and then summing these differences across individuals for a total YPLL. For example, if the selected age limit is 70 years and a person dies at age 30 years, then that person is considered to have lost 40 years of potential life.

Relative risk of death from all causes at age <75 years or younger. Multivariable-adjusted Cox proportional hazards regression was used to estimate, by means of the hazard rate ratio, the risk ratio for death from all causes at age <75 years associated with an ACE Score of 1, 2, 3, 4 or 5, and ≥ 6 compared to an ACE Score of 0. Models were repeated for death at all ages and age <65 years. Multivariable-adjusted models controlled for age, gender, race/ethnicity, education, marital status, and current problems with finances. Relationships between ACEs and premature death were also examined after the addition of health and social problems previously shown to be associated with ACEs (i.e., possible causal intermediates).

Statistical Analysis

Analyses were conducted using SAS v9.1.3 (2002–2003, SAS Institute, Cary, North Carolina). Mortality rates per 1000 person-years were computed by dividing the number of deaths by the person-time experience. Mortality rates were age-standardized using the 2000 Census population for California. The appropriateness of the proportional hazard assumption

was assessed for the variables in the final model; without exception, all covariates in the final model satisfied the proportional hazard assumption.

The ACE Study has been approved by the IRBs of the respective institutions.

Results

Responses to the 8 individual ACE components varied by age such that a higher proportion of participants aged <65 years reported ACEs and had higher ACE Scores than respondents aged ≥ 65 years at baseline (Table 1). However, the overall prevalence of ACEs was high with ≥ 1 ACEs reported by 69.1% of participants aged <65 years and by 53.0% of those aged ≥ 65 years.

The frequency of deaths from all causes and mortality rates by selected study participant characteristics are shown for men and women in Table 2. Of the 16,908 study participants in the follow-up study (followed for 131,681 person-years; M=7.8 years, SE=0.03), 1539 (followed 8255 person-years; M=5.4 years, SE=0.07) died between the baseline appointment date and 31 December 2006. Overall, the age-adjusted rate was 54.7 per 1000 population (crude, 91.0 per 1000). As expected, people who died were older and more often men, nonwhite, unmarried, had a lower education level, and reported current financial problems than those who survived follow-up (or were censored).

The 5 leading causes of death accounted for about 90% of all deaths among study participants. In rank order according to the number of deaths, the leading causes were diseases of the circulatory system (heart disease and stroke) ($n=538$ deaths; crude death rate=31.8 per 1000 population; age-adj rate=19.2 per 1000 population), malignant neoplasms (cancer) ($n=517$; 30.6; 16.4), diseases of the nervous system and sense organs ($n=140$; 8.3;

5.1), diseases of the respiratory system ($n=137$; 8.1; 4.9), and diseases of the digestive system ($n=50$; 3.0; 1.8).

The relationship between ACEs and age-adjusted all-cause mortality rates was unclear inasmuch as a consistent pattern was not observed across the ACE Score (Table 2). After multivariable adjustment, a relationship was observed between the risk of death (at any age) from all causes and ACE Scores of ≥ 6 (hazard ratio [HR]=1.54, 95% CI=0.98–2.40; ref, 0 ACEs); any association between fewer categories of ACEs and the risk of death was very small with hazard ratios clustered around the null (ACE=1: HR=0.97 [95% CI=0.86–1.10]; ACE=2: 1.05 [0.90–1.23]; ACE=3: 0.91 [0.73–1.14]; ACE=4or5: 1.07 [0.85–1.35]).

Overall, the average age-at-death was 77.5 (95% CI=77.0–78.1) years. No meaningful difference in average age-at-death was observed between men and women or between married and unmarried people, while a difference was observed between whites and nonwhites as well as across education levels with people having a high school education or less being older on average at death than those with a college education (Appendix B, available online at www.ajpm-online.net). People with ≥ 6 ACEs died nearly 20 years earlier on average than those without ACEs. Of course, comparisons of average-at-death across groups are not straightforward since the average age-at-death depends to a large extent on the age distribution of the underlying groups being compared.

Overall, the 1539 deaths during follow-up were associated with 15,998 YLL with an average YLL of 10.4 years per death (Table 3). As noted above, standard expected YLL are based on comparing the age of death to standard model life tables for men and women and incorporate the mortality experience from all deaths regardless of age-at-death. Average YLL per death

was nearly 3 times greater among people with ≥ 6 ACEs (25.2 years) than those without ACEs (9.2 years). In order to allow comparisons across groups after controlling for age, age-standardized YLL were computed and were 1.5 times greater among people with ≥ 6 ACEs than among those without ACEs (1028.8 vs 701.5 per 100,000 population). Age-standardized YLL did not increase substantially with an increase in the number of ACEs among those with fewer than 6 ACEs.

The frequency and age-adjusted risk of death prior to age 65 and 75 years and the associated average years of potential life lost (YPLL₆₅ and YPLL₇₅) are shown in Table 4. Roughly 12% ($n=181$) of those who died during follow-up were aged ≤ 65 years at the time of death accounting for a total of 1674 YPLL₆₅ (M=9.2 years, SE=0.68). Men lost a total of 955 YPLL₆₅ (M=9.3 years, SE=0.97), and women lost 719 YPLL₆₅ (M=9.2, SE=0.93). Similarly, about a third ($n=526$) of those who died during follow-up were aged ≤ 75 years at the time of death accounting for a total of 4792 YPLL₇₅ (M=9.1 years, SE=0.41) with a total of 2692 YPLL₇₅ (M=9.4 years, SE=0.57) for men and 2100 YPLL₇₅ (M=8.8, SE=0.58) for women. Average YPLL₆₅ and YPLL₇₅ per death were increased (although not uniformly) across ACE Score categories.

After multivariable adjustment, adults with ≥ 6 ACEs were 1.7 times more likely to die at age 75 or younger (≥ 6 vs 0 ACEs: HR=1.73, 95% CI=1.06, 2.83); any association between fewer categories of ACEs and risk of premature death was again very small with relative hazards clustered around the null. Similar results were observed for all-cause mortality at age 65 or younger (≥ 6 vs 0 ACEs: HR=2.39; 95% CI=1.30–4.39).

Finally, the analysis considered whether health and social problems previously shown to be associated with ACEs accounted for relationships described above. After adding variables for prevalent disease conditions, risk factors, poor mental health, sexual and reproductive health, social problems, and prescription medication utilization (i.e., “ACE-related” conditions) into a model for premature death, risk ratios for the ACE Score were attenuated toward the null, although not completely. For example, after addition of ACE-related conditions, adults with ≥ 6 ACEs were 1.2 (95% CI=0.70, 1.95) times more likely to die at age ≤ 75 years than those without ACEs, about a 30% change in the relative hazard noted above. A similar result was observed for death at age ≤ 65 years.

Discussion

In this prospective cohort study, people exposed to multiple childhood traumatic stressors captured in the ACE Score were at increased risk of premature death compared to people without ACEs. In contrast to prior ACE Study analyses demonstrating strong, graded relationships between the ACE Score and a variety of health behaviors and health outcomes, a graded increase was not observed in the risk of premature death across the number of categories of ACEs. For nearly all measures, the analysis suggested that the burden of premature death was greatest for people with high (≥ 6) ACE Scores, although results were constrained by a small number of cases among those exposed to high levels of ACEs. When health and social problems that may lie in the causal pathway between ACEs and premature mortality were accounted for, the apparent effects of ACEs on the risk of death at younger ages were reduced. Thus, as would be expected, the documented ACE-related conditions among participants appear to account for some, although not all, of the increased risk of premature death observed in the current study.

The observed modest associations between ACEs and all-cause mortality at any age (and associated YLL) are not unexpected for at least two reasons. First, age is inversely related to ACEs (Table 1), and the age structure of the cohort, which is composed of predominantly white, middle-class adults who are enrolled in the Kaiser health plan and who survived to the study period, is skewed toward older age groups. A third of the study sample was aged ≥ 65 years at baseline; 60% were aged ≥ 50 years at baseline. To the extent that aging represents the natural effect of time and the environment on living organisms, it makes intuitive sense that as individuals continue to age into the 7th, 8th and 9th decades one's ability to discern any influence of exposure to traumatic stress during childhood becomes more challenging despite evidence suggesting such events may become "hardwired" into an individual's biology. This is particularly true for mortality outcomes since most deaths occur among people in older age groups.

Secondly, a review of prior ACE Study results reveals that the strongest associations exist between ACEs and mental health or psychosocial-related risk behaviors and outcomes. With the exception of smoking, relationships between ACEs and the major risk factors for chronic disease (e.g., obesity, physical inactivity, hypertension, high blood cholesterol, diabetes) as well as several forms of prevalent chronic disease itself, have been modest with relatively stronger associations at the upper end of the ACE Score distribution.

By extension, it is reasonable to postulate that cumulative exposure to ACEs may accelerate an individual's disease experience making them at increased risk for premature mortality. Although the absolute risks of death prior to age 65 or 75 years by ACE Score were small, the relative risks comparing people with ≥ 6 ACEs to those without were 1.7 and 2.4, respectively.

There are several reasons to believe that these estimates of the relationship between ACEs and premature death are conservative. Some degree of selection bias is inevitable in observational research simply because not all people who are born will survive to the observation period of interest and because the population that does survive often differs from the population that does not (of course, it is not known what these differences in fact are). If prior results from the ACE Study and similar studies are true, then it is reasonable to postulate that people who are exposed to ACEs (particularly multiple ACEs) are more likely (compared to unexposed) to be aborted, die during childhood or young adulthood, institutionalized, or otherwise lost prior to the initiation of the ACE Study. Thus, the association between ACEs and premature all-cause mortality would be biased downward to the extent that people surveyed at baseline differ from those who do not survive to baseline. Some caution must be exercised in making such an assertion with regard to the direction of the bias since this does not always hold for nondichotomous exposures.

The absence of a graded relationship between the ACE Score and risk of premature death may not be unexpected. The finding is consistent in many ways with those of the seminal ACE Study results.¹ As noted above, previously reported relationships between ACEs and the major risk factors for chronic disease and prevalent chronic diseases, which account for more than 75% of deaths during follow-up in this cohort, were modest in the middle of the ACE Score distribution. In contrast, relationships between ACEs and alcohol abuse, illicit drug use, sexual promiscuity, and suicide (which are related to causes of death that constitute a smaller fraction of total death) exhibited strong, graded relationships across the ACE Score.

The study has several strengths. Mortality data were obtained prospectively from a search of the NDI and therefore are not subject to differential misclassification. Examination of the mortality data suggests that the relationship of ACEs to premature death is not limited to any specific cause of death (data not shown). Future analyses will detail relationships of ACEs to increased risk of cause-specific mortality. Also, the ACE Study incorporates multiple forms of childhood traumatic stressors. Studies which examine only one or at most two types of stressors may underestimate the burden of exposure, fail to recognize the interrelationships among different types of traumatic stressors during childhood (see Dong et al⁹), and/or incorrectly attribute long-term consequences to single types of childhood traumatic stress²² despite convincing evidence suggesting that exposure to multiple forms of abuse and traumatic stressors appear to influence health behaviors and outcomes through a cumulative process.

The results of this study are subject to several limitations. The frequency of ACEs may represent an underreporting of their actual occurrence given the sensitive nature of the questions. However, these estimates of the prevalence of childhood exposures are similar to estimates from nationally representative surveys²³⁻²⁴ indicating that the experiences of ACE Study participants are comparable to those of the larger population of adults. For example, the ACE Study shows that 16% of the men and 25% of the women met the case definition for contact sexual abuse; a national telephone survey of adults in the U.S.²⁵ using similar criteria for sexual abuse estimated that 16% of men and 27% of women had been sexually abused. Of the men from the ACE Study study, 30% had been physically abused as boys, which closely parallels the prevalence (31%) found in a recent population-based study of Ontario men that used questions from the same scales.²⁶ The similarity in estimated prevalence of these

childhood exposures between the ACE Study and other population-based studies suggests that these findings are likely to be applicable in other settings.

Although mortality follow-up was available for a maximum of 10 years, statistical power was somewhat limited owing to relatively few deaths during follow-up among people exposed to multiple ACEs. Overall, the sample population under observation is a healthier group identified from the underlying source population based on their attendance at a wellness clinic. Plans for future research include continuing to repeat the NDI search and related analyses in the coming years. As is the case in many observational studies, there may have been unknown or unmeasured confounding factors for which adjustment was not possible. Moreover, measurement error in the assessment or estimation of covariates and their severity may have resulted in incomplete adjustment and residual confounding. Finally, throughout this analysis, the focus was on estimation rather than statistical significance for inference. These data are compatible with a moderate association between ACEs and premature mortality; however, this assumes that there is no bias in the data collected and that the statistical models are correct.²⁷

In conclusion, exposure to ACEs is common and their health consequences are often hidden from view by clinicians and health professionals. In the present study, people exposed to ACEs, particularly those exposed to multiple (in this study ≥ 6) stressors, died younger than those who were not exposed. Some of this increase in risk is explained by ACE-related health and social problems. These results, although tentative, lend further support to the collective body of evidence suggesting that childhood traumatic stressors represent a common pathway to a variety of long-term behavioral, health, and social problems. Additional studies of the

prevalence of ACEs in other populations and examination of relationships with health and social problems are needed.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC or the authors' affiliated institutions.

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References

1. Felitti VJ, Anda RF, Nordenberg D, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The adverse childhood experiences (ACE) study. *Am J Prev Med* 1998;14:245–58.
2. Anda RF, Brown DW, Felitti VJ, Dube SR, Giles WH. Adverse childhood experiences and prescription drug use in a prospective study of adult HMO patients. *BMC Public Health* 2008;8:198.
3. Sabotta EE, Davis RL. Fatality after report to a child abuse registry in Washington State, 1973–1986. *Child Abuse Negl* 1992;16(5):627–35.
4. White HR, Widom CS. Does childhood victimization increase the risk of early death? A 25-year prospective study. *Child Abuse Negl*. 2003;27(7):841–53.
5. Anda RF, Croft JB, Felitti VJ, et al. Adverse childhood experiences and smoking during adolescence and adulthood. *JAMA* 1999;282:1652–8.
6. Dube SR, Anda RF, Felitti VJ, et al. Growing up with parental alcohol abuse: exposure to childhood abuse, neglect, and household dysfunction. *Child Abuse Negl* 2001; 25:1627–40.
7. Edwards VJ, Anda RF, Nordenberg DF, Felitti VJ, Williamson DF, Wright JA. Bias assessment for child abuse survey: factors affecting probability of response to a survey about childhood abuse. *Child Abuse Negl* 2001;25:307–12.
8. Anda RF, Felitti VJ, Bremner JD, et al. The enduring effects of abuse and related adverse experiences in childhood. A convergence of evidence from neurobiology and epidemiology. *Eur Arch Psychiatry Clin Neurosci* 2006;256:174–86.
9. Dong M, Anda RF, Felitti VJ, et al. The interrelatedness of multiple forms of childhood abuse, neglect, and household dysfunction. *Child Abuse Negl* 2004;28:771–84.

10. Dube SR, Williamson DF, Thompson T, Felitti VJ, Anda RF. Assessing the reliability of retrospective reports of adverse childhood experiences among adult HMO members attending a primary care clinic. *Child Abuse Neglect* 2004;28:729–37.
11. Calle EE, Terrell DD. Utility of the National Death Index for ascertainment of mortality among Cancer Prevention Study II participants. *Am J Epidemiol* 1993;137:235–41.
12. Edlavitch SA, Baxter J. Comparability of mortality follow-up before and after the National Death Index. *Am J Epidemiol* 1988;127:1164–78.
13. Stampfer MJ, Willett WC, Speizer FE, et al. Test of the National Death Index. *Am J Epidemiol* 1984;119:837–9.
14. National Center for Health Statistics. National Death Index User's Manual. (Hyattsville, Maryland: National Center for Health Statistics, 2003). Available on request from NCHS.
15. Horm J. Multiple causes of death for the National Health Interview Survey. In Committee on Applied and Theoretical Statistics, National Research Council, Federal Committee on Statistical Methodology, Office of Management and Budget. Record Linkage Techniques—1997 Proceedings of an International Workshop and Exposition (National Academy Press: Washington, DC 1999) pp71–7.
16. National Center for Health Statistics. Office of Analysis and Epidemiology. The 1986–2000 National Health Interview Survey linked mortality files: matching methodology. (Hyattsville, Maryland: National Center for Health Statistics, 2005). Available online at www.cdc.gov/nchs/data/datalinkage/matching_methodology_nhis_final.pdf
17. WHO. Global Burden of Disease Study. Available online at www.who.int/topics/global_burden_of_disease. Accessed 15 January 2009.
18. Murray CJ, Mathers CD, Salomon JA, Lopez AD. Health gaps: An overview and critical appraisal. In Murray et al, eds. Summary Measures of Population Health. (Geneva, Switzerland: WHO Press, 2002).

19. Aragón TJ, Lichtensztajn DY, Katcher BS, Reiter R, Katz MH. Calculating expected years of life lost for assessing local ethnic disparities in causes of premature death. *BMC Public Health* 2008;8:116.
20. Coale AJ, Demeny P, Vaughan B. Regional Model Life Tables and Stable Populations (New York, New York: Academic, 1983).
21. Dempsey M. Decline in tuberculosis: death rate fails to tell entire story. *Am Rev Tuberculosis* 1947;56:157–64.
22. Finkelhor D, Ormrod R, Turner H, Hamby SL. The victimization of children and youth: a comprehensive, national survey. *Child Maltreat* 2005;10:5–25.
23. Finkelhor D, Dziuba-Leatherman J. Children as victims of violence: A national survey. *Pediatrics* 1994;94:413–20.
24. Wyatt GE, Loeb TB, Solis B, Carmona JV, Romero G. The prevalence and circumstances of child sexual abuse: Changes across a decade. *Child Abuse Negl* 1999;23:45–60.
25. Finkelhor D, Hotaling G, Lewis IA, Smith C. Sexual abuse in a national survey of adult men and women: Prevalence, characteristics, and risk factors. *Child Abuse Negl* 1990;14:19–28.
26. MacMillan HL, Fleming JE, Trocme N, et al. Prevalence of child physical and sexual abuse in the community results from the Ontario health supplement. *JAMA* 1997;278:131–5.
27. Rothman KJ, Greenland S, Lash TL. Modern Epidemiology, 3rd Edition. (Philadelphia, Pennsylvania: Lippincott Williams & Wilkins, 2008) pp151–167.

Table 1. Definition and prevalence of adverse childhood experiences (ACEs) occurring during the first 18 years of life, by age

	Age <65 yrs, % (n=11,749)	Age ≥65 yrs, % (n=5588)
Childhood Abuse		
<i>Emotional *</i>	13.0	5.4
<u>(Did a parent or other adult in the household ...)</u>		
(1) Often or very often swear at you, insult you, or put you down?		
(2) Sometimes, often, or very often act in a way that made you afraid that you might be physically hurt?		
<i>Physical</i>	32.3	19.9
<u>(Did a parent or other adult in the household ...)</u>		
(1) Often or very often push, grab, slap, or throw something at you?		
(2) Often or very often hit you so hard that you had marks or were injured?		
<i>Sexual</i>	22.5	17.0
<u>(Did an adult or person at least 5 years older ever ...)</u>		
(1) Touch or fondle you in a sexual way?		
(2) Have you touch their body in a sexual way?		
(3) Attempt oral, anal, or vaginal intercourse with you?		
(4) Actually have oral, anal, or vaginal intercourse with you?		
Household dysfunction		
<i>Substance abuse</i>	32.3	15.4
(1) Live with anyone who was a problem drinker or alcoholic?		
(2) Live with anyone who used street drugs?		
<i>Mental Illness</i>	22.5	12.9
(1) Was a household member depressed or mentally ill?		
(2) Did a household member attempt suicide?		
<i>Mother treated violently</i>	14.9	8.1
<u>(Was your mother (or stepmother) ...)</u>		
(1) Sometimes, often, or very often pushed, grabbed, slapped, or had something thrown at her?		
(2) Sometimes, often, or very often kicked, bitten, hit with a fist, or hit with something hard?		
(3) Ever repeatedly hit over at least a few minutes?		
(4) Ever threatened with or hurt by a knife or gun?		
<i>Incarcerated household member</i>	5.6	2.7
(1) Did a household member go to prison?		
<i>Parental separation or divorce</i>	26.1	17.3
(1) Were your parents ever separated or divorced?		
<i>Categories of adverse childhood experiences, No.</i>		

0	30.9	47.0
1	25.3	27.6
2	17.0	13.7
3	11.0	6.4
4 or 5	12.1	4.8
6, 7, or 8	3.7	0.6

* Respondents were defined as exposed to a category if they responded "yes" to one or more of the questions in that category.

Table 2. Frequency of deaths from all causes and age-standardized mortality rates among 16,908 ACE Study participants, by selected sociodemographic characteristics and number of categories of adverse childhood experiences (ACEs)

	N	Total (N=16,908)		Women (N=9122)		Men (N=7786)	
		Deaths, No.	Mortality Rate*	Deaths, No.	Mortality Rate*	Deaths, No.	Mortality Rate*
Overall, Crude	16,908	1539	11.7	656	9.2	883	14.7
Age-adjusted**		...	7.7	...	6.0	...	9.9
Age (years)							
18–34	1611	8	0.8	2	0.3	6	1.8
35–49	4391	59	1.7	30	1.6	29	2.0
50–64	5410	247	5.7	106	4.6	141	6.8
65–74	3652	514	16.6	230	14.3	284	19.1
≥75	1844	711	52.3	288	41.9	423	62.8
Race/ethnicity**							
White	12,683	1353	7.9	572	6.2	781	10.1
Black	767	48	8.4	20	5.7	28	12.4
Asian	1875	78	6.6	39	5.0	39	8.9
Hispanic	1218	37	5.2	14	3.6	23	8.0
Other	365	23	10.8	11	11.7	12	6.0
Education**							
Less than high school	1218	203	11.9	88	41.1	115	18.9
High school graduate	2976	408	7.8	205	6.5	203	10.1
Some college	6056	487	7.4	206	5.9	281	9.4
College graduate	6658	441	6.5	157	5.3	284	7.5
Married**							
Yes	11,758	1053	7.1	387	5.5	666	8.3
No	5150	486	8.3	269	6.4	217	12.3
Current problems with finances**							
Yes	1967	109	12.7	56	11.1	53	17.2
No	14,941	1430	7.4	600	5.6	830	9.9
Categories of ACEs, No.**							
0	6125	723	7.7	325	11.1	398	5.9
1	4411	408	8.0	160	9.4	248	6.3
2	2682	220	8.4	79	9.9	141	7.1
3	1601	87	9.7	38	14.0	49	3.9
4 or 5	1639	81	22.4	41	6.2	40	21.5
6, 7, or 8	450	20	7.3	13	8.6	7	3.4

* per 1000 person-years

** Rate age-standardized to the 2000 Census population for California

Table 3. Expected years of life lost (YLL), average YLL, and age-standardized YLL from all-cause mortality for 1539 study participants who died between baseline and 31 December 2006, by number of categories of adverse childhood experiences (ACEs)

Categories of ACEs, No.	N	Deaths, No.	YLL	Average YLL	Age-standardized YLL (ASYLL)	ASYLL Ratio
0	6125	723	6675.6	9.2	701.5	1.00*
1	4411	408	4062.0	10.0	609.9	0.87
2	2682	220	2476.8	11.3	679.6	0.97
3	1601	87	1162.5	13.4	723.7	1.03
4 or 5	1639	81	1116.8	13.8	588.0	0.84
6, 7, or 8	450	20	504.0	25.2	1028.8	1.47
Total	16,908	1539	15,997.7	10.4	664.5	

Formulas used for the computation of Years of Life Lost (YLL)

- Standard expected years of life lost were calculated using the formula,

$$YLL = {}_nY_x = ({}_nD_x)({}_ne^s_x),$$

where ${}_nD_x$ is the number of deaths within age interval x and $x+n$. The expected years of life remaining for those deaths (${}_ne^s_x$) was obtained using the formula,

$${}_ne^s_x = e^s_x + ({}_na_x - x) \frac{e^s_{x+n} - e^s_x}{(x+n) - x}$$

where ${}_na_x$ is the average age of death for the age interval, and e^s_x and e^s_{x+n} are life expectancies from the Coale and Demeny life tables at ages x and $x+n$.

- Average YLL were calculated by dividing YLL by the corresponding number of deaths.
- Age-standardized YLL (per 100,000 population) (ASYLL) were calculated according to the formula,

$$ASYLL = \frac{{}_nY_x}{{}_nN_x} \times {}_nw_x$$

where ${}_nY_x$ is the YLL for the age interval, ${}_nN_x$ is the total number of subjects in the age interval, and ${}_nw_x$ is the weight for the age interval. Age-standardized YLL were age-standardized to the 2000 Census population for California.

* People with no ACEs are the ref group for ratio comparisons

Table 4. Frequency and risk of death prior to age 65 or to age 75 years and the associated total and average years of potential life lost (YPLL) for study participants who died between baseline and 31 December 2006, by number of categories of adverse childhood experiences (ACEs)

Categories of ACEs, No.	N	Death prior to age 65 years				Death prior to age 75 years			
		Deaths, No.	Risk*	YPLL ₆₅		Deaths, No.	Risk*	YPLL ₇₅	
				Total	M (SE)			Total	M (SE)
0	6125	61	11.0 (2.44)	501	8.2 (1.09)	203	18.9 (2.53)	1602	7.9 (0.60)
1	4411	39	8.4 (1.93)	326	8.4 (1.53)	140	16.6 (2.08)	1102	7.9 (0.72)
2	2682	35	11.1 (2.09)	318	9.1 (1.64)	75	17.3 (2.30)	830	11.1 (1.18)
3	1601	17	11.7 (3.69)	215	12.6 (2.40)	41	18.6 (3.93)	486	11.9 (1.77)
4 or 5	1639	15	6.2 (1.63)	144	9.6 (2.15)	49	18.2 (2.55)	440	9.0 (1.24)
6, 7, or 8	450	14	24.2 (6.48)	170	12.1 (2.52)	18	30.8 (7.29)	332	18.4 (2.59)
Total	16,908	181	10.4 (1.04)	1674	9.2 (0.68)	526	18.3 (1.11)	4792	9.1 (0.41)

Years of potential life lost with death at age 65, $YPLL_{65} = 65 - \text{age-at-death}$; by definition, deaths after age 65 are not considered

Years of potential life lost with death at age 75, $YPLL_{75} = 75 - \text{age-at-death}$; by definition, deaths after age 75 are not considered

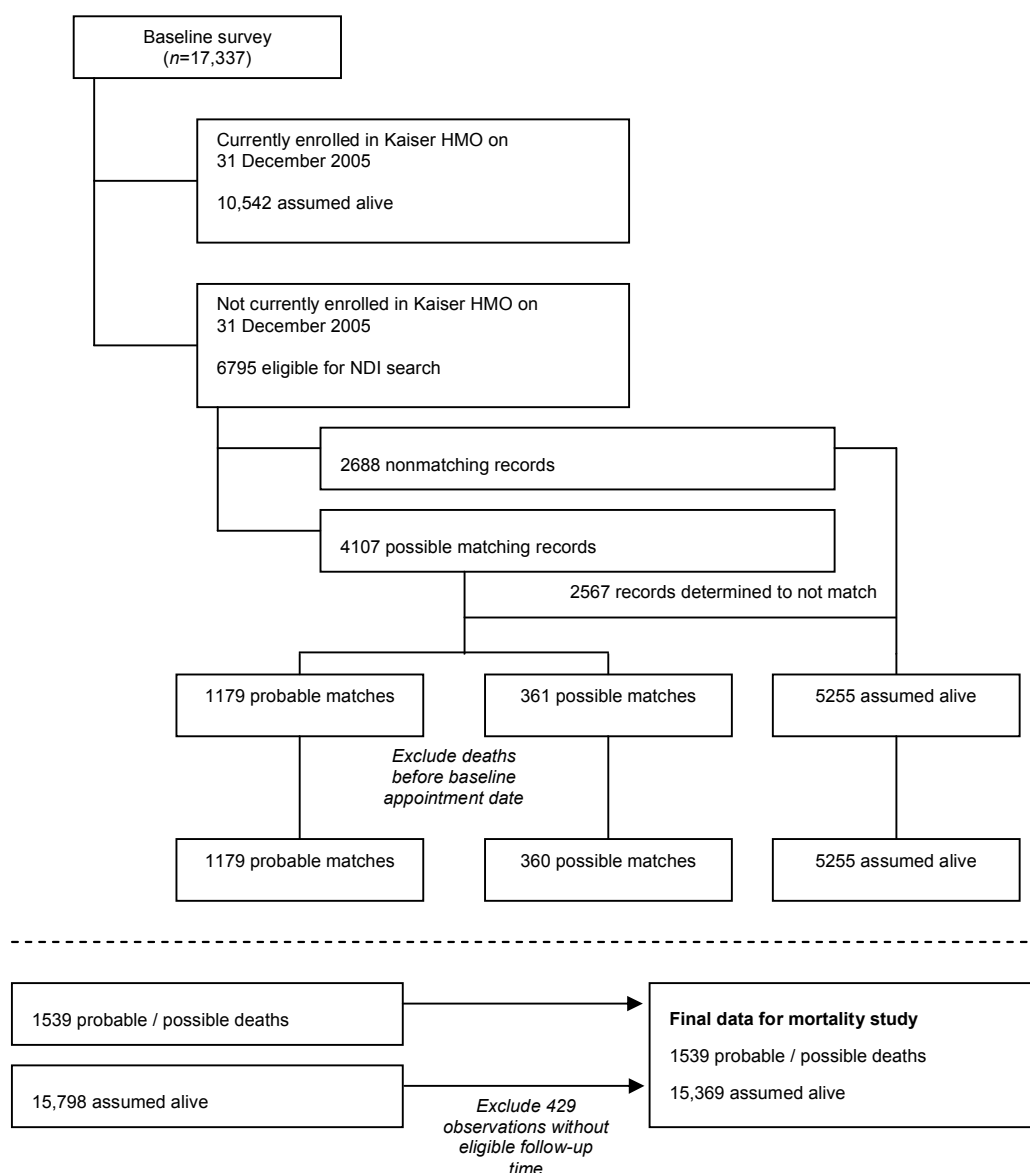
* Age-standardized risk of death (per 1000 population). Standardized to the 2000 Census population for California.

Adverse Childhood Experiences and the Risk of Premature Mortality

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Appendix A

Data map for mortality follow-up period through 31 December 2006



Note: Of the 17,337 study participants at baseline, 10,542 were currently enrolled in the health plan on 31 December, 2005 and assumed to be alive. The vital status of the remaining 6795 participants was unknown, and therefore these participants were eligible for matching to the NDI. Of these 6795 participants, 4107 were identified as potential matching records in the NDI. A total of 1179 participants were identified as probable deaths based on an exact match between all identifying data items sent forward on the ACE Study record and on the NDI record; 361 participants were identified as possible deaths based in part on a probabilistic score for the match computed by NCHS and described in detail elsewhere.¹ We identified one possible death record wherein the death date preceded the baseline study date and subsequently recoded this record from possible death to assumed alive, leaving a total of 1539 study participants who died during the follow-up period (1179 probable; 360 possible).

ACE, Adverse Childhood Experiences; NCHS, National Center for Health Statistics; NDI, National Death Index

References

1. Horn J. Multiple causes of death for the National Health Interview Survey. In: Committee on Applied and Theoretical Statistics, National Research Council, Federal Committee on Statistical Methodology, Office of Management and Budget. Record Linkage Techniques—1997 Proceedings of an International Workshop and Exposition. Washington, DC: National Academy Press, 1999: 71–7.

Appendix B

Average age at baseline and at death from all causes by selected sociodemographic characteristics and number of categories of ACEs

	M (95% CI) x age at baseline (n=16,908)	M (95% CI) ^a age at baseline for those who died during follow-up period (n=1539)	M (95% CI) x age at death (n=1539)
Overall	56.2 (56.0, 56.4)	72.3 (71.7, 72.8)	77.5 (77.0, 78.1)
Gender			
Men	57.3 (57.0, 57.6)	72.6 (72.0, 73.3)	77.8 (77.1, 78.5)
Women	55.2 (54.9, 55.5)	71.8 (71.0, 72.5)	77.2 (76.4, 78.0)
Race/ethnicity			
White	58.6 (58.4, 58.9)	73.0 (72.5, 73.5)	78.3 (77.7, 78.8)
Nonwhite	48.9 (48.5, 49.3)	67.0 (65.6, 68.5)	72.4 (70.9, 73.9)
Education			
Less than high school	63.4 (62.7, 64.2)	74.6 (73.2, 75.9)	79.5 (78.1, 80.9)
High school graduate	60.2 (59.8, 60.8)	73.9 (73.0, 74.9)	79.4 (78.4, 80.4)
Some college	55.4 (55.0, 55.7)	71.0 (70.1, 71.9)	76.2 (75.3, 77.1)
College graduate	53.8 (53.4, 54.1)	71.1 (70.1, 72.0)	76.4 (75.5, 77.4)
Married			
Yes	56.8 (56.6, 57.1)	71.9 (71.3, 72.5)	77.2 (76.5, 77.8)
No	54.8 (54.4, 55.1)	73.1 (72.2, 73.9)	78.4 (77.5, 79.3)
Current problems with finances			
Yes	50.9 (50.3, 51.5)	67.3 (65.4, 69.2)	72.8 (70.9, 74.8)
No	56.9 (56.7, 57.1)	72.6 (72.1, 73.1)	77.9 (77.4, 78.4)
Categories of ACEs (number)			
0	59.3 (58.9, 59.6)	73.9 (73.1, 74.6)	79.1 (78.4, 79.9)
1	56.8 (56.4, 57.2)	72.8 (71.8, 73.7)	78.0 (77.0, 79.0)
2	54.7 (54.2, 55.2)	70.8 (69.4, 72.1)	76.0 (74.7, 77.4)
3	53.0 (52.3, 53.7)	68.1 (66.0, 70.1)	73.5 (71.4, 75.6)
4 or 5	50.9 (50.3, 51.6)	68.3 (66.1, 70.4)	73.6 (71.4, 75.8)
6, 7, or 8	47.4 (46.1, 48.6)	55.5 (51.2, 59.8)	60.6 (56.2, 65.1)

^a Average age-at-death adjusted for all variables in the table
ACE, adverse childhood experience

This piece of the submission is being sent via mail.