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## Lifetime Trauma Exposure and Prospective Cardiovascular Events and All-cause Mortality: Findings from the Heart and Soul Study

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### Abstract

**Objective**—Little is known about the effect of cumulative psychological trauma on health outcomes in patients with cardiovascular disease. The objective of this study was to prospectively examine the association between lifetime trauma exposure and recurrent cardiovascular events or all-cause mortality in patients with existing cardiovascular disease.

**Method**—1,021 men and women with cardiovascular disease were recruited in 2000–2002 and followed annually. Trauma history and psychiatric comorbidities were assessed at baseline using the Computerized Diagnostic Interview Schedule for DSM-IV. Health behaviors were assessed using standardized questionnaires. Outcome data was collected annually, and all medical records were reviewed by two independent, blinded physician adjudicators. We used Cox proportional hazards models to evaluate the association between lifetime trauma exposure and the composite outcome of cardiovascular events and all-cause mortality.

**Results**—During an average of 7.5 years follow-up, there were 503 cardiovascular events and deaths. Compared with the 251 participants in the lowest trauma exposure quartile, the 256 participants in the highest exposure quartile had a 38% greater risk of adverse outcomes (HR 1.38, 95% CI 1.06–1.81), adjusted for age, sex, race, income, education, depression, posttraumatic stress disorder, generalized anxiety disorder, smoking, physical inactivity, and illicit drug abuse.

**Conclusions**—Cumulative exposure to psychological trauma was associated with an increased risk of recurrent cardiovascular events and mortality, independent of psychiatric comorbidities and

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### FINANCIAL DISCLOSURE

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health behaviors. These data add to a growing literature showing enduring effects of repeated trauma exposure on health that are independent of trauma-related psychiatric disorders such as depression and posttraumatic stress disorder.

### Keywords

Cardiovascular disease; psychological trauma; myocardial infarction; depression; post-traumatic stress disorder; cardiovascular mortality

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## INTRODUCTION

Population based studies using standardized definitions of trauma report that at least 50% and perhaps as many as 90% of US adults experience a traumatic event in their lifetime.(1–4) Many researchers have theorized that following trauma a vulnerable subgroup of patients develop psychiatric problems, such as posttraumatic stress disorder (PTSD), or negative coping behaviors that can damage physical health. Indeed, large epidemiologic studies in diverse populations have demonstrated that patients with PTSD, depression, or generalized anxiety disorder (GAD) are at significantly increased risk of developing and dying from cardiovascular disease (CVD), the leading cause of mortality in the United States and worldwide.(5–8)

However, the majority of people who experience trauma will not go on to develop chronic mental health disorders, and relatively few studies have examined the association of psychological trauma with CVD risk independent of psychiatric diagnoses. Two studies have linked greater trauma exposure to CVD independent of some psychiatric risk factors, though both relied on self-report without review of medical records to assess CVD. The Adverse Childhood Experiences (ACE) Study focused on childhood trauma alone and found that exposure to a greater number of categories of traumatic events was associated with greater risk of heart disease after adjusting for anger and depression, each assessed with a single item.(9) Another study examined the presence versus absence of lifetime exposure to trauma and found those who had experienced a traumatic event were more likely to report having angina or heart failure after adjusting for depression and PTSD as determined by a validated clinical interview.(10) To date, no published studies have evaluated the effect of cumulative, lifetime trauma exposure on incident CVD outcomes. Furthermore, prior studies have focused on the development of CVD in healthy populations and not on adverse outcomes in patients with existing CVD. Though exposure to acute stress in laboratory settings and during traumatic events, such as the World Trade Center attacks, has been linked to ischemia in patients with existing CVD, the effect of cumulative trauma exposure has not been studied.(11–13) Finally, though trauma has been associated with higher rates of behavioral CVD risk factors such as tobacco use, illicit substance use, physical inactivity, and medication non-adherence, the extent to which these health behaviors explain any association of trauma and adverse outcomes has not been determined.(14–17)

The high prevalence of exposure to traumatic events highlights the need for further study of the association between trauma and adverse outcomes as well as modifiable behaviors and treatable psychiatric conditions that may mediate this relationship. To address these

questions, we examined the association of trauma exposure with carefully adjudicated adverse outcomes in a large prospective cohort of patients with CVD. We controlled for traditional CVD risk factors and explored potentially mediating psychiatric conditions and behavioral factors.

## **METHODS and MATERIALS**

### **Participants**

The Heart and Soul Study is a prospective cohort study designed to determine the mechanism of association between psychological factors and cardiovascular events in patients with CVD. Methods have been described previously.<sup>(7)</sup> Administrative data were used to identify outpatients with documented coronary artery disease at two Department of Veterans Affairs Medical Centers, one University medical center, and nine public health clinics. Patients were eligible to participate if they had known CVD documented by one of the following: history of myocardial infarction, angiographic evidence of ≥50% stenosis in one or more coronary vessels, prior evidence of inducible ischemia by treadmill or nuclear testing, or a history of coronary revascularization. Between September 11, 2000 and December 20, 2002, a total of 1,024 participants were enrolled. Three participants were excluded because they did not complete the Diagnostic Interview Schedule or were lost to follow-up for cardiovascular event data, leaving 1,021 participants for these analyses. Written informed consent was obtained after complete description of the study to participants. The study was approved by the Institutional Review Boards of the University of California, San Francisco and the San Francisco VA Medical Center.

### **Predictor Variable: Traumatic Events**

A lifetime history of 17 traumatic events was assessed using the Computerized Diagnostic Interview Schedule for DSM-IV (CDIS), a validated computer-based interview administered by trained research personnel.<sup>(18)</sup> This standardized tool includes questions about traumatic events (see Figure 1 for complete list). All responses were coded yes/no, and a cumulative score of exposure to different trauma categories was calculated (range 0 to 17). As there is no established cutpoint for significant trauma exposure, we followed standards from prior large epidemiologic studies that used categories based on the number of types of traumatic events reported.<sup>(9, 19–21)</sup> As the number of events was normally distributed, we examined the effect of quartile of trauma exposure on incident CVD events and also compared patients per standard deviation increase in trauma exposure. The lowest trauma exposure quartile included 251 participants who reported three or fewer traumatic events, the second 268 participants who reported 4 or 5 events, the third 246 participants who reported 6 or 7 events, and the highest 256 participants who reported eight or more traumatic events.

### **Outcome Variable: Adverse Outcomes**

Participants or their designated proxies completed annual telephone interviews to assess mortality and CVD events. For all potential events, medical records, electrocardiograms, and death certificates were retrieved and reviewed by two independent, blinded physician adjudicators. In the event of disagreement, the adjudicators conferred, reconsidered their classification, and requested consultation from a third blinded adjudicator as necessary. The

outcome variables included myocardial infarction, stroke/transient ischemic attack, congestive heart failure, and all-cause mortality. All events were defined using standard criteria as reported previously.(7)

### Potential Psychiatric and Behavioral Mediators

At the baseline visit, participants were assessed for major depressive disorder, GAD and PTSD using the CDIS for DSM-IV. As described above, the CDIS is a validated, standardized psychiatric interview administered by trained research personnel.(18) Health behaviors were assessed using standardized questionnaires. Current use of any tobacco was measured by “yes/no” self-report questionnaire. To evaluate illicit substance abuse, participants were asked “Has a doctor or nurse ever told you that you have drug addiction/abuse?” Alcohol use was measured with the AUDIT-C, a validated screening questionnaire that uses three questions to assess frequency and amount of alcohol use and yields a total score of 0–12. Regular alcohol use was defined as a score of >3. To assess physical activity, we asked “Thinking about the things you do (including recreation, exercise, work and housekeeping), how would you rate yourself as to the amount of exercise you get compared with others your age and sex?” Participants chose from one of the following categories: much less active, somewhat less active, about the same, somewhat more active and much more active. Physical inactivity was defined as report of being much less active or somewhat less active. Self-report has been shown to be a reliable, valid, and accurate method of assessing physical activity and a strong predictor of CVD events.(7) To assess medication adherence, we asked “In the past month, how often did you take your medications as the doctor prescribed?” Possible responses were all of the time (100%), nearly all of the time (90%), most of the time (75%), about half of the time (50%), or less than half the time (<50%). On the basis of prior studies of adherence and CVD events, we defined medication non-adherence as taking prescribed medications 75% or less of the time.(7)

### Additional Covariates

Participants completed questionnaires to determine age, sex, ethnicity, income, and highest education level achieved. Social support was assessed using a 12-item version of the Interpersonal Social Support Evaluation List (ISEL). Each item is scored on a 4-point Likert scale, yielding a total questionnaire score of 12–48. Participants brought their medication bottles to the study visit and a trained research assistant recorded all current medications. Medications were categorized using Epocrates Rx (San Mateo, CA).

We measured height and weight, and calculated body mass index (BMI). Resting systolic and diastolic blood pressure were recorded using a standardized protocol.(7) A fasting blood draw was used to determine Hemoglobin A1c and cholesterol levels. Ejection fraction was measured on a resting echocardiogram using an Acuson Sequoia Ultrasound System (Mountain View, CA). Following the resting echocardiogram, participants completed a symptom-limited, graded exercise treadmill test using a modified Bruce protocol.(7) Exercise capacity was calculated as the total number of metabolic equivalent tasks (METs) achieved at peak exercise (1 metabolic equivalent = 3.5 mL/kg/min of oxygen consumption). At peak exercise, another echocardiogram was obtained, and we calculated the wall motion score index at peak exercise as a measure of inducible ischemia.(7)

## Statistical Analysis

Our objectives were to evaluate the prospective risk of cardiovascular events and all-cause mortality associated with lifetime traumatic events and to explore potential psychiatric comorbidities and health behaviors as mediators of this association. To describe baseline differences in the characteristics of participants by quartile of trauma exposure, we used *t* tests for continuous variables and chi-square tests for dichotomous variables. To evaluate the association of lifetime trauma and CVD events and mortality, we used Cox proportional hazards models to predict prospective CVD outcomes comparing the second, third, and fourth quartiles of trauma exposure to the reference group of the first quartile of trauma exposure. We also used Cox proportional hazards models to compare prospective adverse outcomes associated with each standard deviation increase in the number of trauma categories. We adjusted models for patient characteristics associated with trauma exposure that are known to influence CVD risk (age, sex, race, income, education) as well as psychiatric comorbidities (PTSD, depression, GAD), and health behaviors (smoking, physical activity, illicit drug addiction/abuse). Participants with multiple CVD events were censored at the first outcome.

Finally, we conducted sensitivity analyses to evaluate whether changes over time in psychiatric disorders or health behaviors affected the association of trauma and adverse outcomes. Between September 2005 and December 2007, 667 participants (80% of the 829 survivors) completed a 5-year follow-up examination with repeated measures of health behaviors and psychiatric disorders. We created variables to indicate whether participants developed each potential risk factor between baseline and the follow-up measurement (i.e. did not have depression at baseline, but did have depression at follow-up) and added these to the regression models. All tests of statistical significance were two-tailed. All analyses were performed with SAS version 9.2 (SAS Institute).

## RESULTS

### Patient Characteristics and Trauma Exposure

Of the 1,021 participants, 1,013 (>99%) reported exposure to at least one traumatic event, and the majority experienced multiple traumas (mean number of events 5.6, SD 2.8). The proportion of participants reporting exposure to each type of traumatic event is displayed in Figure 1. Characteristics of participants in each quartile of trauma exposure are shown in Table 1. Individuals in the highest quartile of exposure were on average 2 to 3 years younger than those in the lower quartiles, more likely to be male, more likely to have a lower income, and generally more likely to be white. Many traditional CVD risk factors, including blood pressure and cholesterol, and baseline measurements of CVD severity did not differ by trauma status.

### Trauma, Health Behaviors, and Psychiatric Comorbidities

As shown in Table 1, there was no significant difference in medication non-adherence or alcohol use. However, patients in the highest quartile of traumatic event exposure were more likely to smoke, be physically inactive, report a history of illicit drug addiction/abuse, and meet criteria for PTSD and depression.

## Trauma and adverse outcomes

Over a mean of 7.5 ± standard deviation of 2.8 years of follow up, CVD events and all-cause mortality significantly increased across all quartiles of trauma exposure (Figure 2). Adverse CVD outcomes were more common in patients in the highest trauma quartile, occurring in 140 (55%) participants versus 115 (46%) participants in the lowest trauma quartile, with rates of 37 (14%) vs. 32 (13%) for myocardial infarction, 19 (7%) vs. 10 (4%) for stroke and TIA, 53 (21%) vs. 39 (16%) for congestive heart failure, and 110 (43%) vs. 92 (37%) for all-cause mortality.

In fully adjusted models comparing risk of adverse cardiovascular outcomes in higher trauma quartiles to the reference of the lowest trauma quartile, risk was significantly higher in the fourth trauma quartile (Table 2). Those in this highest trauma quartile had a 38% increased risk of adverse CVD outcomes after adjusting for potential confounders, comorbid psychiatric conditions, and poor health behaviors. Of these covariates, smoking and physical inactivity had the largest effect sizes. Continuous trauma score was also associated with an increase risk of adverse CVD outcomes in fully adjusted models (Table 3). Each standard deviation increase in trauma score associated with an 11% increase in risk for adverse CVD outcomes in adjusted models. Status for psychiatric disorders and negative health behaviors was stable over time in the majority of participants, with few patients developing these conditions (1% for smoking, 1% for illicit substance abuse, 11% for physical inactivity, 3% for depression, and 3% for PTSD). Adjusting for these changes in risk factor status did not substantially alter our findings.

## DISCUSSION

In this cohort of adults with coronary heart disease, we found that greater lifetime traumatic event exposure was associated with a higher risk of prospective CVD events and all-cause mortality over a mean of 7.5 years of follow up. This association was not explained by differences in demographics, health behaviors, or psychiatric diagnoses associated with trauma exposure including post-traumatic stress disorder, generalized anxiety disorder, or depression. Our results represent the first analyses of cumulative lifetime trauma exposure and adverse outcomes in patients with CVD and expand upon prior work on psychological risk factors for the development and progression of CVD.

Several studies in veteran and civilian populations have linked traumatic events to increases in CVD morbidity and mortality, but most have looked at PTSD, rather than trauma exposure, as the variable of interest. Others have focused on specific traumatic events, such as combat exposure,(5, 22) or specific time periods, such as events that occurred during childhood.(23) The association of PTSD with CVD has been found in large epidemiologic studies of male WWII prisoners of war (22) and male Vietnam era veterans (5) and was found to be independent of traditional cardiac risk factors and depression.(8) However, as the majority of patients who experience trauma will not develop PTSD, understanding the independent health consequences of trauma could have substantial public health implications, particularly for sub-populations with high exposure.

The Adverse Childhood Experiences (ACE) Study is one of the largest studies of the chronic physical health effects of psychological trauma.(9, 10) Two weeks after a standardized medical assessment, researchers surveyed 18,175 adult members of a large healthcare organization with a questionnaire on 10 types of childhood trauma. Ischemic heart disease (IHD) was defined by self-report of history of myocardial infarction, exertional angina or nitroglycerin use. After adjusting for age, sex, race, and education level, the number of categories of childhood traumas predicted IHD in a dose dependent fashion.(9) IHD prevalence ranged from 9.9% in those with no trauma to 20.1% in those with 7 or more categories of childhood trauma exposure. We substantially expand on this study of childhood trauma by showing that exposure to greater number of categories of *lifetime* traumatic events is prospectively associated with adverse outcomes in patients with existing cardiovascular disease.

Though there was a significant trend towards increasing risk of adverse CVD outcomes across all four trauma exposure quartiles, in our adjusted models only those patients in the highest trauma quartile had a significantly greater risk of adverse CVD outcomes compared to those in the lowest trauma quartile. In the ACE study, after adjustment for traditional cardiovascular and psychological risk factors, risk of ischemic heart disease was significantly higher in participants with 5 or more types of childhood trauma events compared to those with no events, whereas risk of IHD did not differ for some of the lower trauma levels. It is possible that milder levels of trauma exposure do not increase CVD risk. However, conclusions are limited as both the present study and the ACE study measured exposure through a count of exposure to various types of events and neither evaluated severity of events or whether reported events were recurrent.

Despite this limitation, our study contributes to the growing body of evidence that indicates a causal relationship between exposure to trauma and adverse CVD outcomes and suggests the need for further research into mechanisms linking trauma to CVD. Our findings support studies demonstrating that exposure to traumatic stress has enduring effects on physiology.(24) They further suggest that cumulative trauma exposure is an important risk factor for adverse outcomes in patients with CVD, and that patients do not have to develop a psychiatric disorder or engage in negative health behaviors for this risk to emerge. Understanding the biological, behavioral, and psychosocial mechanisms by which repeated traumatic events lead to poor health outcomes may facilitate the detection of vulnerable individuals and implementation of preventive strategies to reduce the risk of CVD events and death among people with a high exposure history. Prior work has demonstrated that trauma causes neuroendocrinologic alterations in the HPA axis leading to higher concentrations of circulating catecholamines.(25) Patients with CVD also demonstrate increases in inflammation following acute mental stress, and these responses are more dramatic than those observed in healthy controls.(26) These exposure-related acute and chronic biologic changes may increase risk for CVD via endothelial damage and accelerated atherosclerosis.(25)

Integrative models hypothesize that traumatic stress exposure also damages physical health through behavioral and psychological mechanisms.(27) Trauma may lead to unhealthy behaviors such as smoking as well as decreased use of preventive behaviors such as

exercise. Prior cross-sectional and retrospective studies have demonstrated high rates of smoking in diverse populations of patients with PTSD (28) and young adults with trauma exposure.(29) Although few studies have examined the relationship between trauma and physical activity, there is some data to suggest that patients with PTSD may be less likely to engage in vigorous physical activity.(15)

Psychosocial factors involved in the association of trauma exposure and CVD may include social isolation, impairments in occupational functioning, and chronic mental health disorders. Though social support did not differ significantly by trauma status in our sample, participants with greater cumulative trauma exposure had lower income levels and substantially higher rates of mental health disorders. However, even after adjustment for these factors, high exposure to traumatic events remained associated with increased risk of CVD events and death.

Although further research is needed to fully understand the links between trauma and adverse physical health outcomes, our findings have implications for clinical practice. If a patient is not exhibiting or reporting symptoms of a psychiatric disorder, a busy primary care provider may not be prompted to take a detailed social history about exposure to traumatic events. Our results suggest that eliciting a history of traumatic experiences may help identify individuals at higher risk for recurrent adverse outcomes who may benefit from additional care for aggressive risk factor reduction. Based on our data, exposure to a high number of types of trauma may confer the greatest risk, though again, severity of events is also likely to be important and was not evaluated in this study. Integrated or collaborative care models that provide simultaneous access to primary care and mental health services may also be explored to treat the complex, interconnected conditions of psychological trauma and CVD. (30)

The strengths of our study include its prospective design, careful assessment of potential confounders and mediators, and comprehensive assessment of cardiovascular events with medical record confirmation by blinded physician adjudicators. However, our results must be interpreted in light of several limitations. The Heart and Soul Study cohort is composed mostly of urban dwelling men with existing CVD. Though this may limit generalizability, patients with CVD are an important group to study as they are at highest risk for CVD events and mortality and relatively few studies have addressed the impact of trauma on CVD progression. Lifetime exposure to traumatic events was also greater in our sample than in prior reports, though this was expected for several reasons.(1–4) The mean age of our cohort is above 65, which is higher than prior studies that have largely focused on younger populations or have included all adults over 18. Given cumulative exposure to traumatic events has been shown to increase with age, being 60% by age 35 in one study, we would anticipate that an older cohort would have a higher prevalence of events.(2) In addition, our trauma measure was derived from the DSM-IV, which has an expanded list of potential traumatic events that can increase the overall prevalence of trauma exposure.(4) Measuring cumulative trauma exposure presents other challenges as there are no validated schemes to weight the relative psychological impact of different types of trauma and even individuals exposed to the same event may experience it very differently. Similar to multiple prior studies, we used a validated measure of traumatic event exposure and calculated exposure as

the number of types of events reported. (19–21, 23, 31) Prior studies have demonstrated that exposure to a greater number of types of traumatic events is correlated with greater psychological comorbidities and functional impairment. (20, 21, 32, 33) However, we acknowledge that this method may not fully capture variations in the traumatic impact of these events, and additional studies of trauma and CVD outcomes that take into account the impact of events are warranted. In addition, we were unable to examine the effect of repeated exposures to the same type of event or the timeline of traumatic exposures across the lifespan. Given these limitations, we chose a conservative route utilizing standard deviation units and quartiles of trauma exposure as opposed to continuous analyses across single event increases in exposure. Further study using more detailed information on trauma history and severity may allow more in-depth analyses that could identify individuals with the highest risk trauma patterns for targeted interventions to prevent adverse outcomes in patients with CVD.

In summary, we found that greater lifetime exposure to traumatic events predicted future risk of recurrent CVD events and all-cause mortality independent of psychiatric comorbidities and poor health behaviors. Our findings underscore the need for further research on the causal pathways connecting trauma to cardiovascular disease. Interventions that target these mechanisms could improve health and longevity in the large proportion of the population exposed to traumatic events.

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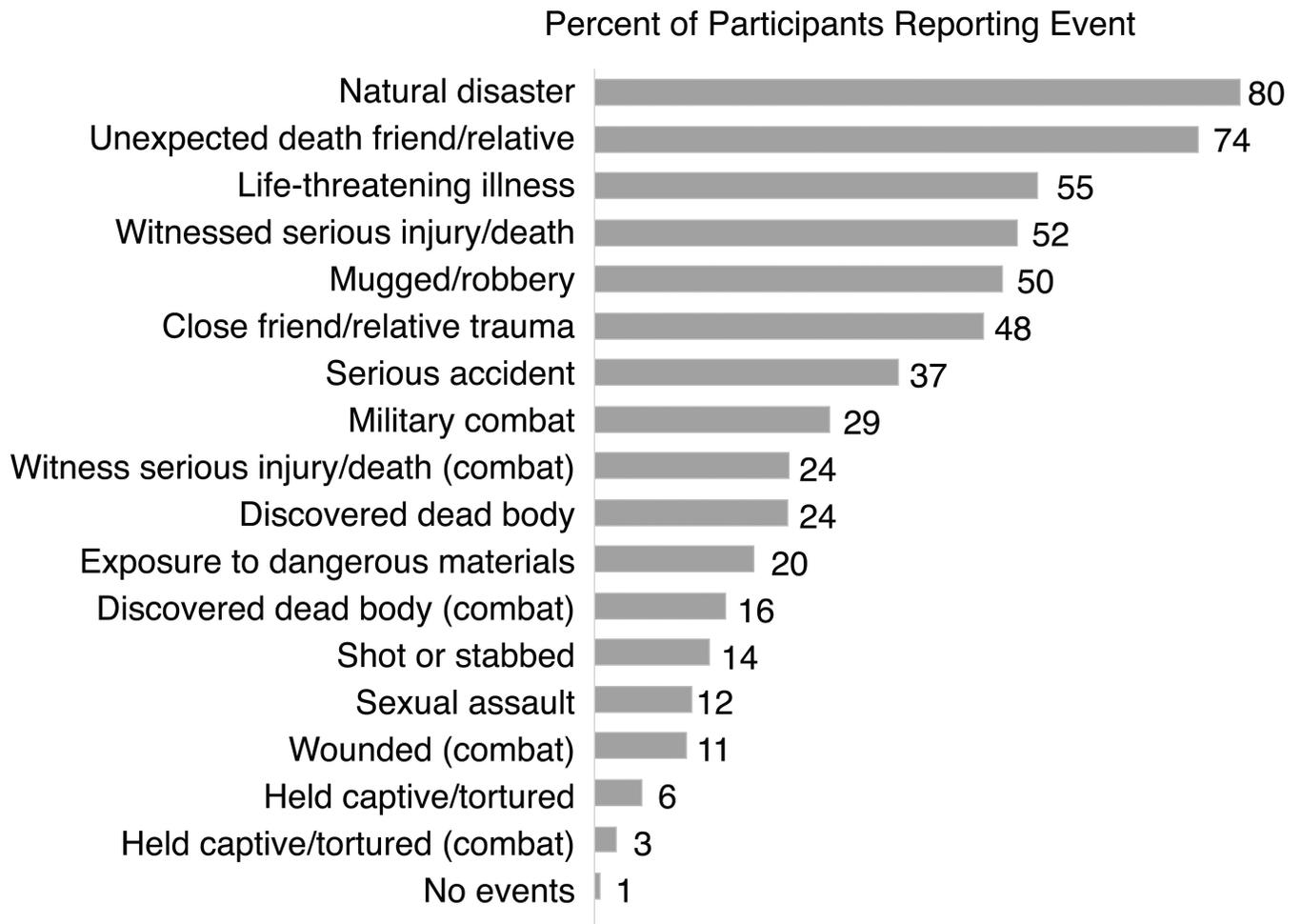
## Acronyms

<b>ACE</b>	Adverse Childhood Experiences
<b>CDIS</b>	Computerized Diagnostic Interview Schedule
<b>CVD</b>	cardiovascular disease
<b>DSM</b>	Diagnostic and Statistical Manual
<b>GAD</b>	generalized anxiety disorder
<b>IHD</b>	ischemic heart disease
<b>METs</b>	metabolic equivalent tasks
<b>PTSD</b>	posttraumatic stress disorder

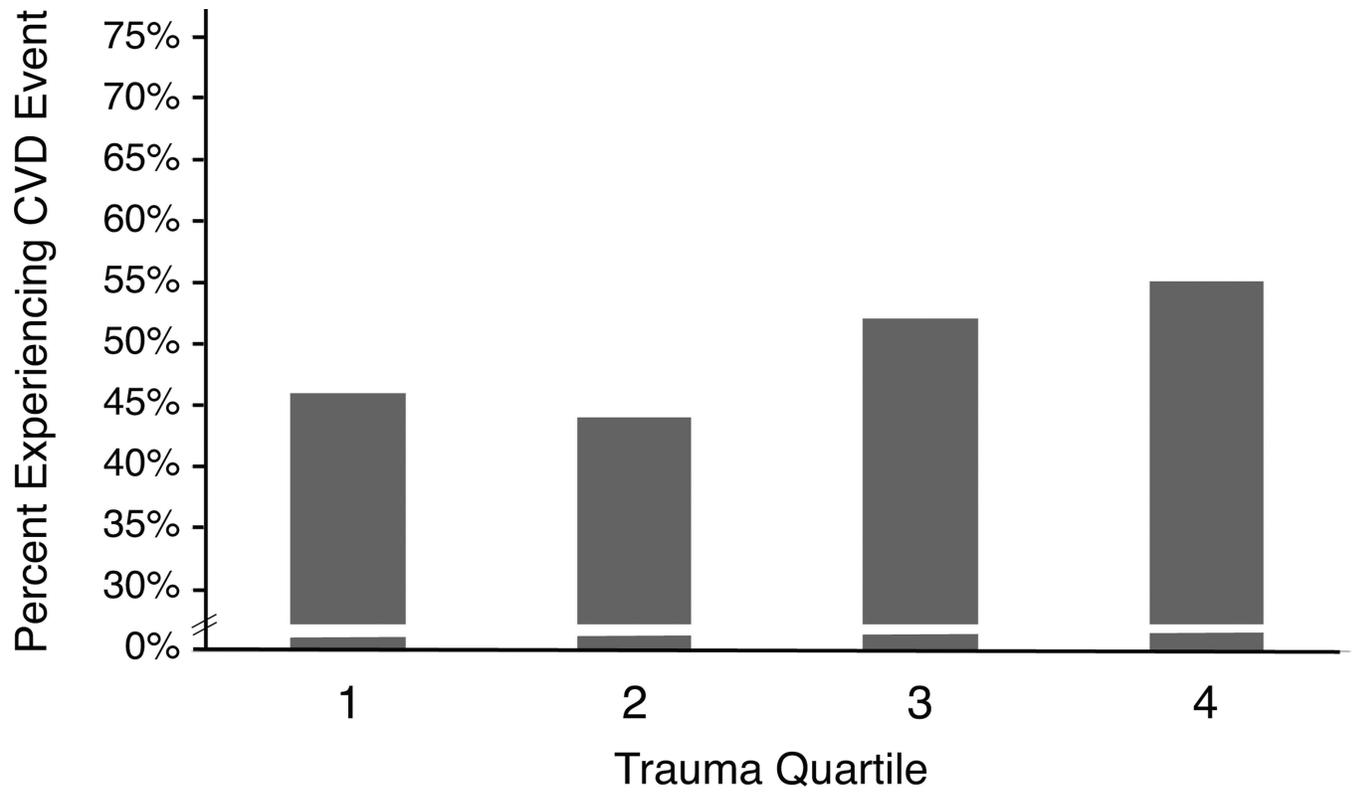
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**Figure 1.**  
Exposure to traumatic events.



**Figure 2.** Adverse CVD outcomes by trauma quartile. *P* for trend of increasing incident CVD events from quartiles 1 through 4 = .01.

Table 1

Participant characteristics by quartile of trauma exposure

	Quartile 1 N=251	Quartile 2 N=268	Quartile 3 N=246	Quartile 4 N=256	P value
<b>DEMOGRAPHICS</b>					
Age (years)	68 (10)	67 (10)	68 (11)	65 (11)	.003
Men	189 (75%)	207 (77%)	213 (87%)	228 (89%)	<.001
White	127 (51%)	164 (61%)	159 (65%)	164 (64%)	.004
Married	107 (43%)	112 (42%)	105 (43%)	110 (43%)	.99
Income <\$20,000/yr	129 (52%)	118 (44%)	102 (42%)	147 (57%)	.002
Education: High school graduate or lower	94 (37%)	78 (29%)	66 (27%)	73 (29%)	.048
<b>BASELINE CVD SEVERITY MEASURES</b>					
Resting Left Ventricular Ejection Fraction (%)	61 (10)	62 (10)	62 (9)	61 (10)	.69
Exercise Capacity in METs	7.3 (3.5)	7.4 (3.4)	7.4 (3.4)	7.1 (3.1)	.57
Ischemia (wall motion score index)	1.2 (.33)	1.1 (.32)	1.2 (.37)	1.2 (.37)	.24
<b>CVD RISK FACTORS/MEDICATIONS</b>					
Body Mass Index	28 (5)	28 (5)	28 (5)	29 (6)	.61
Systolic Blood Pressure	133 (21)	134 (22)	132 (21)	132 (20)	.45
Diastolic Blood Pressure	74 (11)	75 (10)	74 (12)	75 (12)	.80
LDL Cholesterol, mg/DL	106 (37)	104 (32)	104 (31)	104 (34)	.84
HDL Cholesterol, mg/DL	47 (14)	47 (15)	46 (13)	45 (14)	.34
Hemoglobin A1C	5.9 (1.0)	6.1 (1.3)	6.0 (1.0)	5.9 (1.3)	.39
Beta Blocker	142 (57%)	155 (58%)	149 (62%)	146 (58%)	.77
Statin	163 (66%)	173 (65%)	169 (70%)	150 (59%)	.10
Renin-angiotensin Inhibitor	134 (54%)	137 (51%)	124 (51%)	128 (51%)	.85
Aspirin	181 (73%)	187 (70%)	179 (74%)	193 (76%)	.45
<b>HEALTH BEHAVIORS</b>					
Physical Inactivity	80 (32%)	97 (36%)	83 (34%)	111 (43%)	.041
Current Smoking	35 (14%)	46 (17%)	50 (20%)	69 (27%)	.002
Illicit Drug Addiction/Abuse	4 (2%)	13 (5%)	16 (7%)	38 (15%)	<.001
Medication Non-Adherence	25 (10%)	20 (8%)	22 (9%)	16 (6%)	.42
Regular Alcohol Use	64 (26%)	83 (31%)	78 (32%)	67 (26%)	.27

	Quartile 1 N=251	Quartile 2 N=268	Quartile 3 N=246	Quartile 4 N=256	P value
<b>PSYCHOSOCIAL FACTORS</b>					
Post-traumatic Stress Disorder	2 (0.8%)	11 (4%)	25 (10%)	57 (22%)	<.001
Depression	33 (13%)	56 (21%)	65 (26%)	69 (27%)	<.001
Generalized Anxiety Disorder	20 (8%)	24 (9%)	27 (11%)	36(14%)	.12
Social Support	37 (7)	38 (7)	37 (7)	37 (8)	.80

Values shown are mean (SD) or n (%) as appropriate. *P* values are from Chi square tests for categorical variables and *t*-tests for continuous variables.

**Table 2**Association of trauma exposure quartile with adverse cardiovascular outcomes<sup>a</sup>

	<b>Hazard Ratio (95% CI)</b>
<b>Unadjusted</b>	
Trauma Quartile 1	Reference
Trauma Quartile 2	0.98 (0.76, 1.27)
Trauma Quartile 3	1.18 (0.91, 1.51)
Trauma Quartile 4	1.27 (0.99, 1.63)
p-for trend	0.023
<b>Adjusted</b>	
Trauma Quartile 1	Reference
Trauma Quartile 2	1.10 (0.84, 1.43)
Trauma Quartile 3	1.24 (0.95, 1.61)
Trauma Quartile 4	1.38 (1.06, 1.81)
p-for trend	0.012
Age	1.06 (1.05, 1.07)
Sex	1.43 (1.08, 1.89)
Race	1.06 (0.87, 1.29)
Income	1.28 (1.06, 1.55)
Education	1.16 (0.95, 1.42)
Posttraumatic stress disorder	0.58 (0.40, 0.85)
Depression	1.05 (0.80, 1.38)
Generalized anxiety disorder	1.32 (0.94, 1.85)
Smoking	1.54 (1.21, 1.97)
Physical inactivity	1.71 (1.41, 2.07)
Illicit drug addiction/abuse	1.49 (1.03, 2.15)

<sup>a</sup>Single model with all 4 quartiles. *P*-value for trend of hazard ratios is calculated from quartile 1 (reference) through quartile 4

**Table 3**Association of trauma exposure with adverse cardiovascular outcomes<sup>a</sup>

	<b>Hazard Ratio (95% CI)</b>
<b>Unadjusted</b>	<b>1.08 (0.99, 1.18)</b>
<b>Adjusted</b>	
Trauma score*	1.11 (1.01,1.23)
Age	1.06 (1.05, 1.07)
Sex	1.44 (1.09, 1.91)
Race	1.07 (0.88, 1.30)
Income	1.29 (1.06, 1.56)
Education	1.16 (0.95, 1.42)
Posttraumatic stress disorder	0.58 (0.40, 0.85)
Depression	1.05 (0.80, 1.37)
Generalized anxiety disorder	1.31 (0.94, 1.84)
Smoking	1.54 (1.21, 1.97)
Physical inactivity	1.71 (1.41, 2.08)
Illicit drug addiction/abuse	1.49 (1.03, 2.15)

<sup>a</sup> per 1 standard deviation increase in continuous trauma score