

Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults

The Adverse Childhood Experiences (ACE) Study

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Background: The relationship of health risk behavior and disease in adulthood to the breadth of exposure to childhood emotional, physical, or sexual abuse, and household dysfunction during childhood has not previously been described.

Methods: A questionnaire about adverse childhood experiences was mailed to 13,494 adults who had completed a standardized medical evaluation at a large HMO; 9,508 (70.5%) responded. Seven categories of adverse childhood experiences were studied: psychological, physical, or sexual abuse; violence against mother; or living with household members who were substance abusers, mentally ill or suicidal, or ever imprisoned. The number of categories of these adverse childhood experiences was then compared to measures of adult risk behavior, health status, and disease. Logistic regression was used to adjust for effects of demographic factors on the association between the cumulative number of categories of childhood exposures (range: 0–7) and risk factors for the leading causes of death in adult life.

Results: More than half of respondents reported at least one, and one-fourth reported ≥ 2 categories of childhood exposures. We found a graded relationship between the number of categories of childhood exposure and each of the adult health risk behaviors and diseases that were studied ($P < .001$). Persons who had experienced four or more categories of childhood exposure, compared to those who had experienced none, had 4- to 12-fold increased health risks for alcoholism, drug abuse, depression, and suicide attempt; a 2- to 4-fold increase in smoking, poor self-rated health, ≥ 50 sexual intercourse partners, and sexually transmitted disease; and a 1.4- to 1.6-fold increase in physical inactivity and severe obesity. The number of categories of adverse childhood exposures showed a graded relationship to the presence of adult diseases including ischemic heart disease, cancer, chronic lung disease, skeletal fractures, and liver disease. The seven categories of adverse childhood experiences were strongly interrelated and persons with multiple categories of childhood exposure were likely to have multiple health risk factors later in life.

Conclusions: We found a strong graded relationship between the breadth of exposure to abuse or household dysfunction during childhood and multiple risk factors for several of the leading causes of death in adults.

Medical Subject Headings (MeSH): child abuse, sexual, domestic violence, spouse abuse, children of impaired parents, substance abuse, alcoholism, smoking, obesity, physical activity, depression, suicide, sexual behavior, sexually transmitted diseases, chronic obstructive pulmonary disease, ischemic heart disease. (Am J Prev Med 1998;14:245–258) © 1998 American Journal of Preventive Medicine

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Introduction

Only recently have medical investigators in primary care settings begun to examine associations between childhood abuse and adult health risk behaviors and disease.¹⁻⁵ These associations are important because it is now clear that the leading causes of morbidity and mortality in the United States⁶ are related to health behaviors and lifestyle factors; these factors have been called the “actual” causes of death.⁷ Insofar as abuse and other potentially damaging childhood experiences contribute to the development of these risk factors, then these childhood exposures should be recognized as the basic causes of morbidity and mortality in adult life.

Although sociologists and psychologists have published numerous articles about the frequency⁸⁻¹² and long-term consequences¹³⁻¹⁵ of childhood abuse, understanding their relevance to adult medical problems is rudimentary. Furthermore, medical research in this field has limited relevance to most primary care physicians because it is focused on adolescent health,¹⁶⁻²⁰ mental health in adults,²⁰ or on symptoms among patients in specialty clinics.^{22,23} Studies of the long-term effects of childhood abuse have usually examined single types of abuse, particularly sexual abuse, and few have assessed the impact of more than one type of abuse.^{5,24-28} Conditions such as drug abuse, spousal violence, and criminal activity in the household may co-occur with specific forms of abuse that involve children. Without measuring these household factors as well, long-term influence might be wrongly attributed solely to single types of abuse and the cumulative influence of multiple categories of adverse childhood experiences would not be assessed. To our knowledge, the relationship of adult health risk behaviors, health status, and disease states to childhood abuse and household dysfunction²⁹⁻³⁵ has not been described.

We undertook the Adverse Childhood Experiences (ACE) Study in a primary care setting to describe the long-term relationship of childhood experiences to important medical and public health problems. The ACE Study is assessing, retrospectively and prospectively, the long-term impact of abuse and household dysfunction during childhood on the following outcomes in adults: disease risk factors and incidence, quality of life, health care utilization, and mortality. In this initial paper we use baseline data from the study to provide an overview of the prevalence and interrelation of exposures to childhood abuse and household dysfunction. We then describe the relationship between the number of categories of these deleterious childhood exposures and risk factors and those diseases that

underlie many of the leading causes of death in adults.^{6,7,36,37}

Methods

Study Setting

The ACE Study is based at Kaiser Permanente's San Diego Health Appraisal Clinic. More than 45,000 adults undergo standardized examinations there each year, making this clinic one of the nation's largest free-standing medical evaluation centers. All enrollees in the Kaiser Health Plan in San Diego are advised through sales literature about the services (free for members) at the clinic; after enrollment, members are advised again of its availability through new-member literature. Most members obtain appointments by self-referral; 20% are referred by their health care provider. A recent review of membership and utilization records among Kaiser members in San Diego continuously enrolled between 1992 and 1995 showed that 81% of those 25 years and older had been evaluated in the Health Appraisal Clinic.

Health appraisals include completion of a standardized medical questionnaire that requests demographic and biopsychosocial information, review of organ systems, previous medical diagnoses, and family medical history. A health care provider completes the medical history, performs a physical examination, and reviews the results of laboratory tests with the patient.

Survey Methods

The ACE Study protocol was approved by the Institutional Review Boards of the Southern California Permanente Medical Group (Kaiser Permanente), the Emory University School of Medicine, and the Office of Protection from Research Risks, National Institutes of Health. All 13,494 Kaiser Health Plan members who completed standardized medical evaluations at the Health Appraisal Clinic between August–November of 1995 and January–March of 1996 were eligible to participate in the ACE Study. Those seen at the clinic during December were not included because survey response rates are known to be lower during the holiday period.³⁸

In the week after visiting the clinic, and hence having their standardized medical history already completed, members were mailed the ACE Study questionnaire that included questions about childhood abuse and exposure to forms of household dysfunction while growing up. After second mailings of the questionnaire to persons who did not respond to the first mailing, the response rate for the survey was 70.5% (9,508/13,494).

**See
related
Commentary
on pages 354,
356, 361.**

Survey Wave I--complete
71% response (9,508/13,494)*

***All medical evaluations
abstracted***

Follow-up

(Cohort $n=19,000$)

**Survey Wave II--completed,
 $n=15,000$ under evaluation**

***All medical evaluations
abstracted***

Mortality

National Death Index

Morbidity

Hospital Discharge

Outpatient Visits

Emergency Room Visits

Pharmacy Utilization

Figure 1. ACE Study design. *After exclusions, 59.7% of the original wave I sample (8,056/13,494) were included in this analysis.

A second survey wave of approximately the same number of patients as the first wave was conducted between June and October of 1997. The data for the second survey wave is currently being compiled for analysis. The methods for the second mail survey wave were identical to the first survey wave as described above. The second wave was done to enhance the precision of future detailed analyses on special topics and to reduce the time necessary to obtain precise statistics on follow-up health events. An overview of the total ACE Study design is provided in Figure 1.

Comparison of Respondents and Nonrespondents

We abstracted the completed medical evaluation for every person eligible for the study; this included their medical history, laboratory results, and physical findings. Respondent ($n = 9,508$) and nonrespondent ($n = 3,986$) groups were similar in their percentages of women (53.7% and 51.0%, respectively) and in their mean years of education (14.0 years and 13.6 years, respectively). Respondents were older than nonrespondents (means 56.1 years and 49.3 years) and more likely to be white (83.9% vs. 75.3%) although the actual magnitude of the differences was small.

Respondents and nonrespondents did not differ with regard to their self-rated health, smoking, other substance abuse, or the presence of common medical conditions such as a history of heart attack or stroke, chronic obstructive lung disease, hypertension, or diabetes, or with regard to marital status or current family, marital, or job-related problems (data not shown). The health appraisal questionnaire used in the clinic con-

tains a single question about childhood sexual abuse that reads "As a child were you ever raped or sexually molested?" Respondents were slightly more likely to answer affirmatively than nonrespondents (6.1% vs. 5.4%, respectively).

Questionnaire Design

We used questions from published surveys to construct the ACE Study questionnaire. Questions from the Conflicts Tactics Scale³⁹ were used to define psychological and physical abuse during childhood and to define violence against the respondent's mother. We adapted four questions from Wyatt⁴⁰ to define contact sexual abuse during childhood. Questions about exposure to alcohol or drug abuse during childhood were adapted from the 1988 National Health Interview Survey.⁴¹ All of the questions we used in this study to determine childhood experiences were introduced with the phrase "While you were growing up during your first 18 years of life . . ."

Questions about health-related behaviors and health problems were taken from health surveys such as the Behavioral Risk Factor Surveys⁴² and the Third National Health and Nutrition Examination Survey,⁴³ both of which are directed by the Centers for Disease Control and Prevention. Questions about depression came from the Diagnostic Interview Schedule of the National Institute of Mental Health (NIMH).⁴⁴ Other information for this analysis such as disease history was obtained from the standardized questionnaire used in the Health Appraisal Clinic. (A copy of the questionnaires used in this study may be found at www.elsevier.com/locate/amepre.)

Table 1. Prevalence of childhood exposure to abuse and household dysfunction

Category of childhood exposure ^a	Prevalence (%)	Prevalence (%)
Abuse by category		
Psychological		11.1
(<i>Did a parent or other adult in the household . . .</i>)		
Often or very often swear at, insult, or put you down?	10.0	
Often or very often act in a way that made you afraid that you would be physically hurt?	4.8	
Physical		10.8
(<i>Did a parent or other adult in the household . . .</i>)		
Often or very often push, grab, shove, or slap you?	4.9	
Often or very often hit you so hard that you had marks or were injured?	9.6	
Sexual		22.0
(<i>Did an adult or person at least 5 years older ever . . .</i>)		
Touch or fondle you in a sexual way?	19.3	
Have you touch their body in a sexual way?	8.7	
Attempt oral, anal, or vaginal intercourse with you?	8.9	
Actually have oral, anal, or vaginal intercourse with you?	6.9	
Household dysfunction by category		
Substance abuse		25.6
Live with anyone who was a problem drinker or alcoholic?	23.5	
Live with anyone who used street drugs?	4.9	
Mental illness		18.8
Was a household member depressed or mentally ill?	17.5	
Did a household member attempt suicide?	4.0	
Mother treated violently		12.5
(<i>Was your mother (or stepmother)</i>)		
Sometimes, often, or very often pushed, grabbed, slapped, or had something thrown at her?	11.9	
Sometimes, often, or very often kicked, bitten, hit with a fist, or hit with something hard?	6.3	
Ever repeatedly hit over at least a few minutes?	6.6	
Ever threatened with, or hurt by, a knife or gun?	3.0	
Criminal behavior in household		
Did a household member go to prison?	3.4	3.4
	Any category reported	52.1%

^aAn exposure to one or more items listed under the set of questions for each category.

Defining Childhood Exposures

We used three categories of childhood abuse: psychological abuse (2 questions), physical abuse (2 questions), or contact sexual abuse (4 questions). There were four categories of exposure to household dysfunction during childhood: exposure to substance abuse (defined by 2 questions), mental illness (2 questions), violent treatment of mother or stepmother (4 questions), and criminal behavior (1 question) in the household. Respondents were defined as exposed to a category if they responded “yes” to 1 or more of the questions in that category. The prevalence of positive responses to the individual questions and the category prevalences are shown in Table 1.

We used these 7 categories of childhood exposures to abuse and household dysfunction for our analysis. The measure of childhood exposure that we used was simply the sum of the categories with an exposure; thus the possible number of exposures ranged from 0 (unexposed) to 7 (exposed to all categories).

Risk Factors and Disease Conditions Assessed

Using information from both the study questionnaire and the Health Appraisal Clinic’s questionnaire, we chose 10 risk factors that contribute to the leading causes of morbidity and mortality in the United States.^{6,7,36,37} The risk factors included smoking, severe obesity, physical inactivity, depressed mood, suicide attempts, alcoholism, any drug abuse, parenteral drug abuse, a high lifetime number of sexual partners (≥ 50), and a history of having a sexually transmitted disease.

We also assessed the relationship between childhood exposures and disease conditions that are among the leading causes of mortality in the United States.⁶ The presence of these disease conditions was based upon medical histories that patients provided in response to the clinic questionnaire. We included a history of ischemic heart disease (including heart attack or use of nitroglycerin for exertional chest pain), any cancer, stroke, chronic bronchitis, or emphysema (COPD),

diabetes, hepatitis or jaundice, and any skeletal fractures (as a proxy for risk of unintentional injuries). We also included responses to the following question about self-rated health: "Do you consider your physical health to be excellent, very good, good, fair, or poor?" because it is strongly predictive of mortality.⁴⁵

Definition of Risk Factors

We defined severe obesity as a body mass index (kg/meter²) ≥ 35 based on measured height and weight; physical inactivity as no participation in recreational physical activity in the past month; and alcoholism as a "Yes" response to the question "Have you ever considered yourself to be an alcoholic?" The other risk factors that we assessed are self-explanatory.

Exclusions from Analysis

Of the 9,508 survey respondents, we excluded 51 (0.5%) whose race was unstated and 34 (0.4%) whose educational attainment was not reported. We also excluded persons who did not respond to certain questions about adverse childhood experiences. This involved the following exclusions: 125 (1.3%) for household substance abuse, 181 (1.9%) for mental illness in the home, 148 (1.6%) for violence against mother, 7 (0.1%) for imprisonment of a household member, 109 (1.1%) for childhood psychological abuse, 44 (0.5%) for childhood physical abuse, and 753 (7.9%) for childhood sexual abuse. After these exclusions, 8,056 of the original 9,508 survey respondents (59.7% of the original sample of 13,494) remained and were included in the analysis. Procedures for insuring that the findings based on complete data were generalizable to the entire sample are described below.

The mean age of the 8,506 persons included in this analysis was 56.1 years (range: 19–92 years); 52.1% were women; 79.4% were white. Forty-three percent had graduated from college; only 6.0% had not graduated from high school.

Statistical Analysis

We used the Statistical Analysis System (SAS)⁴⁶ for our analyses. We used the direct method to age-adjust the prevalence estimates. Logistic regression analysis was employed to adjust for the potential confounding effects of age, sex, race, and educational attainment on the relationship between the number of childhood exposures and health problems.

To test for a dose-response relationship to health problems, we entered the number of childhood exposures as a single ordinal variable (0, 1, 2, 3, 4, 5, 6, 7) into a separate logistic regression model for each risk factor or disease condition.

Assessing the Possible Influence of Exclusions

To determine whether our results were influenced by excluding persons with incomplete information on any of the categories of childhood exposure, we performed a separate sensitivity analysis in which we included all persons with complete demographic information but assumed that persons with missing information for a category of childhood exposure did not have an exposure in that category.

Results

Adverse Childhood Exposures

The level of positive responses for the 17 questions included in the seven categories of childhood exposure ranged from 3.0% for a respondent's mother (or stepmother) having been threatened with or hurt by a gun or knife to 23.5% for having lived with a problem drinker or alcoholic (Table 1). The most prevalent of the 7 categories of childhood exposure was substance abuse in the household (25.6%); the least prevalent exposure category was evidence of criminal behavior in the household (3.4%). More than half of respondents (52%) experienced ≥ 1 category of adverse childhood exposure; 6.2% reported ≥ 4 exposures.

Relationships between Categories of Childhood Exposure

The probability that persons who were exposed to any single category of exposure were also exposed to another category is shown in Table 2. The relationship between single categories of exposure was significant for all comparisons ($P < .001$; chi-square). For persons reporting any single category of exposure, the probability of exposure to any additional category ranged from 65%–93% (median: 80%); similarly, the probability of ≥ 2 additional exposures ranged from 40%–74% (median: 54.5%).

The number of categories of childhood exposures by demographic characteristics is shown in Table 3. Statistically, significantly fewer categories of exposure were found among older persons, white or Asian persons, and college graduates ($P < .001$). Because age is associated with both the childhood exposures as well as many of the health risk factors and disease outcomes, all prevalence estimates in the tables are adjusted for age.

Relationship between Childhood Exposures and Health Risk Factors

Both the prevalence and risk (adjusted odds ratio) increased for smoking, severe obesity, physical inactivity, depressed mood, and suicide attempts as the number of childhood exposures increased (Table 4). When

Table 2. Relationships between categories of adverse childhood exposure

First Category of Childhood Exposure	Sample Size*	Percent (%) Exposed to Another Category								
		Psychological Abuse	Physical Abuse	Sexual Abuse	Substance Abuse	Mental Illness	Treated Violently	Imprisoned Member	Any One Additional Category	Any Two Additional Categories
Childhood Abuse:										
Psychological	898	—	52*	47	51	50	39	9	93	74
Physical abuse	874	54	—	44	45	38	35	9	86	64
Sexual abuse	1770	24	22	—	39	31	23	6	65	41
Household dysfunction:										
Substance abuse	2064	22	19	34	—	34	29	8	69	40
Mental illness	1512	30	22	37	46	—	26	7	74	47
Mother treated violently	1010	34	31	41	59	38	—	10	86	62
Member imprisoned	271	29	29	40	62	42	37	—	86	64
	median	29.5	25.4	40.5	48.5	38	32	8.5	80	54.5
	range	(22–54)	(19–52)	(34–47)	(39–62)	(31–50)	(23–39)	(6–10)	(65–93)	(40–74)

*Number exposed to first category. For example, among persons who were psychologically abused, 52% were also physically abused. More persons were a second category than would be expected by chance ($P < .001$; chi-square).

persons with 4 categories of exposure were compared to those with none, the odds ratios ranged from 1.3 for physical inactivity to 12.2 for suicide attempts (Table 4).

Similarly, the prevalence and risk (adjusted odds ratio) of alcoholism, use of illicit drugs, injection of illicit drugs, ≥ 50 intercourse partners, and history of a sexually transmitted disease increased as the number of childhood exposures increased (Table 5). In comparing persons with ≥ 4 childhood exposures to those with none, odds ratios ranged from 2.5 for sexually transmitted diseases to 7.4 for alcoholism and 10.3 for injected drug use.

Childhood Exposures and Clustering of Health Risk Factors

We found a strong relationship between the number of childhood exposures and the number of health risk factors for leading causes of death in adults (Table 6). For example, among persons with no childhood exposures, 56% had none of the 10 risk factors whereas only 14% of persons with ≥ 4 categories of childhood exposure had no risk factors. By contrast, only 1% of persons with no childhood exposures had four or more risk factors, whereas 7% of persons with ≥ 4 childhood exposures had four or more risk factors (Table 6).

Relationship between Childhood Exposures and Disease Conditions

When persons with 4 or more categories of childhood exposure were compared to those with none, the odds ratios for the presence of studied disease conditions ranged from 1.6 for diabetes to 3.9 for chronic bronchitis or emphysema (Table 7). Similarly, the odds ratios for skeletal fractures, hepatitis or jaundice, and poor self-rated health were 1.6, 2.3, and 2.2, respectively (Table 8).

Significance of Dose-Response Relationships

In logistic regression models (which included age, gender, race, and educational attainment as covariates) we found a strong, dose-response relationship between the number of childhood exposures and each of the 10 risk factors for the leading causes of death that we studied ($P < .001$). We also found a significant ($P < .05$) dose-response relationship between the number of childhood exposures and the following disease conditions: ischemic heart disease, cancer, chronic bronchitis or emphysema, history of hepatitis or jaundice, skeletal fractures, and poor self-rated health. There was no statistically significant dose-response relationship for a history of stroke or diabetes.

Table 3. Prevalence of categories of adverse childhood exposures by demographic characteristics

Characteristic	Sample size (N)	Number of categories (%) ^a				
		0	1	2	3	4
Age group (years)						
19–34	807	35.4	25.4	17.2	11.0	10.9
35–49	2,063	39.3	25.1	15.6	9.1	10.9
50–64	2,577	46.5	25.2	13.9	7.9	6.6
≥65	2,610	60.0	24.5	8.9	4.2	2.4
Gender ^b						
Women	4,197	45.4	24.0	13.4	8.7	8.5
Men	3,859	53.7	25.8	11.6	5.0	3.9
Race ^b						
White	6,432	49.7	25.3	12.4	6.7	6.0
Black	385	38.8	25.7	16.3	12.3	7.0
Hispanic	431	42.9	24.9	13.7	7.4	11.2
Asian	508	66.0	19.0	9.9	3.4	1.7
Other	300	41.0	23.5	13.9	9.5	12.1
Education ^b						
No HS diploma	480	56.5	21.5	8.4	6.5	7.2
HS graduate	1,536	51.6	24.5	11.3	7.4	5.2
Any college	2,541	44.1	25.5	14.8	7.8	7.8
College graduate	3,499	51.4	25.1	12.1	6.1	5.3
All participants	8,056	49.5	24.9	12.5	6.9	6.2

^aThe number of categories of exposure was simply the sum of each of the seven individual categories that were assessed (see Table 1).

^bPrevalence estimates adjusted for age.

Assessment of the Influence of Exclusions

In the sensitivity analysis where missing information for a category of childhood exposure was considered as no exposure, the direction and strength of the associations between the number of childhood exposures and the risk factors and disease conditions were nearly identical (data not shown). Thus, the results we present appear to be unaffected by our decision to exclude persons for whom information on any category of childhood exposure was incomplete.

Discussion

We found a strong dose response relationship between the breadth of exposure to abuse or household dysfunction during childhood and multiple risk factors for several of the leading causes of death in adults. Disease conditions including ischemic heart disease, cancer, chronic lung disease, skeletal fractures, and liver disease, as well as poor self-rated health also showed a graded relationship to the breadth of childhood exposures. The findings suggest that the impact of these adverse childhood experiences on adult health status is strong and cumulative.

The clear majority of patients in our study who were exposed to one category of childhood abuse or household dysfunction were also exposed to at least one other. Therefore, researchers trying to understand the long-term health implications of childhood abuse may benefit from considering a wide range of related adverse childhood exposures. Certain adult health out-

comes may be more strongly related to unique combinations or the intensity of adverse childhood exposures than to the total breadth of exposure that we used for our analysis. However, the analysis we present illustrates the need for an overview of the net effects of a *group* of complex interactions on a wide range of health risk behaviors and diseases.

Several potential limitations need to be considered when interpreting the results of this study. The data about adverse childhood experiences are based on self-report, retrospective, and can only demonstrate associations between childhood exposures and health risk behaviors, health status, and diseases in adulthood. Second, some persons with health risk behaviors or diseases may have been either more, or less, likely to report adverse childhood experiences. Each of these issues potentially limits inferences about causality. Furthermore, disease conditions could be either over- or under-reported by patients when they complete the medical questionnaire. In addition, there may be mediators of the relationship between childhood experiences and adult health status other than the risk factors we examined. For example, adverse childhood experiences may affect attitudes and behaviors toward health and health care, sensitivity to internal sensations, or physiologic functioning in brain centers and neurotransmitter systems. A more complete understanding of these issues is likely to lead to more effective ways to address the long-term health problems associated with childhood abuse and household dysfunction.

However, our estimates of the prevalence of child-

Table 4. Number of categories of adverse childhood exposure and the adjusted odds of risk factors including current smoking, severe obesity, physical inactivity, depressed mood, and suicide attempt

Health problem	Number of categories	Sample size (N) ^a	Prevalence (%) ^b	Adjusted odds ratio ^c	95% confidence interval
Current smoker ^d	0	3,836	6.8	1.0	Referent
	1	2,005	7.9	1.1	(0.9–1.4)
	2	1,046	10.3	1.5	(1.1–1.8)
	3	587	13.9	2.0	(1.5–2.6)
	4 or more	544	16.5	2.2	(1.7–2.9)
	Total	8,018	8.6	—	—
Severe obesity ^d (BMI ≥ 35)	0	3,850	5.4	1.0	Referent
	1	2,004	7.0	1.1	(0.9–1.4)
	2	1,041	9.5	1.4	(1.1–1.9)
	3	590	10.3	1.4	(1.0–1.9)
	4 or more	543	12.0	1.6	(1.2–2.1)
	Total	8,028	7.1	—	—
No leisure-time physical activity	0	3,634	18.4	1.0	Referent
	1	1,917	22.8	1.2	(1.1–1.4)
	2	1,006	22.0	1.2	(1.0–1.4)
	3	559	26.6	1.4	(1.1–1.7)
	4 or more	523	26.6	1.3	(1.1–1.6)
	Total	7,639	21.0	—	—
Two or more weeks of depressed mood in the past year	0	3,799	14.2	1.0	Referent
	1	1,984	21.4	1.5	(1.3–1.7)
	2	1,036	31.5	2.4	(2.0–2.8)
	3	584	36.2	2.6	(2.1–3.2)
	4 or more	542	50.7	4.6	(3.8–5.6)
	Total	7,945	22.0	—	—
Ever attempted suicide	0	3,852	1.2	1.0	Referent
	1	1,997	2.4	1.8	(1.2–2.6)
	2	1,048	4.3	3.0	(2.0–4.6)
	3	587	9.5	6.6	(4.5–9.8)
	4 or more	544	18.3	12.2	(8.5–17.5)
	Total	8,028	3.5	—	—

^aSample sizes will vary due to incomplete or missing information about health problems.

^bPrevalence estimates are adjusted for age.

^cOdds ratios adjusted for age, gender, race, and educational attainment.

^dIndicates information recorded in the patient's chart before the study questionnaire was mailed.

hood exposures are similar to estimates from nationally representative surveys, indicating that the experiences of our study participants are comparable to the larger population of U.S. adults. In our study, 23.5% of participants reported having grown up with an alcohol abuser; the 1988 National Health Interview Survey estimated that 18.1% of adults had lived with an alcohol abuser during childhood.⁴¹ Contact sexual abuse was reported by 22% of respondents (28% of women and 16% of men) in our study. A national telephone survey of adults in 1990 using similar criteria for sexual abuse estimated that 27% of women and 16% of men had been sexually abused.¹²

There are several reasons to believe that our estimates of the long-term relationship between adverse childhood experiences and adult health are conservative. Longitudinal follow-up of adults whose childhood abuse was well documented has shown that their retrospective reports of childhood abuse are likely to under-

estimate actual occurrence.^{47,48} Underestimates of childhood exposures would result in downwardly biased estimates of the relationships between childhood exposures and adult health risk behaviors and diseases. Another potential source of underestimation of the strength of these relationships is the lower number of childhood exposures reported by older persons in our study. This may be an artifact caused by premature mortality in persons with multiple adverse childhood exposures; the clustering of multiple risk factors among persons with multiple childhood exposures is consistent with this hypothesis. Thus, the true relationships between adverse childhood exposures and adult health risk behaviors, health status, and diseases may be even stronger than those we report.

An essential question posed by our observations is, “Exactly how are adverse childhood experiences linked to health risk behaviors and adult diseases?” The link-

Table 5. Number of categories of adverse childhood exposure and the prevalence and risk (adjusted odds ratio) of health risk factors including alcohol or drug abuse, high lifetime number of sexual partners, or history of sexually transmitted disease

Health problem	Number of categories	Sample size (N) ^a	Prevalence (%) ^b	Adjusted odds ratio ^c	95% confidence interval
Considers self an alcoholic	0	3,841	2.9	1.0	Referent
	1	1,993	5.7	2.0	(1.6–2.7)
	2	1,042	10.3	4.0	(3.0–5.3)
	3	586	11.3	4.9	(3.5–6.8)
	4 or more	540	16.1	7.4	(5.4–10.2)
	Total	8,002	5.9	—	—
Ever used illicit drugs	0	3,856	6.4	1.0	Referent
	1	1,998	11.4	1.7	(1.4–2.0)
	2	1,045	19.2	2.9	(2.4–3.6)
	3	589	21.5	3.6	(2.8–4.6)
	4 or more	541	28.4	4.7	(3.7–6.0)
	Total	8,029	11.6	—	—
Ever injected drugs	0	3,855	0.3	1.0	Referent
	1	1,996	0.5	1.3	(0.6–3.1)
	2	1,044	1.4	3.8	(1.8–8.2)
	3	587	2.3	7.1	(3.3–15.5)
	4 or more	540	3.4	10.3	(4.9–21.4)
	Total	8,022	0.8	—	—
Had 50 or more intercourse partners	0	3,400	3.0	1.0	Referent
	1	1,812	5.1	1.7	(1.3–2.3)
	2	926	6.1	2.3	(1.6–3.2)
	3	526	6.3	3.1	(2.0–4.7)
	4 or more	474	6.8	3.2	(2.1–5.1)
	Total	7,138	4.4	—	—
Ever had a sexually transmitted disease ^d	0	3,848	5.6	1.0	Referent
	1	2,001	8.6	1.4	(1.1–1.7)
	2	1,044	10.4	1.5	(1.2–1.9)
	3	588	13.1	1.9	(1.4–2.5)
	4 or more	542	16.7	2.5	(1.9–3.2)
	Total	8023	8.2	—	—

^aSample sizes will vary due to incomplete or missing information about health problems.

^bPrevalence estimates are adjusted for age.

^cOdds ratios adjusted for age, gender, race, and educational attainment.

^dIndicates information recorded in the patient's chart before the study questionnaire was mailed.

ing mechanisms appear to center on behaviors such as smoking, alcohol or drug abuse, overeating, or sexual behaviors that may be consciously or unconsciously used because they have immediate pharmacological or psychological benefit as coping devices in the face of the stress of abuse, domestic violence, or other forms of

family and household dysfunction. High levels of exposure to adverse childhood experiences would expectedly produce anxiety, anger, and depression in children. To the degree that behaviors such as smoking, alcohol, or drug use are found to be effective as coping devices, they would tend to be used chronically. For

Table 6. Relationship between number of categories of childhood exposure and number of risk factors for the leading causes of death^a

Number of categories	Sample size	% with number of risk factors				
		0	1	2	3	4
0	3,861	56	29	10	4	1
1	2,009	42	33	16	6	2
2	1,051	31	33	20	10	4
3	590	24	33	20	13	7
≥4	545	14	26	28	17	7
Total	8,056	44	31	15	7	3

^aRisk factors include: smoking, severe obesity, physical inactivity, depressed mood, suicide attempt, alcoholism, any drug use, injected drug use, ≥50 lifetime sexual partners, and history of a sexually transmitted disease.

Table 7. Number of categories of adverse childhood exposure and the prevalence and risk (adjusted odds ratio) of heart attack, cancer, stroke, COPD, and diabetes

Disease condition ^d	Number of categories	Sample size (N) ^a	Prevalence (%) ^b	Adjusted odds ratio ^c	95% confidence interval
Ischemic heart disease	0	3,859	3.7	1.0	Referent
	1	2,009	3.5	0.9	(0.7–1.3)
	2	1,050	3.4	0.9	(0.6–1.4)
	3	590	4.6	1.4	(0.8–2.4)
	4 or more	545	5.6	2.2	(1.3–3.7)
	Total	8,022	3.8	—	—
Any cancer	0	3,842	1.9	1.0	Referent
	1	1,995	1.9	1.2	(1.0–1.5)
	2	1,043	1.9	1.2	(1.0–1.5)
	3	588	1.9	1.0	(0.7–1.5)
	4 or more	543	1.9	1.9	(1.3–2.7)
	Total	8,011	1.9	—	—
Stroke	0	3,832	2.6	1.0	Referent
	1	1,993	2.4	0.9	(0.7–1.3)
	2	1,042	2.0	0.7	(0.4–1.3)
	3	588	2.9	1.3	(0.7–2.4)
	4 or more	543	4.1	2.4	(1.3–4.3)
	Total	7,998	2.6	—	—
Chronic bronchitis or emphysema	0	3,758	2.8	1.0	Referent
	1	1,939	4.4	1.6	(1.2–2.1)
	2	1,009	4.4	1.6	(1.1–2.3)
	3	565	5.7	2.2	(1.4–3.3)
	4 or more	512	8.7	3.9	(2.6–5.8)
	Total	7,783	4.0	—	—
Diabetes	0	3,850	4.3	1.0	Referent
	1	2,002	4.1	1.0	(0.7–1.3)
	2	1,046	3.9	0.9	(0.6–1.3)
	3	587	5.0	1.2	(0.8–1.9)
	4 or more	542	5.8	1.6	(1.0–2.5)
	Total	8,027	4.3	—	—

^aSample sizes will vary due to incomplete or missing information about health problems.

^bPrevalence estimates are adjusted for age.

^cOdds ratios adjusted for age, gender, race, and educational attainment.

^dIndicates information recorded in the patient's chart before the study questionnaire was mailed.

example, nicotine is recognized as having beneficial psychoactive effects in terms of regulating affect⁴⁹ and persons who are depressed are more likely to smoke.^{50,51} Thus, persons exposed to adverse childhood experiences may benefit from using drugs such as nicotine to regulate their mood.^{49,52}

Consideration of the positive neuroregulatory effects of health-risk behaviors such as smoking may provide biobehavioral explanations⁵³ for the link between adverse childhood experiences and health risk behaviors and diseases in adults. In fact, we found that exposure to higher numbers of categories of adverse childhood experiences increased the likelihood of smoking by the age of 14, chronic smoking as adults, and the presence of smoking-related diseases. Thus, smoking, which is medically and socially viewed as a “problem” may, from the perspective of the user, represent an effective immediate solution that leads to chronic use. Decades later, when this “solution” manifests as emphysema, cardiovascular disease, or malignancy, time and the

tendency to ignore psychological issues in the management of organic disease make improbable any full understanding of the original causes of adult disease (Figure 2). Thus, incomplete understanding of the possible benefits of health risk behaviors leads them to be viewed as irrational and having solely negative consequences.

Because adverse childhood experiences are common and they have strong long-term associations with adult health risk behaviors, health status, and diseases, increased attention to primary, secondary, and tertiary prevention strategies is needed. These strategies include prevention of the occurrence of adverse childhood experiences, preventing the adoption of health risk behaviors as responses to adverse experiences during childhood and adolescence, and, finally, helping change the health risk behaviors and ameliorating the disease burden among adults whose health problems may represent a long-term consequence of adverse childhood experiences.

Table 8. Number of categories of adverse childhood exposure and the prevalence and risk (adjusted odds ratio) of skeletal fracture, hepatitis or jaundice, and poor self-rated health

Disease condition	Number of categories	Sample size (N) ^a	Prevalence (%) ^b	Adjusted odds ratio ^c	95% confidence interval
Ever had a skeletal fracture	0	3,843	3.6	1.0	Referent
	1	1,998	4.0	1.1	(1.0–1.2)
	2	1,048	4.5	1.4	(1.2–1.6)
	3	587	4.0	1.2	(1.0–1.4)
	4 or more	544	4.8	1.6	(1.3–2.0)
	Total	8,020	3.9	—	—
Ever had hepatitis or jaundice	0	3,846	5.3	1.0	Referent
	1	2,006	5.5	1.1	(0.9–1.4)
	2	1,045	7.7	1.8	(1.4–2.3)
	3	590	10.2	1.6	(1.2–2.3)
	4 or more	543	10.7	2.4	(1.8–3.3)
	Total	8,030	6.5	—	—
Fair or poor self-rated health	0	3,762	16.3	1.0	Referent
	1	1,957	17.8	1.2	(1.0–1.4)
	2	1,029	19.9	1.4	(1.2–1.7)
	3	584	20.3	1.4	(1.1–1.7)
	4 or more	527	28.7	2.2	(1.8–2.7)
	Total	7,859	18.2	—	—

^aSample sizes will vary due to incomplete or missing information about health problems.

^bPrevalence estimates are adjusted for age and gender.

^cOdds ratios adjusted for age, gender, race, and educational attainment.

^dIndicates information recorded in the patient's chart before the study questionnaire was mailed.

Primary prevention of adverse childhood experiences has proven difficult^{54,55} and will ultimately require societal changes that improve the quality of family and household environments during childhood. Recent research on the long-term benefit of early home visitation on reducing the prevalence of adverse childhood experiences is promising.⁵⁶ In fact, preliminary data from the ACE Study provided the impetus for the Kaiser Health Plan to provide funding to participate at 4 locations (including San Diego County, California) in the Commonwealth Fund's "Healthy Steps" program. This program extends the traditional practice of pediatrics by adding one or more specialists in the developmental and psychosocial dimensions of both childhood and parenthood. Through a series of office visits, home visits, and a telephone advice line for parents, these specialists develop close relationships between children and their families from birth to 3 years of age. This approach is consistent with the recommendation of the U.S. Advisory Board on Child Abuse and Neglect that a universal home visitation program for new parents be developed^{57,58} and provides an example of a family-based primary prevention effort that is being explored in a managed care setting. If these types of approaches can be replicated and implemented on a large scale, the long-term benefits may include, somewhat unexpectedly, substantial improvements in overall adult health.

Secondary prevention of the effects of adverse childhood experiences will first require increased recognition of their occurrence and second, an effective un-

derstanding of the behavioral coping devices that commonly are adopted to reduce the emotional impact of these experiences. The improbability of giving up an immediate "solution" in return for a nebulous long-term health benefit has thwarted many well-intended preventive efforts. Although articles in the general medical literature are alerting the medical community to the fact that childhood abuse is common,⁵⁹ adolescent health care is often inadequate in terms of psychosocial assessment and anticipatory guidance.⁶⁰ Clearly, comprehensive strategies are needed to identify and intervene with children and families who are at risk for these adverse experiences and their related outcomes.⁶¹ Such strategies should include increased communication between and among those involved in family practice, internal medicine, nursing, social work, pediatrics, emergency medicine, and preventive medicine and public health. Improved understanding is also needed of the effects of childhood exposure to domestic violence.^{19,62} Additionally, increased physician training⁶³ is needed to recognize and coordinate the management of all persons affected by child abuse, domestic violence, and other forms of family adversity such as alcohol abuse or mental illness.

In the meantime, tertiary care of adults whose health problems are related to experiences such as childhood abuse⁵ will continue to be a difficult challenge. The relationship between childhood experiences and adult health status is likely to be overlooked in medical practice because the time delay between exposure

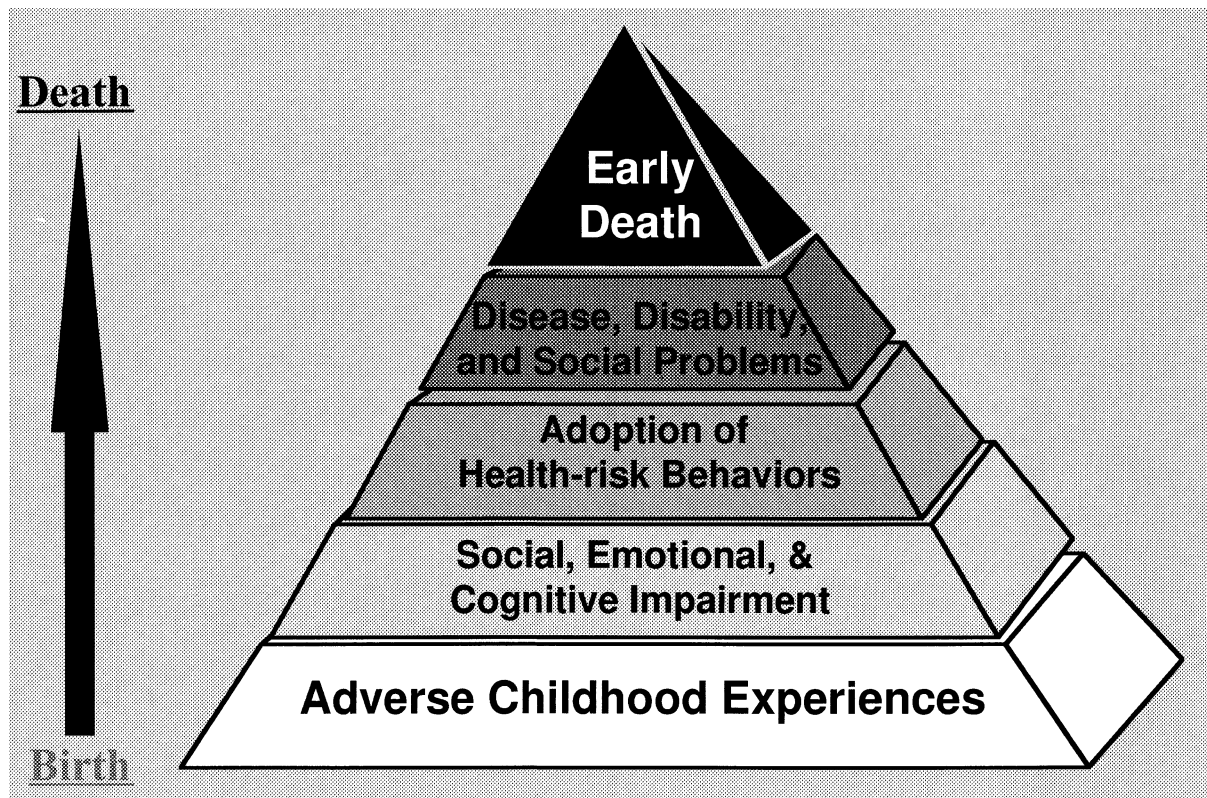


Figure 2. Potential influences throughout the lifespan of adverse childhood experiences.

during childhood and recognition of health problems in adult medical practice is lengthy. Moreover, these childhood exposures include emotionally sensitive topics such as family alcoholism^{29,30} and sexual abuse.⁶⁴ Many physicians may fear that discussions of sexual violence and other sensitive issues are too personal even for the doctor-patient relationship.⁶⁵ For example, the American Medical Association recommends screening of women for exposure to violence at every entrance to the health system;⁶⁶ however, such screening appears to be rare.⁶⁷ By contrast, women who are asked about exposure to sexual violence say they consider such questions to be welcome and germane to routine medical care,⁶⁸ which suggests that physicians' fears about patient reactions are largely unfounded.

Clearly, further research and training are needed to help medical and public health practitioners understand how social, emotional, and medical problems are linked throughout the lifespan (Figure 2). Such research and training would provide physicians with the confidence and skills to inquire and respond to patients who acknowledge these types of childhood exposures. Increased awareness of the frequency and long-term consequences of adverse childhood experiences may also lead to improvements in health promotion and disease prevention programs. The magnitude of the difficulty of introducing the requisite changes into

medical and public health research, education, and practice can be offset only by the magnitude of the implications that these changes have for improving the health of the nation.

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Research article

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Adverse childhood experiences and prescription drug use in a cohort study of adult HMO patients

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Abstract

Background: Prescription drugs account for approximately 11% of national health expenditures. Prior research on adverse childhood experiences (ACEs), which include common forms of child maltreatment and related traumatic stressors, has linked them to numerous health problems. However, data about the relationship of these experiences to prescription drug use are scarce.

Method: We used the ACE Score (an integer count of 8 different categories of ACEs) as a measure of cumulative exposure to traumatic stress during childhood. We prospectively assessed the relationship of the Score to prescription drug use in a cohort of 15,033 adult HMO patients (mean follow-up: 6.1 years) and assessed mediation of this relationship by documented ACE-related health and social problems.

Results: Nearly 1.2 million prescriptions were recorded; prescriptions rates increased in a graded fashion as the ACE Score increased (p for trend < 0.0001). Compared to persons with an ACE Score of 0, persons with a Score ≥ 5 had rates increased by 40%; graded relationships were seen for all age groups (18–44, 45–64, and 65–89 years) (p for trend < 0.01). Graded relationships were observed for the risk of being in the upper decile of number of classes of drugs used; persons with scores of ≥ 5 had this risk increased 2-fold. Adjustment for ACE-related health problems reduced the strength of the associations by more than 60%.

Conclusion: ACEs substantially increase the number of prescriptions and classes of drugs used for as long as 7 or 8 decades after their occurrence. The increases in prescription drug use were largely mediated by documented ACE-related health and social problems.

Background

A growing body of literature suggests that child maltreatment and traumatic stressors have long-term consequences for adult health behavior and adult health outcomes. Adults with a history of child maltreatment

have been shown to be at increased risk of multiple health risk behaviors and risk factors for chronic disease including overweight or obesity [1,2], smoking [3-5], and physical inactivity [6], and some have reported associations with higher prevalences of heart [7-9], lung [10], and

liver[11] disease, diabetes [9], and depression or depressive disorders [12-17] – chronic conditions associated with higher health care service utilization.

Health care resources are scarce, and therefore research focused on explaining and/or predicting utilization of health care services is both of interest and of importance to policymakers. Use of prescription drugs, one of the most rapidly growing sectors of health care in the US, has increased substantially over the past 10 to 15 years, although use of some prescription drugs, such as hormone replacement therapy [18] and alpha- (α -) blockers [19], has decreased. In 2000, three in five US adults filled at least one prescription. [20] Nationally, the number of purchased prescription drugs increased 75% between 1993 and 2005 from 2.0 to 3.5 billion per year. [21,22] In 2004 an estimated 45% of American adults were taking prescription drugs on a regular basis and 27% were taking them occasionally [23].

Increases in prescribed drug use are reflected in expenditures for these medications. Spending on prescription drugs in the United States in 2003 was nearly \$180 billion, or 11% of total national health expenditures, and was more than four times the amount spent on prescription drugs in 1990.[24] Future spending on prescription drugs is projected to increase 10.5% between 2005 and 2013, but this may turn out to be an underestimate as the projection was made before the passage of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 [25].

Few studies have assessed the relationship of child maltreatment and related traumatic stressors to the use of prescription drugs in adulthood. [26-29] Our earlier analyses of data from the Adverse Childhood Experiences (ACE) Study have demonstrated that an integer count of the number of categories of abuse, exposure to domestic violence, and other forms of serious household dysfunction

(the ACE Score) [30] experienced during childhood has a strong graded relationship to a wide variety of health and social problems from adolescence to adulthood (Table 1). [2,3,6,7,11,12,31-43] Therefore, we hypothesized that the ACE Score would be associated with increased rates and number of classes of prescriptions drugs used during an average of 6.1 years of follow-up of adults in the ACE Study cohort.

Methods
Study population

The ACE Study methods have been described in detail elsewhere. [3,6,31] Briefly, more than 50,000 adult members of the Kaiser Health Plan in San Diego, California are evaluated annually for wellness care at Kaiser Permanente's San Diego Health Appraisal Clinic (HAC) which includes a standardized health history, psychosocial evaluations, and physical examination. Appointments for most members are obtained by self-referral with 20% referred by their health care provider. [6] A review of continuously enrolled (between 1992 and 1995) Kaiser Permanente members aged 25 years or older in San Diego revealed that 81% of those members had been evaluated at the Health Appraisal Clinic. [6] The ACE Study was approved by the institutional review board of Kaiser Permanente and written informed consent was given by study participants.

Within two weeks of their HAC visit, each member who completed the standardized evaluation during the baseline survey period (August 1995 to October 1997) was mailed a study questionnaire that contained questions about childhood exposure to abuse, neglect, domestic violence, and other forms of serious and interrelated household dysfunction. [30] A total of 17 421 (68%) responded; 84 persons had incomplete information on race and educational attainment leaving an analytic sample of 17 337 persons [32].

Table 1: Health and social problems shown to have a graded relationship to the ACE Score

Type of Problem	Outcomes Associated with Adverse Childhood Experiences
Prevalent Diseases	Ischemic heart disease ^{6,7} cancer, ⁶ chronic lung disease, ⁶ skeletal fractures, ⁶ sexually transmitted diseases, ^{6,32,33} and liver disease ^{6,11}
Risk Factors for Common Diseases/Poor Health	Smoking, ^{3,6,31,32} alcohol abuse, ^{12,31,32,34} promiscuity, ^{6,31,32,35} obesity, ^{2,6,31} illicit drug use, ^{6,31,32,36} injected drug use, ^{6,31,36} multiple somatic symptoms, ³¹ poor self-rated health, ⁶ high perceived risk of AIDS ³⁵
Poor Mental Health	Depressive disorders, ^{6,31,32,37} anxiety, ³¹ hallucinations, ^{31,38} panic reactions, ³¹ sleep disturbances, ³¹ memory disturbances, ^{31,39} poor anger control, ³¹ risk of perpetrating or being a victim of domestic violence ³¹
Sexual and Reproductive Health	Early age at first intercourse, ^{31,35} sexual dissatisfaction, ³¹ teen pregnancy, ⁴⁰ unintended pregnancy, ⁴¹ teen paternity, ⁴² fetal death ⁴⁰
General Health and Social Problems	High perceived stress, ³¹ difficulty with job performance, ⁴³ relationship problems, ⁴³ marriage to an alcoholic ³⁴

* A complete bibliography of ACE Study publications listed by topic area is available.⁵⁷

Table 2: Definition and prevalence of each category of adverse childhood experience

Childhood Abuse	
<i>Emotional</i>	10.3%
<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 that you might be physically hurt?	
Physical	28.0%
<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?	
Sexual	20.4%
<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	
Substance abuse	26.6%
1) Live with anyone who was a problem drinker or alcoholic?	
2) Live with anyone who used street drugs?	
Mental illness	19.0%
1) Was a household member depressed or mentally ill?	
2) Did a household member attempt suicide?	
Mother treated violently	12.6%
(Was your mother (or stepmother)):	
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?	
Incarcerated household member	4.5%
1) Did a household member go to prison?	
Parental separation or divorce	22.8%
1) Were your parents ever separated or divorced?	
Number of adverse childhood experiences (ACE Score)	
0	36.4%
1	26.2%
2	15.9%
3	9.3%
4	6.1%
5 or more	6.1%

* Percentages based on a total of 15,033 adults included in the analysis sample

Eligibility for the Prospective (Follow-up) Phase of the Study

Follow-up data on the use of prescription drugs was available from Kaiser Permanente from January 1, 1997 through December 31, 2004. We excluded 18 persons aged 90 years or older to facilitate direct age standardization to the 2000 US population. We also excluded 1053 (6%) persons whose membership had lapsed prior to their evaluation at the HAC or before January 1, 1997 or whose member record number was not considered valid.

In addition, among persons who disenrolled and reenrolled at least once (median/mean: 1 time; range: 1–6 times) during the follow-up period, we excluded the 1233 (7%) persons whose ratio of time disenrolled/total possible time enrolled during follow-up exceeded 20%; we considered such persons to have inadequate continuity of follow-up to merit inclusion in the prospective analysis. Thus, the final sample retained 15 033 of the 17 337 persons included in the baseline survey (87%).

To assess any influence of including persons with discontinuous follow-up who had a ratio as described of ($\leq 20\%$), we repeated the analyses included herein after excluding any persons whose follow-up was discontinuous.

Relationship of the ACE Score to Exclusion from Follow-up

We used logistic regression to assess the probability that the ACE Score might be related to excluding from follow-up. In this analysis, the risks (ORs) of exclusion from follow-up for persons with 1, 2, 3, or ≥ 4 ACEs were 1.0 (0.9–1.1), 1.0 (0.9–1.2), 1.2 (1.0–1.4) and 1.1 (0.9–1.3), respectively, and thus we ruled out exclusion from follow-up as a potential source of bias.

Definitions of Adverse Childhood Experiences (ACEs)

All questions used to define ACEs pertained to the respondents' first 18 years of life (≤ 18 years of age) (Table 2). Questions adapted from the Conflict Tactics Scale (CTS) [44] had 5 response categories: "never", "once or twice", "sometimes", "often", or "very often". We defined 3 types of childhood abuse: emotional abuse (2 questions), physical abuse (2 questions), or contact sexual abuse (4 questions) by Wyatt. [45] We also defined 5 exposures to household dysfunction during childhood: exposure to substance abuse (defined by 2 questions) [46], mental illness (2 questions), violent treatment of mother or stepmother (4 questions) [44], criminal behavior in the household (1 question), and parental separation or divorce (1 question). Respondents were defined as exposed to a category if they responded "yes" to 1 or more of the questions in that category.

To assess the cumulative effect of early trauma and stress on use of prescription drugs, the total number of these categories of childhood exposures (range: 0–8) was summed to create the ACE Score (Table 2). The statistical characteristics and validity of the ACE Score have been published elsewhere [30].

Rates of Prescription Drug Use

To calculate rates of prescription drug use, we divided total claims for prescription drugs by the cumulative person-time at risk during follow-up. Person-time at risk was calculated using electronic enrollment data files provided by Kaiser Permanente. Because pharmacy claims data were not available before January 1, 1997, we designated this date as beginning of follow-up for persons enrolled before January 1, 1997. We counted prescription medications through December 31, 2004 (latest available data).

We calculated the maximum possible person-time at risk as the difference between December 31, 2004 and the later of either January 1, 1997 or the baseline appointment date for persons who were continuously enrolled.

For persons with periods of disenrollment from their baseline appointment date to December 31, 2004, follow-up time was calculated as the maximum possible person-time less periods of disenrollment.

Use of Multiple Classes of Prescription Drugs

The Kaiser pharmacy database includes 15 classes of drugs: anti-infectives, endocrine and metabolic, cardiovascular, respiratory, gastrointestinal, genitourinary, central nervous system, analgesics and anesthetics, neuromuscular, topical products, biologics, antineoplastics, nutritional, hematological agents, and other drugs. On an *a priori* basis we chose the approximate age-specific upper decile of the number of classes of prescription drugs used during follow-up to define persons as having used multiple classes of pharmaceuticals. The approximate upper deciles for the age groups 18–44 years, 45–64 years, and 65–89 years were 8, 10, and 11, respectively; the prevalence of persons in each of these age-specific groups was 17%, 12%, and 15%, respectively (total = 14%).

Statistical Analysis

Analyses were completed using SAS v8.2 (SAS Institute, Cary, NC). [47] We used the 2000 US Standard Population for direct age-standardization of prevalences and risks.

To assess the independent relationship between the ACE Score and the rate of prescription drug use, we used rate ratios derived from multivariable-adjusted negative binomial regression models employing PROC GENMOD. [47] To allow for differing lengths of follow-up, the log of person-time was incorporated as the offset in the model. Rate ratios were obtained by exponentiating estimated regression coefficients. Age, race/ethnicity, educational attainment and sex were forced into all models.

We used multivariable adjusted logistic regression to assess the relationship of the ACE Score to prescription of multiple classes of drugs and included the following covariates: age at baseline, sex, race (white, nonwhite), and education ($<$ high school, high school, some college, college graduate). All statistical inferences were based on a significance level of α (2-sided) = 0.05.

Assessment of Mediation by Documented ACE-related Health and Social Problems

Previously, we have reported graded relationships between the ACE Score and multiple health and social outcomes (Table 1) that ultimately lead a physician to prescribe medication. Therefore, we hypothesized that the presence of these conditions would mediate the relationship of the ACE Score to use of prescription pharmaceuticals. To examine this issue, we used logistic regression models without (Model A) and with (Model B) each of

the health and social problems from Table 1 (coded dichotomously (yes/no). We compared the reduction in the strength of the relationship (odds ratio) between Model A and Model B using the risk decrement which was expressed as a percent and calculated as follows:

$$\frac{\text{Model A odds ratio} - \text{Model B odds ratio}}{\text{Model A odds ratio} - 1} \times 100.$$

Results

Characteristics of Study Population

The study population included 8134 women (54%) and 6899 men (46%). The mean age (standard deviation) was 57 (15) years. Seventy-six percent were white, 11% Hispanic, 4% Black, 7% Asian, < 1% Native American, and 2% other; 40% were college graduates; 36% had some college education; and 17% were high school graduates. Only 7% had not graduated from high school. The mean length of follow-up was 6.1 (SD, 2.4) years.

The prevalence of each of the 8 individual ACEs and the ACE Score are presented in Table 2. A total of 1 188 052 prescriptions were written during 95 883 person-years of follow-up. The age-standardized prescription rate was 9.6 per person-year (data not shown).

Prescription Rates by ACE Score

As the ACE Score increased, rates of prescription drug use increased in a graded fashion (Table 3). This relationship was graded for each age group but was attenuated among persons 65–89 years. However, the trend was statistically significant for all age groups (Table 3).

Risk of Being Prescribed Multiple Classes of Drugs

As the ACE Score increased, the risk (adjusted odds ratio) of having been prescribed multiple classes of pharmaceuticals also increased in a graded fashion for all age groups (Table 4).

Relationship Between Prescription Rates and Multiple Classes Drugs Used

As the number of classes of drugs used increased, the number of prescriptions also increased (Pearson's correlation = .69; $p < 0.001$). Both the mean and the median rates of prescriptions increased dramatically as the number of classes increased from 0 to 14 (data not shown).

Mediation by ACE-related Health and Social Problems

For persons of all ages, the ACE Score had a graded relationship to rates of prescription drug use (Table 5); for persons with ACE Scores ≥ 5 , the rate increased by more than 40% (Table 5). When we entered the variables for the health and social problems (Table 1) into a model for rates of prescriptions, the relative rates were reduced for each level of the ACE Score; these reductions ranged from 67–70% (median, 69%)(Table 5).

Similarly, for persons of all ages, the risk of being prescribed multiple classes drugs increased in a graded fashion as the ACE Score increased (Model A, Table 5); for persons with ACE Scores ≥ 5 , the risk was increased 2-fold. Entry of the ACE-related health problems into this model reduced the risks (ORs) by 26–67% (median: 61%).

Discussion

In this large study of HMO patients we found that rates of prescriptions increased in a graded fashion as the ACE Score increased. This pattern was particularly evident in the younger age groups – whose rates were increased by as much as 60% for persons with ACE Scores of 5 or more. Previous research has shown ACEs to be associated with earlier onsets of health risks such as smoking [3], alcohol [34] and illicit drug use [36], and sexual intercourse [31,35]. Thus, ACEs may "accelerate" the onset of health risks and illnesses, in the process increasing the use of prescription drugs among younger persons. If this is the case, the greatest relative effects on prescription rates would be expected among younger persons.

Table 3: Prescription drug rates (per person per year) by age group and ACE Score

ACE Score	Age 18–44 years		Age 45–64 years		Age 65–89 years	
	Rate	RR* (95% CI)	Rate	RR* (95% CI)	Rate	RR* (95% CI)
0	5.03	1.00 (referent)	10.18	1.00 (referent)	17.27	1.00 (referent)
1	5.99	1.14 (1.00–1.29)	11.19	1.09 (1.02–1.17)	16.92	0.99 (0.94–1.05)
2	6.86	1.30 (1.13–1.50)	11.33	1.12 (1.04–1.21)	18.10	1.08 (1.00–1.16)
3	6.95	1.33 (1.13–1.56)	12.11	1.17 (1.06–1.28)	17.83	1.04 (0.93–1.15)
4	7.64	1.46 (1.23–1.73)	12.59	1.24 (1.11–1.39)	19.43	1.12 (0.98–1.29)
5 or more	8.84	1.63 (1.38–1.93)	15.48	1.45 (1.30–1.62)	20.67	1.25 (1.05–1.48)
Overall	6.45		11.32		17.47	
p-value, trend		< 0.0001		< 0.0001		0.0025

* Relative rate (RR) and 95% confidence interval (CI) adjusted for age, sex, race, education

Table 4: Prevalence of multiple prescription medication classes (upper decile by age) during follow-up by age group and ACE Score

ACE Score	Age 18–44 years		Age 45–64 years		Age 65–89 years	
	Top 10% (%)	OR* (95% CI)	Top 10% (%)	OR* (95% CI)	Top 10% (%)	OR* (95% CI)
0	12.67	1.00 (referent)	10.14	1.00 (referent)	14.06	1.00 (referent)
1	16.27	1.39 (1.06–1.82)	11.51	1.14 (0.93–1.41)	15.14	1.14 (0.94–1.39)
2	17.54	1.53 (1.14–2.04)	12.08	1.21 (0.96–1.53)	14.56	1.11 (0.87–1.43)
3	18.42	1.51 (1.09–2.09)	13.44	1.38 (1.05–1.80)	16.72	1.26 (0.90–1.76)
4	18.48	1.47 (1.04–2.07)	16.38	1.65 (1.22–2.24)	22.42	1.83 (1.24–2.72)
5 or more	25.27	2.11 (1.54–2.89)	21.52	2.22 (1.68–2.92)	19.23	1.56 (0.93–2.60)
Overall	16.97		12.31		14.98	
p-value, trend		< 0.0001		< 0.0001		0.0020

* Odds ratio (OR) and 95% confidence interval (CI) adjusted for age, sex, race, education

Among older persons, the graded relationship between the ACE Score and prescription rates was attenuated. This could be due to differential morbidity and mortality because ACEs influence a multitude of health and social problems (Table 1). Older persons affected by ACEs might expectedly have higher levels of multimorbidity [31] or severe health problems (such as ischemic heart disease [7] or liver disease [11]), requiring ongoing specialty care. In this scenario, older persons would be less likely to visit a clinic for wellness care and hence, less likely to have enrolled in the study. Moreover, ACE Scores tend to be lower among older persons, [6] possibly as a result of increased mortality over time leading to a decreased likelihood that persons with high levels of ACEs would survive to be in the older age groups included in the study.

Our finding that the risk of being prescribed multiple classes of drugs during follow-up increased in a strong graded fashion as the ACE Score increased lends further support for the idea that ACEs matter long after they occur. We found a 2-fold increase for young and middle-aged persons and 1.7-fold for the older persons with Scores ≥ 5 . Thus, there was little evidence of attenuation among older persons as was observed for rates of prescription use. This is likely due to the choice of the upper decile of number of drug classes – an extreme measure – which may have selected persons with comorbid conditions that resulted from exposure to ACEs. We have previously shown that the mean number of a variety of health-related problems [31] and the number of risk factors for the leading causes of death increases as the ACE Score increases [6].

When we controlled for documented ACE-related health and social problems (Table 1), the apparent effects of ACEs on rates of prescription drug use were reduced by 67–76% (median, (69%); similarly, the risk of using a high number of classes of drugs during follow-up was reduced by 26–67% (median, 61%). Thus, as would be expected, the documented ACE-related conditions among participants appear to account for the majority, although

not all, of the increase use of prescription medications we observed. Because screening for childhood traumatic stressors is not yet a routine part of adult medical care, some clinicians are likely identifying and treating these conditions without a full understanding of their origins in the long-term neurobiologic effects [31,48,49] of childhood stressors.

Relationships between child maltreatment and prescription drug use in adulthood among adult survivors of child maltreatment have been examined previously, but the relationships remain unclear as studies are often limited by study design, use of clinical populations versus community-based samples, self-reported health care service utilization measures, examination of only one or two types of maltreatment, and suboptimal statistical analyses as in the case of no multivariable adjustment of comparisons. In our study, the multivariable-adjusted relative rate of prescriptions as well as the relative risk of use of a high number of classes of drugs increased with a higher ACE Score. In a study of 3333 women aged 18–64 years who were members of a large health maintenance organization in the northwestern United States, Bonomi and colleagues [26] observed that women with a history of both physical and sexual childhood abuse had more pharmacy fills (adjusted incidence rate ratio = 1.57; 95% CI: 1.33–1.86) than women without a history of child physical or sexual abuse. In a study of 150 women aged 17–49 years seen consecutively for non-emergency medical care by a family practitioner in a health maintenance organization, Sansone and colleagues [29] found a significant association between sexual abuse and the number of prescribed medications, obtained from a physician review of patient medical records, during the 12-months following completion of a clinic survey; lifetime physical or emotional abuse were not associated with use. Participants were not queried for abuse that occurred only during childhood; rather, for each type of abuse participants provided an age range during which the event(s) occurred.

Table 5: Rates of prescription drugs and risk (odds ratio) of multiple classes prescribed by ACE Score with and without adjustment for potential mediating health-related conditions shown to have a graded relationship to the ACE Score

Prescription drug rates				
ACE Score	Rate PPPY*	Model A RR† (95% CI)	Model B RR‡ (95% CI)	% Decrease due to mediation
0	8.41	1.00 (referent)	1.00 (referent)	...
1	9.40	1.06 (1.01–1.11)	1.02 (0.98–1.07)	67
2	9.96	1.13 (1.07–1.19)	1.04 (0.99–1.10)	69
3	10.28	1.15 (1.08–1.23)	1.05 (0.99–1.12)	67
4	11.58	1.25 (1.16–1.35)	1.06 (0.98–1.15)	76
5 or more	12.05	1.44 (1.33–1.56)	1.13 (1.05–1.23)	70
Overall	9.59			
p-value, trend		< 0.0001	0.0016	Median = 69

Multiple prescription medication classes				
ACE Score	Proportion in Top Decile*	Model A OR† (95% CI)	Model B OR‡ (95% CI)	% Decrease due to mediation
0	10.84	1.00 (referent)	1.00 (referent)	...
1	13.49	1.19 (1.05–1.35)	1.14 (1.00–1.29)	26
2	14.19	1.24 (1.08–1.43)	1.08 (0.93–1.26)	67
3	15.70	1.33 (1.13–1.58)	1.11 (0.93–1.33)	67
4	17.76	1.57 (1.30–1.90)	1.22 (1.00–1.50)	61
5 or more	20.71	2.00 (1.67–2.40)	1.41 (1.15–1.73)	59
Overall	14.05			
p-value, trend		< 0.0001	0.0026	Median = 61

PPPY, per person per year

* Age standardized using the method of direct standardization and the 2000 US standard population

† Adjusted for age, sex, race, education

‡ Adjusted for age, sex, race, education, and all documented health-related problems shown to have a graded relationship to the ACE Score (see Table 1)

Using data from women members of a health maintenance organization, Farley and Patsalides [27] report significantly more prescription medications obtained from medical record review among women with a history of childhood physical and sexual abuse ($n = 27$) compared to women without a history of either form of abuse ($n = 26$). The study is limited by a low response rate (14%) for the mailed survey, the absence of any quantitative data on the prescription drug use, and the absence of any multivariable adjustment in the statistical comparisons of abuse groups. In a clinical sample of 75 women with fibromyalgia, Alexander and associates [28] observed an increased use of pain medications and greater outpatient service use among women with a history of sexual or physical abuse compared to those without such a history. The study did not stipulate when the abuse occurred (i.e., childhood or adolescence vs adulthood) and did not include multivariable-adjusted statistical analyses.

The analyses herein have several strengths. Prescriptions were obtained prospectively from electronic, administrative pharmacy claims data and therefore are not subject to differential misreporting. The relationship of ACEs to prescription drug use is not limited to any specific class of

drugs (data not shown). Future analyses will detail the relationship of ACEs to increased use of individual classes of drugs.

Our results should be interpreted keeping the following limitations in mind. Because of the sensitive nature of questions about ACEs and affective problems, the responses probably represent an underreporting of their actual occurrence. However, our estimates of the prevalence of childhood exposures are similar to estimates from nationally representative surveys [50,51] indicating that the experiences of our participants are comparable to those of the larger population of adults. For example, in our study we found that 16% of the men and 25% of the women met the case definition for contact sexual abuse; a national telephone survey of adults conducted by Finkelhor and colleagues [52] using similar criteria for sexual abuse estimated that 16% of men and 27% of women had been sexually abused. Of the men in our study, 28% had been physically abused as boys, which closely parallels the percentage (31%) found in a population-based study of men in Ontario that used questions from the same scales. [53] The similarity in estimates of the prevalence of these childhood exposures between the ACE Study and other

population-based studies suggests that our findings are likely to be applicable in other settings. Also, when utilizing retrospective reports of adverse childhood experiences, several factors may inevitably lead to variability in the responses over time. These include difficulty recalling the experiences due to the time lapse between the events in question and the research survey, variability in responses may occur due to the sensitive nature of the questions and the subjects' knowledge of the "social taboos" of responding to such questions, and incomplete or total inability to recall the experiences due to memory impairments as a result of stressful childhood experiences. Dube and associates [54] observed that retrospective responses to childhood abuse and related forms of serious household dysfunction are generally stable over time concluding that there is good to excellent reliability in the reports of adverse childhood experiences during adulthood.

Conclusion

The mind-body dichotomy that persists in Western medical training may lead clinicians away from understanding the role that childhood trauma and stress has on the health of their adult patients. Childhood stressors are known to produce changes in the developing brain that affect emotions, behavior, and cognition [55] which in turn can impair health and quality of life via numerous pathways (Table 1). These traumatic pathophysiological insults may be "silent" until much later in life, [55,56] leading clinicians to prescribe medications to treat symptoms and illnesses without knowledge of their potential origins in the disruptive effects of ACEs on neurodevelopment. As improvements in the treatment of persons affected by traumatic stress evolve, understanding the role of these childhood experiences on adult health will become increasingly important in making decisions about prognosis, diagnosis, and treatment.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Study conception and design: RFA, DWB. Acquisition of data: RFA, VJF, SRD. Analysis and interpretation of data: RFA, DWB, WHG. Drafting of manuscript: RFA, DWB, VJF, SRD, WHG. Critical revision: RFA, DWB, VJF, SRD, WHG. All authors read and approved the final manuscript.

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The Social-Ecological Model: A Framework for Prevention

The ultimate goal is to stop violence before it begins. Prevention requires understanding the factors that influence violence. CDC uses a four-level social-ecological model to better understand violence and the effect of potential prevention strategies.¹ This model considers the complex interplay between individual, relationship, community, and societal factors. It allows us to understand the range of factors that put people at risk for violence or protect them from experiencing or perpetrating violence. The overlapping rings in the model illustrate how factors at one level influence factors at another level.



Besides helping to clarify these factors, the model also suggests that in order to prevent violence, it is necessary to act across multiple levels of the model at the same time. This approach is more likely to sustain prevention efforts over time than any single intervention.

Individual

The first level identifies biological and personal history factors that increase the likelihood of becoming a victim or perpetrator of violence. Some of these factors are age, education, income, substance use, or history of abuse. Prevention strategies at this level are often designed to promote attitudes, beliefs, and behaviors that ultimately prevent violence. Specific approaches may include education and life skills training.

Relationship

The second level examines close relationships that may increase the risk of experiencing violence as a victim or perpetrator. A person's closest social circle-peers, partners and family members-influences their behavior and contributes to their range of experience. Prevention strategies at this level may include parenting or family-focused prevention programs, and mentoring and peer programs designed to reduce conflict, foster problem solving skills, and promote healthy relationships.

Community

The third level explores the settings, such as schools, workplaces, and neighborhoods, in which social relationships occur and seeks to identify the characteristics of these settings that are associated with becoming victims or perpetrators of violence. Prevention strategies at this level are typically designed to impact the social and physical environment – for example, by reducing social isolation, improving economic

and housing opportunities in neighborhoods, as well as the climate, processes, and policies within school and workplace settings.

Societal

The fourth level looks at the broad societal factors that help create a climate in which violence is encouraged or inhibited. These factors include social and cultural norms that support violence as an acceptable way to resolve conflicts. Other large societal factors include the health, economic, educational and social policies that help to maintain economic or social inequalities between groups in society.

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