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Henok Mulatu Teferi Date

Racial disparities in the association between childhood and adult life stress and adverse cardiovascular outcomes among patients with a history of myocardial infarction in Georgia, USA.

By

Henok Mulatu Teferi
Degree to be awarded: Master of Public Health

Department: Global Epidemiology

_____

Viola Vaccarino, MD, PhD
Committee Chair

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By

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MD., Arba Minch University, 2017
M.Sc., Umeå University, 2022

Thesis Committee Chair: Viola Vaccarino, MD, PhD

An abstract of
A thesis submitted to the faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Global Epidemiology
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Abstract

Background: Although studies have identified associations between overall childhood life stress and adverse cardiovascular outcomes among myocardial infarction (MI) patients, limited studies have assessed the association of specific forms of childhood stress with adverse cardiovascular outcomes and the role of adult life stress in these associations. This study aimed to assess 1) racial disparities in childhood and adult life stress and its association with adverse cardiovascular outcomes; 2) the association of specific forms of childhood stress with cardiovascular outcomes; and 3) the role of adult life stress and race/ethnicity in these associations.

Methods: Data from the Myocardial infarction and mental stress 2 (MIMS2) study from Emory's affiliated hospitals was used. The analytical sample included 300 MI patients aged between 18-60 years. The study outcome was time to composite adverse cardiovascular event. Childhood general trauma, physical, emotional, and sexual abuse were assessed with the Early Trauma Inventory. Logistic and linear regression were used to assess differences by race in childhood and adult stress. Kaplan-Meier survival curves were used to assess event free survival differences by race. Cox-proportional hazard regression was used to estimate hazard ratio and 95% confidence interval.

Results: Black participants (55.8%) had higher prevalence of overall childhood life stress than 'White and other races' (41.6%). The mean difference in adult life stress between Black and 'White and other races' was 1.04 score point (95% CI: -0.08, 2.17). After controlling for sex and age, Blacks had higher odds of childhood general trauma (OR=2.0; 95% CI: 1.22-3.41) and physical abuse (OR=2.0; 1.18-3.4) than 'Whites and other races.' Black had higher risk of a composite adverse cardiovascular event at the study end point compared to 'White and other races' (HR=2.2; 95% CI: 1.29-3.79). Black participants who experienced overall childhood life stress (HR=1.9; 95% CI: 1.02-3.58) and specifically, general trauma (HR=1.9; 95% CI: 1.01-3.78) were more likely to develop adverse cardiovascular outcomes at the study end point than White and other races.

Conclusion: This study identified racial disparities in childhood and adult stress, particularly general trauma, was significantly associated with adverse cardiovascular outcomes among Black individuals. Race-specific interventions to address childhood stress and reduce future adverse cardiovascular outcomes is recommended.

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Introduction

Cardiovascular disorders (CVD) continue to be a significant public health concern and the primary cause of mortality globally and within the United States (1). The World Health Organization (WHO) reports that CVD accounts for a total of 17.9 million deaths annually worldwide (2). Adverse cardiovascular events such as acute myocardial infarction (MI), hypertension, stroke, and heart failure, are the primary contributors to CVD-related morbidity and mortality (1). Individuals who have previously experienced an MI are more susceptible to serious cardiovascular consequences (1).

Several studies have investigated the impact of childhood life stress on the development of risk factors for cardiovascular disease and its subsequent adverse outcomes (3–7). Adverse childhood life events may include a wide range of stressors experienced during childhood, including household dysfunction (such as parental substance use, domestic violence, and parental death), childhood maltreatment (including emotional, physical, and sexual abuse), homelessness, bullying, economic hardship, and the death of a close family member (3).

Previous studies have shown an association between adverse childhood life stressors and an increased prevalence of CVD risk factors and adverse health behaviors in adulthood, including obesity, hypertension, smoking, alcohol use, diabetes, and physical inactivity (3,4,6,8–10). An association between stress experienced during childhood and adverse cardiovascular outcomes has also been reported. A systematic review and meta-analysis that included a total of 10 studies,

has shown a pooled estimate of 2.09 times higher odds of developing MI among those with a high cumulative burden of stressful events during childhood compared to their counterparts (11). Furthermore, a recent literature review revealed that those who have had four or more adverse childhood events have two times a higher risk of developing CVD in comparison to those who had fewer than four stressful events throughout childhood (10). A study conducted among individuals who had a previous history of MI also showed a higher risk of experiencing adverse cardiovascular events, such as the recurrence of MI, hospitalization due to heart failure, and mortality, among those who had experienced a greater number of stressful events during childhood (12).

Various studies examined the behavioral, mental, and biological pathways through which childhood life stressors contribute to the risk and progression of CVD (3,5,10). Two main biological pathways have been proposed. Individuals who have experienced childhood stressful events are more likely to have a persistent increase in stress hormones, including cortisol and catecholamines leading to long-term disruptions in cardiometabolic function and an increased risk of CVD (3,10). Additionally, chronic stress throughout childhood may lead to changes in inflammatory processes leading to the persistent production of pro-inflammatory mediators, which may contribute to the development of CVD (3,5,10). A previous study conducted among patients with a history of MI also showed the potential mediation effect of C-reactive protein in the association between early life stress and a composite CVD endpoint including death or recurrent MI (12). In addition to biological pathways, psychosocial factors linked to early life adversity, including depression, anxiety, and substance abuse, may play a role in the development of adverse cardiovascular outcomes among those who experienced childhood stress (3,5,10). A

prior study conducted in China also identified a significant association between adverse adulthood experiences and incident cardiovascular disorders (13). The mediation role of adult life stress in the association between childhood life stress and CVD outcomes have also been identified (13).

Racial/ethnic disparities in childhood life stress and their association with adverse health outcomes have been reported by several studies (14–18). A study conducted in a nationally representative sample of 11,404 in the United States reported a higher prevalence of childhood stressful events among non-Hispanic Black adults, followed by Hispanics and non-Hispanic Whites (15). Another studies also reported similar findings (19–21). Moreover, a study conducted among a racially diverse population showed a higher association between adverse childhood events and obesity among racial minorities compared to non-Hispanic White adults (16). However, studies are not consistent, as some reported a higher frequency of childhood life stress such as sexual, emotional and physical abuse among White compared to Black individuals (22,23).

Although previous studies have described an association between childhood life stress and adverse cardiovascular outcomes and potential mechanistic pathways, few have examined differences by race. Furthermore, studies mainly focused on assessing the composite effect of adverse childhood events rather than considering specific childhood life events separately. Identifying whether specific childhood life stressors are implicated in adverse outcomes would be important to develop a targeted intervention for improving health outcomes. In addition, few studies have assessed the relative importance of adult life stress and childhood stress for adverse CVD outcomes. Exposure to childhood adversity predisposes to physical and behavioral

adversity throughout life (24). Understanding the separate impact of childhood stress and adult life stress may help to identify the timing and type of interventions that are most relevant to mitigate adverse adult outcomes. Therefore, this study aimed: 1) To assess racial differences in childhood and adult life stress as well as adverse cardiovascular outcomes among patients with a recent MI; 2) To assess separately the association of different types of childhood stress, including general trauma, physical, emotional and sexual abuse, with adverse cardiovascular outcomes; 3) To assess the role of adult-life stress in this association; 4) To assess if these associations are modified by race/ethnicity.

Methods

Data source, study design and sampling

This study used data from the myocardial infarction and mental stress 2 (MIMS-2) study. The MIMS-2 is a prospective study that included participants from Emory-affiliated Hospitals in Atlanta, Georgia, which includes Emory University Hospital, Emory Hospital Midtown, Saint Joseph's Hospital, and Grady Memorial Hospital. MI patients were included if they were between the age of 18-61 years old and had a history of MI (type 1) with the past eight months (using standard criteria through chart review, suggestive ECG findings and elevated troponin levels). The MIMS-2 study recruited a total of 425 participants, 313 with history of MI and 112 community controls without history of MI. Only the MI patients were followed for events, so the 112 participants without a history of MI were excluded from this analysis. Among the MI patients, 13 participants had missing values for childhood life stress and were excluded. Thus, a total of 300 participants were included in our final analysis (Figure 1).

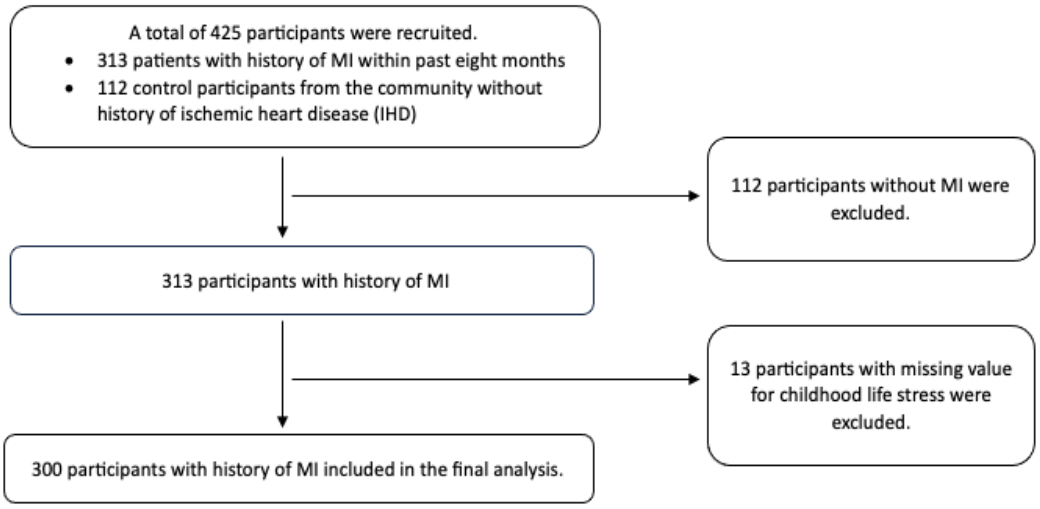


Figure 1: Sampling strategy of the study participants.

Measurements

Study Outcome

The outcome variable in this study was the time to the occurrence of a composite outcome measures including type 1 MI, stroke, death due to cardiovascular disorders and hospitalization due to decompensated heart failure (HF). The patients were followed for a median of four years from the onset of enrollment to collect information on subsequent hospitalizations or death. Data on subsequent cardiovascular events was collected from the patient's medical records supplemented with follow-up phone calls with the participants or their proxies. Deaths from cardiovascular causes included severe MI, fatal cerebrovascular accidents, and fatalities due to cardiac arrhythmia or HF. Each event was determined independently by cardiologists participating in the study who did not have access to any additional study data. The social security death index and patient contacts were also used to collect data on CVD-related deaths.

Study Exposures

The exposure variables in this study were four childhood life stressful events, which include general trauma, physical abuse, emotional abuse and sexual abuse. The Early Trauma Inventory Self-Report Short Form (ETI-SR-SF), a validated 27 item self-report questionnaire was used to assess domains of early life stress (25). Consistent with previous literature (26), cut-off points for each of the four domains of childhood stress were used to categorize them into binary variables based on the mean plus one standard deviation of published data from healthy individuals (25). *General trauma* was categorized as 'yes' if the participants scored >=3.4 out of the 11 questions used to measure the general trauma, otherwise it was categorized as 'no'. *Physical abuse* was categorized as 'yes' if the participant scored >=2.3 out of the five questions asked for physical abuse, otherwise it was categorized as 'no'. Similarly, *emotional abuse* was categorized as 'yes' if the participants score was >=2.1 out of the five questions asked for emotional abuse, otherwise it was categorized as 'no'. Finally, *sexual abuse* was categorized as 'yes' if the score is >=0.8 out of the six questions asked for sexual abuse, otherwise it was categorized as 'no'. Overall childhood life stress was categorized as 'yes' if the participants score >=6.8 on the entire ETI-SR-SF and 'no' if they scored <6.8.

Covariates

Baseline socioeconomic factors (age, sex, educational status, smoking status), clinical factors (history of hypertension, diabetes, body mass index, and high blood cholesterol) and medication use (beta blocker, aspirin, statin and ACE inhibitors) were measured at the baseline visit using standardized questionnaires and physical examination. Adult life stress was measured using the adult trauma inventory (ATI), a 33-item questioner that assessed the various stressful events after

the age of 18 years old, on a scale of "yes" or "no". Race was grouped into two categories ('Black' and 'Whites and other races') and assessed as an effect modifier variable.

Statistical analysis

Frequency and percentages (for categorical variables) as well as mean and standard deviations (for continuous variables) were used to describe the sociodemographic, adult life stress, clinical and medication related characteristics of the participants by overall and the four domains of childhood life stress events (general trauma, physical abuse, emotional abuse, and sexual abuse). Logistic regression was used to assess the association between race and the overall as well as the four categorized domains of childhood life stress events and bar charts were used to visually present the results of the disparities. Linear regression was used to assess the association between race and adult life stress from the ATI scale, which was treated as a continuous variable.

Kaplan- Meier survival curves were used to illustrate differences in the outcome by race ('Black' vs 'Whites and others') in survival. Cox-proportional hazard regression was used to estimate the hazard ratio (HR) at 95% confidence interval for the associations between overall and specific forms of childhood life stress events (general trauma, physical abuse, emotional abuse, and sexual abuse) and the study end point individually, both overall and stratified by race. A total of four cox-regression models were conducted for each of the exposure variables. In model 1, unadjusted regression analysis was conducted between each of the overall and the four domains of the childhood life stress events and the study endpoint. Model 2 was adjusted for sociodemographic factors; model 3 was adjusted for model 2 variables plus clinical factors and medications, and finally model 4 was adjusted for factors in model 2 and 3 plus adult-life stress events.

The supplementary analysis was conducted to assess the association between childhood life stress events (treated as a continuous and standardized variable to ensure comparability of the regression coefficients) and the study endpoint, stratifying by race to examine the modifying effect of race. This analysis also aimed to compare the strength of the association of stress events in both childhood and adult life. In addition, the association between adult life stress (as a continuous and standardized variable) and the study end point was also examined and presented as a supplementary table. Both childhood and adult life stress variables were standardized by subtracting the mean score from each participant's score and then dividing it by the standard deviation. This produced a z-score with a mean of zero and a standard deviation of one for each variable, enabling the examination of the variable's effect in relation to other standardized variables in the regression models. All data analysis was conducted by SAS version 9.4 (SAS institute).

Ethical considerations

The MIMS-2 study received ethical approval from the Emory University Institutional Review Board and informed consent was provided for each of the participants before enrolling into the study.

Results

Characteristics of the study participants

The mean age of participants included in this study was 50.9 years (SD=6.6) and 50.0% were women. Among these participants, more than half (66.0%) were Black, while the remaining races included White (28.0 %), Asian /Asian Indian (2.0%), West Indian (1.0%), Native

American (1.0%) and unknown races (2.0%). More than half of the participants attended at least a high school (69.0%), and ever smoked a cigarette (55.3%) (Table 1). The majority of the participants had hypertension (81.3%) and dyslipidemia (80.0%), and 31.3% had diabetes. Regarding their medications, the majority were on aspirin (81.7%), beta blockers (86%), and statin (84.7%), while 46.7% were on angiotensin converting enzyme (ACE) inhibitors (Table 1).

Overall Childhood and adult life stress events

The overall prevalence of childhood life stress was 51.0%, while the mean score of adult life stress was 9.6 (SD=4.7). The mean score of adult life stress was higher among those who experienced childhood life stress events (11.7 (SD=4.6)) compared to those who did not (7.2 (SD=3.6)) (Table 1).

Table 1: Characteristics of the study participants by overall childhood and adult life stress events (n=300)

	Whole Sample n (%)	**Overall childhood life stress**	
		Yes	No
Total, n (%)	300 (100%)	152 (50.6)	148 (49.3)
Adult life stress, mean (SD)	9.6 (4.7)	11.7 (4.6)	7.3 (3.7)
Demographic factors			
Age, mean (SD)	50.9 (6.6)	50.6(6.5)	51.1(6.8)
Sex, n (%)			
Female	150 (50.0)	73 (48.0)	77 (52.0)
Race, n (%)			
Black (African American)	198 (66.0)	110 (72.4)	88 (59.5)
Level of education[1]**, n (%)**			
> high school	177 (69.0)	80 (52.6)	97 (65.5)
Ever smoker (yes), n (%)	166 (55.3)	103 (67.8)	63 (42.6)
Clinical factors, n (%)			
Hypertension (yes)	244 (81.3)	130 (85.5)	114 (77.0)
Diabetes (yes)	94 (31.3)	58 (38.2)	36 (24.3)
Obesity (BMI>30)	155 (51.7)	90 (59.2)	65 (43.9)
Dyslipidemia (yes)	240 (80.0)	123 (80.9)	117 (79.1)
Medications, n (%)			
ASA	245 (81.7)	120 (79.0)	125 (84.5)
Beta blockers	258 (86.0)	130 (85.5)	128 (86.5)
Statin	254 (84.7)	129 (84.9)	125 (84.5)
ACE inhibitors	140 (46.7)	83 (54.6)	57 (38.5)

Similarly, the mean age of participants who experienced overall childhood life stress, and who did not, was equivalent (50.6 vs 51.1). The majority of participants who experienced a childhood life stress were Black (72.4%) and almost half of them were women (48.0%). Those with

childhood stressful events, compared to those without these events, were more likely to smoke, to be hypertensive and to have dyslipidemia (80.9%) (Table 1).

Specific forms of Childhood life stress events

Among the four forms of the childhood life stress, general trauma has the highest prevalence (44.3%) followed by physical abuse (39.0%), sexual abuse (33.0%) and emotional abuse (26.7%). There was no meaningful difference in mean age of participants among those who had general trauma (51.3 (SD=6.3)), physical abuse (50.8 (SD=6.5)), emotional abuse (50.9 (SD=6.9)), and sexual abuse (50.5 (6.8)). Compared to men, a lower percentage of women experienced general trauma (44.4%) and physical abuse (39.3%). However, the proportion of women was higher for those who reported emotional abuse (55.0%) and sexual abuse (64.7%). While more than half of participants who had general trauma (52.6%), physical abuse (52.1%) and sexual abuse (60.6%) had a high school education or higher, less than half of participants who had emotional abuse (48.8%) had a high school education or higher (Table 2).

Table 2: Characteristics of the study participants by specific childhood life stress events (n=300)

	Childhood life stress n (%)							
	General trauma		Physical abuse		Emotional abuse		Sexual abuse	
	Yes	No	Yes	No	Yes	No	Yes	No
Total, n (%)	133 (44.3)	167 (55.7)	117 (39.0)	183 (61.0)	80 (26.7)	220 (73.3)	99 (33.0)	201 (67.0)
Adult life stress (Mean, SD)	12.4 (4.5)	7.3 (3.5)	11.4 (5.0)	8.4 (4.1)	12.1 (4.9)	8.6 (4.2)	11.5 (4.8)	8.6 (4.4)
Demographic factors								
Age, mean (SD)	51.3 (6.3)	50.5 (6.9)	50.8 (6.5)	50.9 (6.7)	50.9 (6.9)	50.8 (6.5)	50.5 (6.8)	51.0 (6.5)
Sex								
Female	59 (44.4)	91 (54.5)	46 (39.3)	104 (56.8)	44 (55.0)	106 (48.2)	64 (64.7)	86 (42.8)
Race								
Black (African American)	97 (72.9)	101 (60.5)	85 (72.7)	113 (61.8)	54 (67.5)	144 (65.5)	71 (71.7)	127 (63.2)
Level of education[1]								
> high school	70 (52.6)	107 (64.1)	61 (52.1)	116 (63.4)	39 (48.8)	138 (62.7)	60 (60.6)	117 (58.2)
Ever smoker (yes)	92 (69.2)	74 (44.3)	78 (66.7)	88 (48.1)	53 (66.3)	113 (51.4)	64 (64.7)	102 (50.8)
Clinical factors								
Hypertension (yes)	110 (82.7)	134 (80.2)	96 (82.1)	148 (80.9)	69 (86.3)	175 (79.6)	82 (82.8)	162 (80.6)
Diabetes (yes)	47 (35.3)	47 (28.1)	46 (39.3)	48 (26.2)	34 (42.5)	60 (27.3)	35 (35.4)	59 (29.4)
Obesity (BMI>30)	68 (51.1)	87 (52.1)	65 (55.6)	90 (49.2)	47 (58.8)	108 (49.1)	62 (62.6)	93 (46.3)
Dyslipidemia (yes)	110 (82.7)	130 (77.8)	93 (79.5)	147 (80.3)	62 (77.5)	178 (80.9)	76 (76.8)	164 (81.6)
Medications								
ASA	103 (77.4)	142 (85.0)	94 (80.3)	151 (82.5)	60 (75.0)	185 (84.1)	79 (79.8)	166 (82.6)
Beta blockers	108 (81.2)	150 (89.8)	101 (86.3)	157 (85.8)	69 (86.3)	189 (85.9)	82 (82.8)	176 (87.6)
Statin	111 (83.5)	143 (85.6)	98 (83.8)	156 (85.3)	65 (81.3)	189 (85.9)	82 (82.8)	172 (85.6)
ACE inhibitors	67 (50.4)	73 (43.7)	60 (51.3)	80 (43.7)	43 (53.8)	97 (44.1)	47 (47.5)	93 (46.3)

Racial differences in childhood life stress events

The overall prevalence of childhood life stress among Black participants was 55.8% while it was 41.6% among all the other races combined (p=0.02). The age and sex adjusted logistic regression

model showed a statistically significant association between race/ethnicity and the overall as well as two forms of childhood life stresses (general trauma and physical abuse).

After adjusting for age and sex, the odds of having overall childhood life stress and general trauma among 'Black' participants was 1.9 (OR=1.9; 95% CI: 1.13-3.08) and 2.0 times (OR=2.0; 95% CI: 1.22-3.41) the odds among 'White and other' races. Similarly, the odds of experiencing a physical abuse among 'Black' was 2.0 times the odds among 'White and other' races (OR=2.0;95% CI: 1.18-3.42) (Figure 2). However, the association between race/ethnicity and emotional abuse and sexual abuse were not statistically significant.

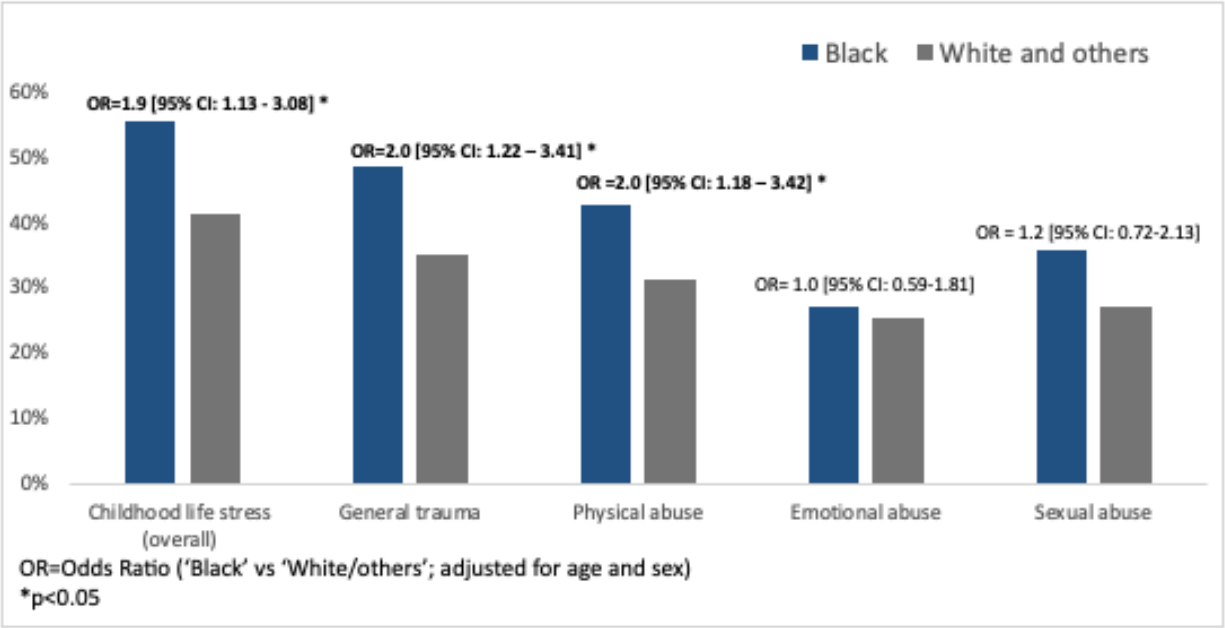


Figure 2: Racial differences in specific forms of childhood stress adjusted for age and sex.

Racial differences in adult life stress events

The mean difference in the adult life stress using the adult trauma inventory between 'Black' and 'White and other' races was 1.04 [95% CI: -0.08, 2.17]. Sex and age adjusted linear regression for the association of race/ethnicity ('Black' vs 'White and others') with adult life stress events showed a statistically significant association, where Black participants had a 1.25 (95% CI: 0.12-

2.38) higher score points in adult trauma inventory compared to 'Whites and other' races (figure 3).

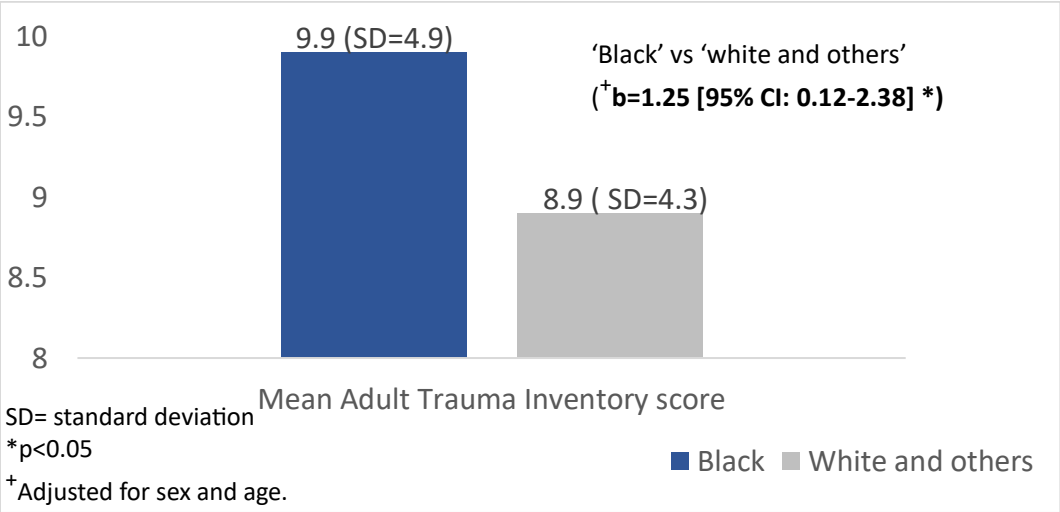
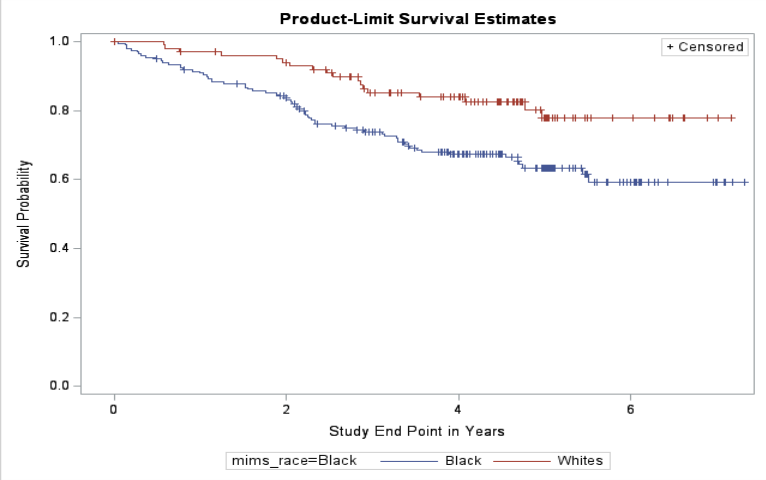


Figure 3: Racial differences in mean adult life stressful events.

Racial Differences in time to adverse cardiovascular outcomes

Black participants had a lower outcome-free survival probability compared to non-Black counterparts (Figure 4). In unadjusted cox-regression analysis, the hazard of developing the composite adverse cardiovascular outcome was 2.1 times higher among Black participants compared to non-Black participants (HR=2.1; 95% CI: 1.26-3.57). After adjusting for sociodemographic factors, the association did not substantially change (HR=2.2; 95% CI:1.29-3.79) (Figure 4).



HR = 2.1 (95% CI: 1.26-3.57)
‡HR= 2.2(95% CI: 1.29-3.79)
‡Adjusted for sociodemographic factors (age, sex, educational status)

Figure 4: Kaplan-Meier survival curves for composite outcome free survival after 'MI' by race/ ethnicity.

The association between childhood life stress and cardiovascular outcomes

The fully adjusted hazard of developing composite adverse cardiovascular outcomes at the study end point among participants who experienced overall childhood life stress events (ETISF>=6.8) was 1.9 (95% CI: 1.13-3.39) times those who did not experience childhood life stress events (Table 3). This associations persisted when examining childhood life stress as a continuous variable and as a standardized variable (see supplementary table 1).

In this adjusted model, Black participants who experienced childhood life stress had a 1.9 times higher hazard (95% CI: 1.02 to 3.59) of developing composite adverse cardiovascular outcomes at the endpoint compared to those who did not experience childhood life stress. Meanwhile, the hazard among Whites and other participants who experienced childhood life stress was 2.3 times that of those who did not, but this association was not statistically significant (95% CI: 0.48-10.77) (Table 3).

Of the four types of childhood life stress, those who experienced general trauma had a higher hazard of adverse cardiovascular outcomes (HR=1.9; 95% CI: 1.02-3.81) at the study endpoint among Black participants but no association was found among Whites or other races (Table 3). Emotional abuse was significant for Whites and other races in the unadjusted model but not after adjusting for sociodemographic factors in model 2. Physical and sexual abuse were not significantly associated to the composite adverse cardiovascular outcomes at the study endpoint for both "Black' and 'White and other races' (Table 3).

Table 3: Cox regression analysis of the association between the four forms of childhood life stress and study end point (n=300)

	Overall	Black	White and others
	HR [95% CI]	HR [95% CI]	HR [95% CI]
Number of events, n (%)	85 (28.3)	67 (33.8)	18 (17.6)
ETISF Overall (>=6.8 vs <6.8)			
Model 1	**1.8 [1.18-2.84] ***	1.4[0.88-2.35]	**2.9 [1.11-8.10] ***
Model 2	**1.9 [1.18-2.96] ***	1.5 [0.89-2.47]	**3.1 [1.08-8.85] ***
Model 3	**1.8 [1.08-2.86] ***	1.7 [0.97-2.87]	2.2 [0.49-10.28]
Model 4	**1.9 [1.13-3.39] ***	**1.9 [1.02-3.59] ***	2.3 [0.48-10.77]
General trauma (Yes vs No)			
Model 1	1.3 [0.87-2.05]	1.1 [0.44-2.95]	1.3 [0.79-2.05]
Model 2	1.3 [0.85-2.05]	1.3 [0.79-2.16]	0.9 [0.33-2.60]
Model 3	1.4 [0.88-2.19]	1.6 [0.94-2.65]	0.7 [0.19-2.36]
Model 4	1.5 [0.86-2.56]	**1.9 [1.02-3.81] ***	0.6 [0.18-2.35]
Physical abuse (Yes vs No)			
Model 1	1.1 [0.72-1.72]	0.9 [0.56-1.57]	1.3 [0.49-3.49]
Model 2	1.1 [0.72 -1.76]	1.0 [0.61-1.68]	1.1 [0.34-3.13]
Model 3	1.1 [0.65-1.72]	1.1 [0.59-1.85]	1.0 [0.31-3.47]
Model 4	1.0 [0.61-1.71]	1.0 [0.56 -1.93]	1.0 [0.31-3.47]
Emotional abuse (Yes vs No)			

Model 1	**1.6 [1.04-2.54] ***	1.4 [0.81-2.27]	**2.8 [1.12-7.19] ***
Model 2	**1.6 [1.01-2.55] ***	1.4 [0.92-2.34]	2.7 [0.97-7.22]
Model 3	1.4 [0.85-2.20]	1.3 [0.76-2.27]	3.1 [0.79-11.72]
Model 4	1.4 [0.83-2.25]	1.3 [0.74-2.39]	3.1 [0.79-11.8]
Sexual abuse (Yes vs No)			
Model 1	1.2 [0.74-1.79]	1.1 [0.65-1.75]	1.2 [0.46-3.25]
Model 2	1.1 [0.67-1.76]	1.0 [0.63-1.72]	1.3 [0.46 -3.84]
Model 3	1.1 [0.71-1.78]	1.1 [0.64-1.77]	1.5 [0.41-5.20]
Model 4	1.1 [0.67-1.79]	1.1 [0.61- 1.81]	1.5 [0.34-5.36]

Model 1: Unadjusted
Model 2: Adjusted for demographic factors (age, sex, educational status, ever smoking)
Model 3: Adjusted for clinical factors (hypertension, diabetes, body mass index, high blood cholesterol) and medications (aspirin, beta-blocker, statin, ACE-inhibitor use) plus model 2 factors.
Model 4: Adjusted for adult-life stress plus model 2 and 3 factors.
*$p<0.05$

The supplementary analysis also showed a positive and statistically significant linear association of childhood general trauma (b=5.0; 95% CI: 4.13-5.94), physical abuse (b=3.1; 95% CI: 2.03-4.09), emotional abuse (b=3.5; 95% CI: 2.38-4.65), and sexual abuse (b=2.9; 95% CI: 1.89-4.06) with adult life stress. However, there was no statistically significant association between adult life stress and time to a composite adverse cardiovascular outcome at the study end point in all models (Supplementary table 1).

Discussion

This study showed disparities in childhood and adult life stress and adverse cardiovascular outcome between ‘Black’ and ‘White and other’ races. It showed an association between childhood life stress and time to adverse composite cardiovascular events. Additionally, stratification by race identified no substantial difference by race in the association of overall early life events, while general trauma tended to be more strongly associated with the outcome

among Black participants and emotional abuse among participants of other races. Furthermore, the study identified that adult life stress did not play a role in the causal pathway in the association between childhood life stress and the time to composite adverse cardiovascular outcomes among patients with a history of MI.

This study showed a higher prevalence of overall childhood life stress as well as of specific types of childhood life stress including general trauma and physical abuse among Black compared to White and other races. This result supports (19–21) as well as differs from (22,23) prior studies. The inconsistencies in the findings could be due to the differences in the sample included and the study design followed in the different studies. For example, two studies which showed a higher prevalence of childhood life stress among White compared to Black individuals were conducted among high-risk populations, where one was conducted among a sample of low-income women and the other among youth from high-risk families in child abuse and neglect, measuring the childhood life stress prospectively unlike our study (22,23). In addition, our study specifically assessed the association among post-MI patients unlike the other studies. Poor socioeconomic status may be one of the major contributors of childhood life stress for Black individuals, as economic constraints can expose them to violence and household dysfunction (3). In addition, views on adversity might differ across different racial and ethnic groups, potentially due to varying cultures or norms. For example, when presented with identical situations, one racial or ethnic group may perceive them as adverse, while another race might not (23).

A high mean score in adult life stress was identified among Black participants compared to those who were ‘White and other’ races. This finding is supported by prior studies that showed a high

level of overall stress among Black individuals compared to other races (27,28). Prior studies, as well as our analysis, indicate that adverse childhood life stress events are directly and positively correlated with adult life stress (13). This implies that Black individuals who have a high prevalence of adverse childhood experiences in our sample are more likely to experience stress in adulthood. Additionally, the role of poor socioeconomic status among Black individuals may predispose them to various stressful environments, and insufficient financial support may hinder their ability to resolve these challenges (3).

This study identified associations between childhood life stress and adverse cardiovascular outcomes among 'Black' and 'White and other' races. Among Black, the association between childhood life stress and adverse cardiovascular outcomes, which was initially close to the null and not statistically significant, became larger and significant after adjusting for adult life stress. However, after adjusting for adult life stress, childhood life stress showed a statistically significant effect on adverse composite cardiovascular outcomes, indicating that childhood life stress affects cardiovascular outcomes independently of adult life stress. This finding differs from a previous study conducted in China, which showed that adverse adult experiences partially mediated the association between childhood life stress and cardiovascular outcomes (13). The difference in the results between this study and the study conducted in China may be attributable to variations in the study population and the outcomes measured. The study in China used a community-based cohort which included participants aged above 45 years old and looked at incident CVD cases, while our study included patients with history of MI and examined a composite adverse CVD outcome.

Among the four forms of childhood life stress, the association of general trauma with the composite adverse cardiovascular outcome, which was initially close to the null, became more pronounced and statistically significant after adjusting for adult life stress only among Black participants. Among Black patients with a history of MI, general trauma in childhood was the most important early life stress exposure that was associated with the composite adverse cardiovascular outcomes independent of the adult life stress. This effect was not seen among White and other racial groups. Compared to other racial groups, Black participants are more susceptible to live in a neighborhood with a high violence and poor socioeconomic conditions, which may help explain these finding (29).

In contrast to the findings of a Chinese study (13), adult life stress did not appear to influence the association between childhood life stress and composite adverse cardiovascular outcomes in either groups. These diverging results may be due to differences in the populations included by the studies. The Chinese study used community-based data, whereas our study included patients with a history of MI. Additionally, the Chinese study had a larger sample size (n=5936), which likely provided greater statistical power to detect a statistically significant association. Given these differences, additional research to examine the role of adult life stress in these associations is recommended.

Strength and limitations

The strength of our study lies in the fact that more than half of our participants are Black, a group that has been historically underrepresented in prior cardiovascular research. In addition, this study is the first to assess racial disparities in the association between childhood life stress events and a composite adverse cardiovascular outcome among patients with a history of MI. Despite its

strengths, this study may also have some limitations. Since childhood and adult life stress were assessed retrospectively based on patients' response, responses might be susceptible to recall bias. In addition, the sample was small, which limited our ability to obtain robust estimates when examining subgroups. Our study sample was also based on institutions in Atlanta, which may affect the generalizability of the findings.

Conclusion

This study showed significant racial disparities in the prevalence of childhood and adult life stress among post-MI patients. Childhood life stress was independently associated with the risk of adverse composite cardiovascular outcomes, regardless of adult life stress, and there were no significant differences by race in this association. The influence of specific types of childhood stress on cardiovascular risk varied by race, with general trauma being most important among Black individuals, and emotional stress being more influential among White and other races.

Policy Implication

This study has important policy implications, including the need to develop and evaluate screening and intervention programs that address the adverse effects of childhood stress, particularly across different racial/ethnic groups. Comprehensive targeted interventions that address the long-term effects of childhood stress in adults who had considerable stress in the early years should be tested. Focused studies should examine the impact of these strategies to reduce the risk of adverse outcomes among individuals with an MI.

References

1. Institute of Medicine (US). A nationwide framework for surveillance of cardiovascular and chronic lung diseases. National Academies Press Washington, DC; 2011.

2. Cardiovascular diseases [Internet]. [cited 2023 Oct 12]. Available from: https://www.who.int/health-topics/cardiovascular-diseases

3. Suglia SF, Koenen KC, Boynton-Jarrett R, Chan PS, Clark CJ, Danese A, et al. Childhood and adolescent adversity and cardiometabolic outcomes: a scientific statement from the American Heart Association. Circulation. 2018;137(5):e15–28.

4. Allen H, Wright BJ, Vartanian K, Dulacki K, Li HF. Examining the prevalence of adverse childhood experiences and associated cardiovascular disease risk factors among low-income uninsured adults. Circ Cardiovasc Qual Outcomes. 2019;12(9):e004391.

5. Miller GE, Chen E, Parker KJ. Psychological stress in childhood and susceptibility to the chronic diseases of aging: moving toward a model of behavioral and biological mechanisms. Psychol Bull. 2011;137(6):959.

6. Flores-Torres MH, Comerford E, Signorello L, Grodstein F, Lopez-Ridaura R, de Castro F, et al. Impact of adverse childhood experiences on cardiovascular disease risk factors in adulthood among Mexican women. Child Abuse Negl. 2020;99:104175.

7. Jackson DB, Testa A, Woodward KP, Qureshi F, Ganson KT, Nagata JM. Adverse childhood experiences and cardiovascular risk among young adults: findings from the 2019 Behavioral Risk Factor Surveillance System. Int J Environ Res Public Health. 2022;19(18):11710.

8. Chang X, Jiang X, Mkandarwire T, Shen M. Associations between adverse childhood experiences and health outcomes in adults aged 18–59 years. PloS One. 2019;14(2):e0211850.

9. Campbell JA, Walker RJ, Egede LE. Associations between adverse childhood experiences, high-risk behaviors, and morbidity in adulthood. Am J Prev Med. 2016;50(3):344–52.

10. Godoy LC, Frankfurter C, Cooper M, Lay C, Maunder R, Farkouh ME. Association of adverse childhood experiences with cardiovascular disease later in life: a review. JAMA Cardiol. 2021;6(2):228–35.

11. Jacquet-Smailovic M, Brennstuhl MJ, Tarquinio CL, Tarquinio C. Relationship between cumulative adverse childhood experiences and myocardial infarction in adulthood: A systematic review and meta-analysis. J Child Adolesc Trauma. 2021;1–14.

12. Almuwaqqat Z, Wittbrodt M, Young A, Lima BB, Hammadah M, Garcia M, et al. Association of early-life trauma and risk of adverse cardiovascular outcomes in young and middle-aged individuals with a history of myocardial infarction. JAMA Cardiol. 2021;6(3):336–40.

13. Wang W, Liu Y, Yang Y, Jiang W, Ni Y, Han X, et al. Adverse childhood and adulthood experiences and risk of new-onset cardiovascular disease with consideration of social support: a prospective cohort study. BMC Med. 2023;21(1):297.

14. Elkins J, Miller KM, Briggs HE, Kim I, Mowbray O, Orellana ER. Associations between adverse childhood experiences, major depressive episode and chronic physical health in adolescents: Moderation of race/ethnicity. Soc Work Public Health. 2019;34(5):444–56.

15. Vásquez E, Udo T, Corsino L, Shaw BA. Racial and ethnic disparities in the association between adverse childhood experience, perceived discrimination and body mass index in a national sample of US older adults. J Nutr Gerontol Geriatr. 2019;38(1):6–17.

16. Vásquez E, Quiñones A, Ramirez S, Udo T. Association between adverse childhood events and multimorbidity in a racial and ethnic diverse sample of middle-aged and older adults. Innov Aging. 2019;3(2):igz016.

17. Lam-Hine T, Riddell CA, Bradshaw PT, Omi M, Allen AM. Racial differences in associations between adverse childhood experiences and physical, mental, and behavioral health. SSM-Popul Health. 2023;101524.

18. Brown LL, Mitchell UA, Ailshire JA. Disentangling the stress process: Race/ethnic differences in the exposure and appraisal of chronic stressors among older adults. J Gerontol Ser B. 2020;75(3):650–60.

19. Cronholm PF, Forke CM, Wade R, Bair-Merritt MH, Davis M, Harkins-Schwarz M, et al. Adverse childhood experiences: Expanding the concept of adversity. Am J Prev Med. 2015;49(3):354–61.

20. Zhang X, Monnat SM. Racial/ethnic differences in clusters of adverse childhood experiences and associations with adolescent mental health. SSM-Popul Health. 2022;17:100997.

21. Richards TN, Schwartz JA, Wright E. Examining adverse childhood experiences among Native American persons in a nationally representative sample: Differences among racial/ethnic groups and race/ethnicity-sex dyads. Child Abuse Negl. 2021;111:104812.

22. Fagan AA, Novak A. Adverse childhood experiences and adolescent delinquency in a high-risk sample: A comparison of white and black youth. Youth Violence Juv Justice. 2018;16(4):395–417.

23. Mersky JP, Janczewski CE. Racial and ethnic differences in the prevalence of adverse childhood experiences: Findings from a low-income sample of US women. Child Abuse Negl. 2018;76:480–7.

24. Nelson CA, Bhutta ZA, Harris NB, Danese A, Samara M. Adversity in childhood is linked to mental and physical health throughout life. bmj [Internet]. 2020 [cited 2024 Apr 7];371. Available from: https://www.bmj.com/content/371/bmj.m3048.abstract

25. Bremner JD, Bolus R, Mayer EA. Psychometric properties of the early trauma inventory–self report. J Nerv Ment Dis. 2007;195(3):211.

26. Zhao J, Bremner JD, Goldberg J, Quyyumi AA, Vaccarino V. MAOA genotype, childhood trauma and subclinical atherosclerosis: a twin study. Psychosom Med. 2013;75(5):471.

27. Lu MC, Chen B. Racial and ethnic disparities in preterm birth: the role of stressful life events. Am J Obstet Gynecol. 2004;191(3):691–9.

28. Sternthal MJ, Slopen N, Williams DR. Racial disparities in health: how much does stress really matter? 1. Bois Rev Soc Sci Res Race. 2011;8(1):95–113.

29. Kim SJ, Kery C, An J, Rineer J, Bobashev G, Matthews AK. Racial/Ethnic disparities in exposure to neighborhood violence and lung cancer risk in Chicago. Soc Sci Med. 2024;340:116448.

Supplemental Tables

Table 1. Cox-regression analysis between adult life stress and the study endpoint (n=300)

		Black	White and others
	HR [95% CI]	HR [95% CI]	HR [95% CI]
Adult life stress			
Model 1	1.0 [0.99-1.09]	1.0[0.97-1.07]	**1.1 [1.00-1.23] ***
Model 2	1.0 [0.99-1.09]	1.0 [0.96-1.06]	1.1 [0.99-1.23]
Model 3	1.0 [0.97-1.06]	1.0 [0.96-1.06]	1.0 [0.88-1.15]
Model 4	0.9 [0.92-1.03]	0.9[0.90- 1.03]	0.9 [0.85-1.16]
Adult life stress (standardized)			
Model 1	1.2 [0.97-1.48]	1.1 [0.85-1.35]	**1.7 [1.04-2.68]**
Model 2	1.2 [0.95-1.47]	1.1 [0.83-1.35]	1.6 [0.96-2.68]
Model 3	1.1 [0.85-1.31]	1.0 [0.80-1.29]	1.0[0.55-1.96]
Model 4	0.9 [0.66-1.15]	0.8 [0.62-1.15]	0.9 [0.46-1.98]

Model 1: Unadjusted
Model 2: Adjusted for demographic factors (age, sex, educational status, ever smoking)
Model 3: Adjusted for clinical factors (hypertension, diabetes, body mass index, high blood cholesterol) and medications (aspirin, beta-blocker, statin, ACE-inhibitor use) plus model 2 factors.
Model 4: Adjusted for Early-life stress plus model 2 and 3 factors (n=297 due to missing value).

Table 2. Cox-regression analysis between a continuous Early-life stress (ETI-SR-SF) and the study endpoint (n=300)

		Black	White and others
	HR [95% CI]	HR [95% CI]	HR [95% CI]
Early life stress			
Model 1	**1.0 [1.00-1.08] ***	1.0 [0.99-1.07]	1.1[0.99-1.15]
Model 2	**1.0 [1.00-1.08] ***	1.0[0.99-1.07]	1.1[0.99-1.19]
Model 3	1.0 [0.99-1.07]	1.0[0.99-1.08]	1.0[0.90-1.20]
Model 4	**1.1 [1.00-1.11] ***	1.1[0.99-1.11]	1.0[0.89-1.23]
Early life stress (standardized)			
Model 1	**1.3 [1.05-1.57]**	1.2 [0.93-1.47]	1.5 [0.97-2.29]
Model 2	**1.3 [1.04-1.59]**	1.2 [0.93-1.50]	1.6[0.96-2.72]
Model 3	1.2 [0.98-1.52]	1.2 [0.94-1.52]	1.3 [0.55-2.91]
Model 4	**1.3 [1.00-1.78]**	1.3 [0.98-1.85]	1.3 [0.51-3.38]

*$p<0.05$
Model 1: Unadjusted
Model 2: Adjusted for demographic factors (age, sex, educational status, ever smoking)

Model 3: Adjusted for clinical factors (hypertension, diabetes, body mass index, high blood cholesterol) and medications (aspirin, beta-blocker, statin, ACE-inhibitor use) plus model 2 factors.
Model 4: Adjusted for adult life stress plus model 2 and 3 factors.
*p<0.05

Table 3. Linear regression analysis between childhood life stress events and adult-life stress (n=300)

		b	95% CI
General trauma			
	No	**ref**	
	Yes	**5.0**	**4.13-5.94 ***
Physical abuse			
	No	**ref**	
	Yes	**3.1**	**2.03-4.09 ***
Emotional abuse			
	No	**ref**	
	Yes	**3.5**	**2.38-4.65 ***
Sexual abuse			
	No	**ref**	
	Yes	**2.9**	**1.89-4.06 ***

*p<0.05