Stress, Resilience, and Cardiovascular Disease Risk Among Black Women

Results From the Women's Health Initiative

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BACKGROUND: Empirical data on the link between stress and cardiovascular disease (CVD) risk among black women is limited. We examined associations of stressful life events and social strain with incident CVD among black women and tested for effect modification by resilience.

METHODS AND RESULTS: Our analysis included 10 785 black women enrolled in the Women's Health Initiative Observational Study and Clinical Trials cohort. Participants were followed for CVD for up to 23 years (mean, 12.5). Multivariable Cox regression was used to estimate hazard ratios and 95% CIs for associations between stress-related exposures and incident CVD. We included interactions between follow-up time (age) and stressful life events because of evidence of nonproportional hazards. Effect modification by resilience was examined in the sub-cohort of 2765 women with resilience and stressful life events measures. Higher stressful life events were associated with incident CVD at ages 55 (hazard ratio for highest versus lowest quartile=1.80; 95% CI, 1.27–2.54) and 65 (hazard ratio for highest versus lowest quartile=1.40; 95% CI, 1.16–1.68), but not at older ages. Adjustment for CVD risk factors attenuated these associations. Similar associations were observed for social strain. In the sub-cohort of women with updated stressful life events and resilience measures, higher stressful life events were associated with incident CVD in multivariable-adjusted models (hazard ratio=1.61; 95% CI, 1.04–2.51). Resilience did not modify this association nor was resilience independently associated with incident CVD.

CONCLUSIONS: In this cohort of older black women, recent reports of stressful life events were related to incident CVD. Resilience was unrelated to incident CVD.

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Key Words: atherosclerosis ■ cardiovascular diseases ■ diabetes mellitus ■ hypertension ■ risk

WHAT IS KNOWN

- Black women have a higher burden of cardiovascular disease (CVD) compared with their white counterparts.
- Stress is modestly associated with higher risk of CVD in mostly white study populations.

WHAT THE STUDY ADDS

- Higher baseline stressful life events and social strain were associated with higher CVD risk among black women; however, adjustment for traditional CVD risk factors attenuated these associations.
- In a sub-cohort of women with updated stressful life events and resilience measures, higher stressful life events were independently associated with higher incident CVD.
- Resilience was not independently associated with CVD risk nor did it modify the association between stressful life events and CVD risk.

Cardiovascular disease (CVD) mortality has declined dramatically in the United States. This decline has paralleled advances in primary prevention, including improved hypertension treatment and control, smoking reductions, and the prevalent use of statins, as well as the use of early interventions in those with atherosclerotic events.[1,2] Age-adjusted annual heart disease mortality fell by 56% between 1950 and 1996, whereas age-adjusted annual stroke rates fell by 70% during the same period.[3] However, these reductions have not been equitably experienced across the US population. In particular, black women continue to experience a higher burden of CVD compared with their white counterparts.[3–5] These differences appear to persist, even after accounting for traditional CVD risk factors. As such, the continued disparate health outcomes experienced by black women mandate additional research into the etiology and preventive strategies for CVD among black women.

Stress is hypothesized to contribute to CVD through inflammation, endothelial dysfunction, and atherosclerosis.[6] In an analysis of the Women's Health Initiative (WHI) Observational Study (OS),[7] higher social strain and stressful life events were associated with increased risk of coronary heart disease and stroke in models adjusted for sociodemographic characteristics and depressive symptoms; however, subsequent inclusion of potential mediating factors, including alcohol use, cigarette smoking, hypertension, waist circumference, high cholesterol, diabetes mellitus, physical activity, and dietary quality attenuated these relationships. These associations were not modified by race, suggesting similar relationships among white and black women.

Stress may be particularly relevant for black women, given the discriminatory environment in which these women may live. However, research on the relationship between stress and CVD among black women is sparse. Furthermore, resilience, or the ability to bounce back from adversity, may mitigate some of the harmful effects of stress and CVD risk factors. Emerging data suggest that at-risk populations, including individuals stigmatized because of their race/ethnicity, have developed culturally-specific mechanisms that help them not only survive, but also thrive.[8] Although the potential moderating effect of resilience has not been specifically explored in the context of stress and CVD among black women, resilience has been identified as a protective factor in the relationship between substance abuse, violence, and HIV/AIDS with depressive symptoms among black women.[9]

We sought to build on the prior WHI analysis by examining the association between stress and incident CVD in a larger population of black women and evaluating whether resilience modifies this relationship. We hypothesized that higher self-reports of stressful life events and social strain are associated with increased incident CVD among black women. Moreover, we postulated that high levels of resilience may attenuate the harmful effects of stress on CVD development among black women.

METHODS

Study Population

Because of the sensitive nature of the data collected for this study, requests to access the dataset from qualified researchers trained in human subject confidentiality protocols may be sent to the Women's Health Initiative at www.whi.org. Full details of the WHI have been described previously.[10–12] Briefly, between 1993 and 1998, postmenopausal women between the ages of 50 and 79 years were recruited from 40 clinical sites across the US into 1 or more randomized clinical trials (WHI-CT, n=68 132) or an OS (WHI-OS, n=93 676). Women in the WHI-OS were either unwilling or ineligible to be included in the WHI-CT.[13] Moreover, black women were oversampled in the WHI-OS. The WHI-CT and WHI-OS were closed in 2004 to 2005, and participants were invited to continue follow-up in the WHI Extension Study 1 (2005–2010), Extension Study 2 (2010–2015), and Extension Study 3 (2015–2020). Written informed consent was obtained from all study participants. Ethics approval was obtained from institutional review boards at all participating institutions. A standardized written protocol, centralized training of staff, and quality assurance visits by the Clinical Coordinating Center were used to ensure uniform data collection.[13]

Our study sample was drawn from the 161 808 women participating in either the WHI-CT or WHI-OS. Of these, we excluded non-black women (n=147 190), women missing baseline stressful life events or social strain measures (n=1322), women with a history of CVD at baseline (n=2435), and women who were missing follow-up time (n=76), leaving 10 785 women in our analytic sample.

Exposure Variables

At baseline, women completed questionnaires on stressful life events and social strain. The stressful life events questionnaire was adapted from the Beta-Blocker Heart Attack Trial and modified for women of older age.[14] Participants indicated whether any of 11 life changes had occurred over the past year: spouse died, spouse had serious illness, close friend died, had major problems with money, experienced a divorce or break up, close friend divorced, major conflict with children or grandchildren, lost job, physically abused, verbally abused, and pet died. Additionally, women were asked to appraise each of the 11 life events that occurred based on the degree of upset that it caused on a scale of 1 (did not upset me) to 3 (upset me very much), generating a scale ranging from 0 to 33, with higher scores indicating greater stressful events.

Social strain was derived from 4 items from a previously validated measure of negative aspects of social relationships.[15] Participants were asked how many of the people who were important to them got on their nerves, asked too much of them, did not include them, or tried to get them to do things they do not want to do. Responses to each item ranged from 1 (none) to 5 (all), yielding a social strain score ranging from 4 to 20, with higher scores indicating greater social strain.

Resilience, or the ability to bounce back from stressful situations, was assessed during the WHI Extension Study 2 and quantified with the modified Brief Resilience Scale.[16] Of the 6 items included in the original Brief Resilience Scale, scoring of 3 items was available in the WHI study. Participants are asked to rate the following statements on a scale of 1 to 6: "I tend to bounce back quickly after hard times; It does not take me long to recover from a stressful event; I have a hard time making it through stressful events." Scores range from 3 to 18, with higher scores indicating higher resilience.

Other Covariates

At baseline, participants completed self-administered questionnaires detailing demographic characteristics, medical and reproductive history, previous use of postmenopausal hormone therapy, physical activity, smoking history, alcohol use, diet, and other risk factors. Physical activity was quantified with questions on frequency, duration, and intensity of participation in different forms of physical activity. Weekly recreational physical activity was calculated by multiplying an assigned energy expenditure level for each category of activity by the hours exercised per week to calculate total metabolic equivalents per week (METs per week). Participants also underwent a clinic visit where trained staff measured each participant's height and weight using a standardized protocol. Body mass index was calculated based on these height and weight measurements.

Outcome Variables

The primary outcome of our analysis was time to any CVD event, including coronary heart disease (angina and myocardial infarction), revascularization procedure (coronary revascularization, percutaneous transluminal coronary angioplasty, carotid revascularization, and coronary artery bypass graft), carotid artery disease, peripheral artery disease, stroke/transient ischemic attack, heart failure, and CVD-related death. These events were centrally adjudicated using standardized case definitions and clinical criteria and updated annually through December 31, 2015 (end of Extension Study 2). Death certificate and medical record reviews were used to determine cause of death. A 94% rate of agreement between local and central clinical adjudicators for cause of death in WHI has been previously reported.[17]

Statistical Analysis

Summary statistics of baseline characteristics according to stressful life events and social strain were evaluated with χ^2 tests or *t* tests, respectively. Stressful life events and social strain were investigated in 4 categories (based on quartiles) and as continuous variables. We estimated hazard ratios (HRs) and 95% CIs for the association between stressful life events, social strain, and incident CVD using the Cox proportional hazards regression model. Age at study randomization/enrollment was used as the underlying time scale, and women who died from non-CVD events were censored. We tested the proportional hazards assumption by examining the Wald test for the multiplicative interaction between our main exposure variables, stressful life events and social strain, and follow-up time (natural log scale). Due to evidence of nonproportional hazards for baseline stressful life events, but not social strain, we included a multiplicative interaction between baseline stressful life events and age to allow for nonproportional hazards. We present age-specific HRs and 95% CIs to illustrate the time-varying relationship of baseline stress on incident CVD as women age. All models were adjusted for known CVD risk factors, including diabetes mellitus status (no, yes), body mass index (<25 kg/m^2, 25–30 kg/m^2, ≥30 kg/m^2), physical activity (>0–3.75 MET-h/wk, 3.75–8.75 MET-h/wk, 8.75–17.5 MET-h/wk, ≥17.5 MET-h/wk), hypertension history (none, treated hypertension, or untreated hypertension), use of antihyperlipidemia drugs (no, yes), smoking status (never, past, and current), and education (less than high school or general equivalency diploma, high school diploma or general equivalency diploma, some college, college graduate or higher).

We also examined whether resilience modified the effect of stressful life events and incident CVD using the likelihood-ratio procedure, comparing models with and without an interaction term between resilience and stressful life events. This analysis included the subset of black women who responded to the Extension Study 2 questionnaire. We did not examine interactions with social strain, as this was not included in the Extension Study 2 questionnaire. Analyses were conducted using STATA software (version 11, STATA Corp, Texas). All *P* values were 2-sided with the probability of a type I error set at <5%.

RESULTS

Study Population

Compared with black women in the lowest quartile of stressful life events, women in the highest quartile of stressful life events were younger at baseline, had lower educational attainment, were less physically active, and had a higher proportion of current smoking, obesity,

Table 1. **Baseline Characteristics of Study Participants by Stressful Life Events, Women's Health Initiative Observational and Clinical Trials, n=10 785**

	Stressful Life Events			
	Q1 (0–1)	Q2 (2–3)	Q3 (4–6)	Q4 (7–30)
	(n=2495)	(n=2917)	(n=2966)	(n=2407)
Age at WHI entry mean (SD)	61.7 (7)	61.4 (7.1)	60.8 (7)	60.0 (6.8)
Education				
Missing	22 (1%)	31 (1%)	31 (1%)	42 (2%)
Less than high school diploma or GED	226 (9%)	256 (9%)	291 (10%)	317 (13%)
High school diploma or GED	342 (14%)	397 (14%)	395 (13%)	323 (13%)
Some college	897 (36%)	1066 (37%)	1170 (39%)	1014 (42%)
College graduate or higher	1008 (40%)	1167 (40%)	1079 (36%)	711 (30%)
Smoking status				
Missing	46 (2%)	35 (1%)	45 (2%)	35 (1%)
Never smoked	1286 (52%)	1444 (50%)	1425 (48%)	1133 (47%)
Past smoker	933 (37%)	1142 (39%)	1122 (38%)	932 (39%)
Current smoker	230 (9%)	296 (10%)	374 (13%)	307 (13%)
BMI				
Missing	25 (1%)	28 (1%)	25 (1%)	23 (1%)
<25 kg/m^2	443 (18%)	506 (17%)	464 (16%)	329 (14%)
25 to 29 kg/m^2	886 (36%)	984 (34%)	991 (33%)	712 (30%)
≥30 kg/m^2	1141 (46%)	1399 (48%)	1486 (50%)	1343 (56%)
Hormone use				
Missing	4 (<1%)	2 (<1%)	4 (<1%)	6 (<1%)
Never	1446 (58%)	1701 (58%)	1727 (58%)	1456 (60%)
Past user	383 (15%)	420 (14%)	443 (15%)	352 (15%)
Current user <5 y	267 (11%)	291 (10%)	313 (11%)	263 (11%)
Current user 5 to <10 y	141 (6%)	195 (7%)	187 (6%)	126 (5%)
Current user ≥10 y	254 (10%)	308 (11%)	292 (10%)	204 (8%)
Type of hormone use				
Missing	4 (<1%)	2 (<1%)	4 (<1%)	6 (<1%)
Never user	1446 (58%)	1701 (58%)	1727 (58%)	1456 (60%)
Past user of either E alone or E+P	383 (15%)	420 (14%)	443 (15%)	352 (15%)
E alone	498 (20%)	599 (21%)	574 (19%)	458 (19%)
E+P	164 (7%)	195 (7%)	218 (7%)	135 (6%)
Oral contraceptive use				
Missing	0	0	0	1 (<1%)
Yes	905 (36%)	1142 (39%)	1216 (41%)	1039 (43%)
Diabetes mellitus status				
Missing	6 (<1%)	7 (<1%)	5 (<1%)	2 (<1%)
Yes	222 (9%)	279 (10%)	301 (10%)	287 (12%)
Use of antihyperlipidemia drugs				
Missing	125 (5%)	186 (6%)	188 (6%)	173 (7%)
Yes	328 (13%)	391 (13%)	359 (12%)	303 (13%)
Hypertension history				
Missing	112 (4%)	164 (6%)	169 (6%)	145 (6%)
Never hypertensive	1187 (48%)	1333 (46%)	1335 (45%)	1050 (44%)
Treated hypertensive	993 (40%)	1191 (41%)	1200 (40%)	973 (40%)

(*Continued*)

Table 1. Continued

	Stressful Life Events			
	Q1 (0–1)	Q2 (2–3)	Q3 (4–6)	Q4 (7–30)
	(n=2495)	(n=2917)	(n=2966)	(n=2407)
Untreated hypertensive	203 (8%)	229 (8%)	262 (9%)	239 (10%)
Physical activity				
Missing	77 (3%)	125 (4%)	135 (5%)	108 (4%)
None	513 (21%)	639 (22%)	641 (22%)	565 (23%)
>0–3.75 MET-h/wk	436 (17%)	478 (16%)	540 (18%)	461 (19%)
3.75–8.75 MET-h/wk	515 (21%)	584 (20%)	614 (21%)	473 (20%)
8.75–17.5 MET-h/wk	463 (19%)	513 (18%)	502 (17%)	404 (17%)
≥17.5 MET-h/wk	491 (20%)	578 (20%)	534 (18%)	396 (16%)
WHI trial membership				
OS	1340 (54%)	1495 (51%)	1444 (49%)	1180 (49%)
E only	158 (6%)	177 (6%)	224 (8%)	187 (8%)
E+P	108 (4%)	154 (5%)	158 (5%)	126 (5%)
DM	741 (30%)	878 (30%)	904 (30%)	704 (29%)
E+P and DM	148 (6%)	213 (7%)	236 (8%)	210 (9%)

DM indicates dietary modification; E, estrogen; GED, general equivalency diploma; MET, metabolic equivalent; OS, observational study; and P, progestin.

oral contraceptive use, and diabetes mellitus (Table 1). Black women in the highest quartile of social strain were more commonly never users of menopausal hormone therapy compared with those in the lowest quartile of social strain (Table 2).

Baseline Stressful Life Events, Social Strain, and Incident CVD

During a mean 12.5 years of follow-up, 1863 women (17%) experienced a CVD event, at a mean age of 72.6 years. Angina was the most common CVD event (n=636; 34%), followed by stroke (n=348; 19%), coronary heart disease (n=308; 17%), and congestive heart failure (n=302, 16%). In univariable models, higher baseline reports of stressful life events were associated with higher incident CVD at ages 55 (HR for highest versus lowest quartile =1.80; 95% CI, 1.27–2.54) and 65 (HR for highest versus lowest quartile =1.40; 95% CI, 1.16–1.68). In multivariable models that adjusted for established CVD risk factors, the association between stressful life events and incident CVD was no longer significant (Table 3 and Figure). Similarly, we observed a univariable association between higher baseline reports of social strain and incident CVD (HR for highest versus lowest quartile =1.30; 95% CI, 1.13–1.49) that was attenuated in the multivariable models (HR, 1.13; 95% CI, 0.97–1.31). Associations between established CVD risk factors and CVD events were in the expected directions in the multivariable-adjusted model. For example, diabetes mellitus (HR, 2.25; 95% CI, 1.98–2.56), obesity HR, 1.18; 95% CI, 1.06–1.32), physical inactivity (HR, 1.27; 95% CI, 1.09–1.49), and current smoking (HR, 2.05; 95% CI, 1.76–2.38) were all related to higher CVD event risk.

Modifying Role of Resilience

Among the 10 785 black women included in the baseline analyses, 2765 (25.6%) had data on resilience and stressful life events from the Extension Study 2 questionnaire. Associations between resilience, stressful life events, and baseline factors are shown in Table 4. Black women in the highest quartile of resilience reported lower stress, had higher educational attainment, were less likely to be obese, more commonly used oral contraceptives, less commonly used antihyperlipidemia drugs, and were more physically active compared with black women in the lower quartile of resilience.

Of the Extension Study 2 cohort, 202 (7.3%) experienced a CVD event, with a mean age at first CVD event of 79.5 years (SD, 6.6 years; range, 64.6–96.3 years). We observed no interaction between resilience and stressful life events in either a univariable (P=0.74) or multivariable Cox proportional hazards model for incident CVD (P=0.48). Therefore, we present the multivariable-adjusted main effects of stressful life events and resilience in relation to incident CVD in Table 5. Similar to estimates in the overall cohort, higher stressful life events was positively associated with incident CVD (HR for highest versus lowest quartile =1.61; 95% CI, 1.04–2.51; Q2 versus Q1 HR, 1.83; 95% CI, 1.19–2.82) even after accounting for CVD risk factors. However, resilience was not associated with incident

Table 2. Baseline Characteristics of Study Participants by Social Strain, Women's Health Initiative Observational and Clinical Trials, n=10 785

	Social Strain			
	Q1 (4)	Q2 (5–6)	Q3 (7–9)	Q4 (10–20)
	(n=2649)	(n=3220)	(n=2477)	(n=2439)
Age at WHI entry mean (SD)	61.3 (7)	60.8 (7)	60.3 (6.8)	61.8 (7.2)
Education				
Missing	22 (1%)	40 (1%)	39 (2%)	25 (1%)
Less than high school diploma or GED	207 (8%)	288 (9%)	376 (15%)	219 (9%)
High school diploma or GED	308 (12%)	459 (14%)	368 (15%)	322 (13%)
Some college	1011 (38%)	1289 (40%)	1009 (41%)	838 (34%)
College graduate or higher	1101 (42%)	1144 (36%)	685 (28%)	1035 (42%)
Smoking status				
Missing	52 (2%)	43 (1%)	36 (1%)	30 (1%)
Never smoked	1297 (49%)	1593 (49%)	1173 (47%)	1225 (50%)
Past smoker	1016 (38%)	1220 (38%)	936 (38%)	957 (39%)
Current smoker	284 (11%)	364 (11%)	332 (13%)	227 (9%)
BMI				
Missing	27 (1%)	34 (1%)	17 (1%)	23 (1%)
<25 kg/m^2	503 (19%)	524 (16%)	298 (12%)	417 (17%)
25–29 kg/m^2	895 (34%)	1052 (33%)	738 (30%)	888 (36%)
≥30 kg/m^2	1224 (46%)	1610 (50%)	1424 (57%)	1111 (46%)
Hormone use				
Missing	6 (<1%)	4 (<1%)	3 (<1%)	3 (<1%)
Never	1456 (55%)	1919 (60%)	1483 (60%)	1472 (60%)
Past user	452 (17%)	450 (14%)	351 (14%)	345 (14%)
Current user <5 y	275 (10%)	340 (11%)	259 (10%)	260 (11%)
Current user 5 to <10 y	180 (7%)	190 (6%)	157 (6%)	122 (5%)
Current user ≥10 y	280 (11%)	317 (10%)	224 (9%)	237 (10%)
Type of hormone use				
Missing	6 (<1%)	4 (<1%)	3 (<1%)	3 (<1%)
Never user	1456 (55%)	1919 (60%)	1483 (60%)	1472 (60%)
Past user of either E alone or E+P	452 (17%)	450 (14%)	351 (14%)	345 (14%)
E alone	561 (21%)	618 (19%)	489 (20%)	461 (19%)
E+P	174 (7%)	229 (7%)	151 (6%)	158 (6%)
Oral contraceptive use				
Missing	1 (<1%)	0	0	0
Yes	1026 (39%)	1343 (42%)	1025 (41%)	908 (37%)
Diabetes mellitus status				
Missing	6 (<1%)	4 (<1%)	5 (<1%)	5 (<1%)
Yes	235 (9%)	311 (10%)	306 (12%)	237 (10%)
Use of antihyperlipidemia drugs				
Missing	178 (7%)	212 (7%)	163 (7%)	119 (5%)
Yes	342 (13%)	404 (13%)	346 (14%)	289 (12%)
Hypertension history				
Missing	157 (6%)	192 (6%)	132 (5%)	109 (4%)
Never hypertensive	1229 (46%)	1445 (45%)	1060 (43%)	1171 (48%)
Treated hypertensive	1037 (39%)	1314 (41%)	1028 (42%)	978 (40%)

(*Continued*)

Table 2. Continued

	Social Strain			
	Q1 (4)	Q2 (5–6)	Q3 (7–9)	Q4 (10–20)
	(n=2649)	(n=3220)	(n=2477)	(n=2439)
Untreated hypertensive	226 (9%)	269 (8%)	257 (10%)	181 (7%)
Physical activity				
Missing	128 (5%)	147 (5%)	97 (4%)	73 (3%)
None	539 (20%)	718 (22%)	589 (24%)	512 (21%)
>0–3.75 MET-h/wk	472 (18%)	580 (18%)	456 (18%)	407 (17%)
3.75–8.75 MET-h/wk	520 (20%)	656 (20%)	497 (20%)	513 (21%)
8.75–17.5 MET-h/wk	490 (18%)	531 (16%)	426 (17%)	435 (18%)
≥17.5 MET-h/wk	500 (19%)	588 (18%)	412 (17%)	499 (20%)
WHI trial membership				
OS	1304 (49%)	1579 (49%)	1236 (50%)	1340 (55%)
E only	178 (7%)	239 (7%)	188 (8%)	141 (6%)
E+P	141 (5%)	171 (5%)	113 (5%)	121 (5%)
DM	827 (31%)	978 (30%)	739 (30%)	683 (28%)
E+P and DM	199 (8%)	253 (8%)	201 (8%)	154 (6%)

DM indicates dietary modification; E, estrogen; GED, general equivalency diploma; MET, metabolic equivalent; OS, observational study; and P, progestin.

CVD (HR for lowest versus highest quartile =0.95; 95% CI, 0.63–1.42).

DISCUSSION

In this large study of older black women, we observed associations between baseline reports of higher stressful life events and increased incident CVD that diminished with age. Moreover, the age-specific associations were subsequently attenuated when conventional CVD risk factors were accounted. Likewise, higher social strain was related to incident CVD, but associations were attenuated with CVD risk factor adjustment. In the sub-cohort of women with updated information on stressful life events, we observed a significant association with CVD that was independent of CVD risk factors. Yet, contrary to our hypothesis, the relationship between stressful life events and incident CVD was not modified by resilience, nor was resilience independently related to incident CVD in the sub-cohort.

Epidemiological research conducted among male and female study populations support a link between psychosocial factors and CVD.[18,19] For example, a London-based study of psychological distress in 4374 men and 1895 women reported increased risk of coronary heart disease associated with higher baseline levels of psychological distress; associations among women were of a smaller magnitude compared with men.[20] In the INTERHEART study, a large, international, case-control study, general stress, adverse life events, and financial stress were consistently associated with myocardial infarction risk, independent of smoking behavior and socioeconomic status for both men and women.[21] Moreover, adverse childhood events, depression, and anger were more strongly related to ischemic heart disease risk than traditional risk factors in a study including 9367 women and 7970 men.[22] However, it is widely known that sex is an important biological variable. In the female-only Nurses' Health Study II, trauma and posttraumatic stress disorder were associated with elevated incident CVD.[23] Inclusion of race along with female sex is a focal point in understanding the impact of psychosocial factors and incident CVD.

Few studies have investigated stress and CVD in study populations with large numbers of black women, which is unfortunate given that black women are disproportionately affected by various psychosocial challenges, including more limited access to healthcare through insurance,[24] generally lower median household income,[25] less access to healthy food options,[26] and higher exposure to crime[27] when compared with white women. Moreover, there is evidence to suggest that race-related stress is associated with cardiovascular health.[28] These factors may act independently and interactively to uniquely increase CVD risk among black women.

In the Jackson Heart Study cohort, a cross-sectional analysis found that higher levels of stress were positively associated with CVD risk factors, including hypertension, diabetes mellitus, and obesity—findings consistent with our own data.[29] In a prior WHI analysis including women of any race, baseline reports of higher stressful life events and social strain were associated with CVD; however, associations were attenuated with adjustment for traditional risk factors.[7] Fur-

Table 3. Age-Specific Hazard Ratios (HRs) and 95% CIs for Associations of Stressful Life Events, Social Strain, and CVD Risk Among Black Women in the Women's Health Initiative, n=10 785

	Univariable Model		Multivariable Model*	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Stressful life events (at age 55)				
Q4 (7–30) vs Q1 (0–1)	1.80 (1.27–2.54)	<0.001	1.32 (0.91–1.92)	0.15
Q3 (4–6) vs Q1 (0–1)	1.25 (0.88–1.77)	0.21	1.13 (0.78–1.63)	0.51
Q2 (2–3) vs Q1 (0–1)	1.03 (0.72–1.46)	0.89	0.84 (0.57 –1.23)	0.36
Stressful life events (at age 65)				
Q4 (7–30) vs Q1 (0–1)	1.40 (1.16–1.68)	<0.001	1.14 (0.94–1.40)	0.19
Q3 (4–6) vs Q1 (0–1)	1.13 (0.94–1.36)	0.19	1.05 (0.86–1.28)	0.62
Q2 (2–3) vs Q1 (0–1)	1.04 (0.86–1.26)	0.68	0.94 (0.77–1.15)	0.55
Stressful life events (at age 75)				
Q4 (7–30) vs Q1 (0–1)	1.13 (0.97–1.31)	0.11	1.01 (0.86–1.19)	0.88
Q3 (4–6) vs Q1 (0–1)	1.04 (0.9–1.19)	0.61	0.99 (0.85–1.14)	0.85
Q2 (2–3) vs Q1 (0–1)	1.05 (0.92–1.2)	0.45	1.04 (0.90–1.20)	0.60
Stressful life events (at age 85)				
Q4 (7–30) vs Q1 (0–1)	0.94 (0.73–1.19)	0.60	0.91 (0.70–1.18)	0.48
Q3 (4–6) vs Q1 (0–1)	0.96 (0.77–1.20)	0.73	0.93 (0.73–1.18)	0.57
Q2 (2–3) vs Q1 (0–1)	1.06 (0.86–1.32)	0.57	1.13 (0.90–1.43)	0.29
Stressful life events (at age 95)				
Q4 (7–30) vs Q1 (0–1)	0.79 (0.55–1.13)	0.20	0.83 (0.56–1.22)	0.34
Q3 (4–6) vs Q1 (0–1)	0.90 (0.64–1.25)	0.53	0.89 (0.62–1.27)	0.52
Q2 (2–3) vs Q1 (0–1)	1.08 (0.77–1.49)	0.67	1.22 (0.86–1.74)	0.26
Social strain		0.001		0.39
Q4 (10–20) vs Q1 (4)	1.30 (1.13–1.49)		1.13 (0.97–1.31)	
Q3 (7–9) vs Q1 (4)	1.24 (1.09–1.42)		1.09 (0.95–1.25)	
Q2 (5–6) vs Q1 (4)	1.14 (1.01–1.30)		1.04 (0.90–1.21)	
Diabetes mellitus status				
Yes vs no	2.61 (2.32–2.93)	<0.001	2.25 (1.98–2.56)	<0.001
BMI		<0.001		<0.001
<25 vs 25–29 kg/m^2	0.79 (0.68–0.93)		0.79 (0.67–0.93)	
≥30 vs 25–29 kg/m^2	1.39 (1.25–1.54)		1.18 (1.06–1.32)	
Physical activity		<0.001		0.01
None	1.44 (1.24–1.68)		1.27 (1.09–1.49)	
>0–3.75 vs ≥17.5 MET-h/wk	1.47 (1.26–1.72)		1.28 (1.09–1.51)	
3.75–8.75 vs ≥17.5 MET-h/wk	1.26 (1.08–1.47)		1.16 (0.99–1.37)	
8.75–17.5 vs ≥17.5 MET-h/wk	1.16 (0.98–1.36)		1.10 (0.93–1.30)	
Hypertension history		<0.001		<0.001
Treated hypertensive vs never hypertensive	1.71 (1.55–1.9)		1.46 (1.31–1.63)	
Untreated hypertensive vs never hypertensive	1.44 (1.22–1.72)		1.31 (1.09–1.56)	
Use of antihyperlipidemia drugs				
Yes vs no	1.42 (1.25–1.6)	<0.001	1.24 (1.09–1.41)	<0.001
Smoking status		<0.001		<0.001
Past smoker vs never smoked	1.21 (1.09–1.33)		1.24 (1.12–1.38)	
Current smoker vs never smoked	1.86 (1.62–2.13)		2.05 (1.76–2.38)	
Education		<0.001		<0.001
Less than high school diploma/GED vs college graduate or higher	1.99 (1.72–2.31)		1.61 (1.37–1.90)	
High school diploma/GED vs college graduate or higher	1.38 (1.19–1.59)		1.14 (0.98–1.34)	
Some college vs college graduate or higher	1.27 (1.14–1.41)		1.19 (1.06–1.34)	

*Adjusted for stressful life events, social strain, diabetes mellitus status, BMI, physical activity, hypertension history, use of antihyperlipidemia drugs, smoking status, and education.

BMI indicates body mass index; GED, general equivalency diploma; and MET, metabolic equivalent.

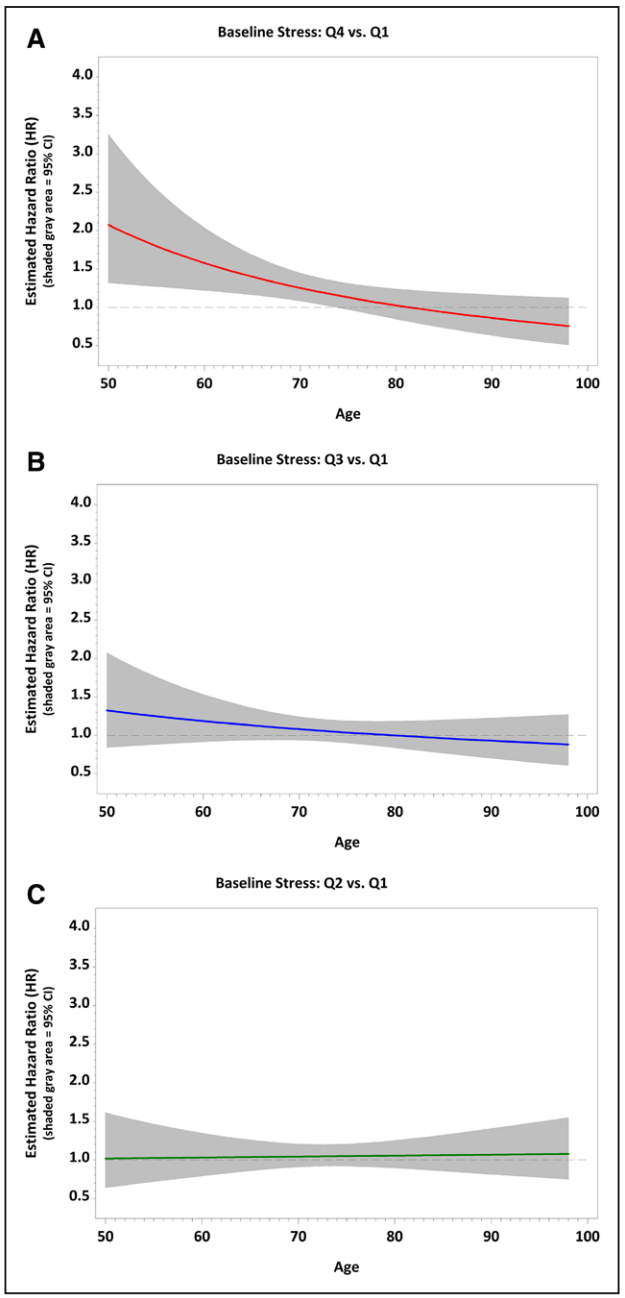

Figure. Plots of the multivariable-adjusted hazard ratios and 95% CIs for associations between baseline stressful life events and cardiovascular disease (CVD) risk according to age among black women in the Women's Health Initiative.
A, Quartile 4 vs quartile 1. **B**, Quartile 3 vs quartile 1. **C**, Quartile 2 vs quartile 1.

ther, effect modification by race was not observed in the prior WHI study, suggesting that associations were similar among white and black women. In the current WHI analysis of black women, we observed an association between baseline reports of stressful life events and incident CVD that was also attenuated in multivariable models. However, in the sub-cohort of women with updated assessments of stressful life events, the association of higher stressful life events and incident CVD was independent of traditional risk factors. Of note, women in quartiles 2 and 4 of stressful life events had significantly higher CVD risk than women in quartile 1. The lack of a clear dose-response relationship might suggest that the scale used to measure stressful life events is inadequate in capturing the full multidimensional nature of stress. In addition, the WHI study assessed an acute measure of stressful life events, ie, events occurring in the preceding year. As such, we hypothesize that the age-related waning effect of stressful life events on incident CVD reflects a distance from events that no longer impact cardiovascular health. The observation that an updated assessment of stressful life events (evaluated during Extension Study 2) was independently associated with CVD reinforces this concept. Additional studies with assessment of cumulative or chronic stress are needed to understand pathways that lend to modification and mediation of stress and disease.

The association between stress and disease was first introduced by Selye[30] and later adapted within the context of specific diseases, including CVD. Stress is hypothesized to contribute to CVD through direct and indirect routes. The biological response to stress includes raised blood pressure, reduced insulin sensitivity, increased hemostasis, and endothelial dysfunction, all of which could conceivably contribute to CVD.[31] Moreover, repeated exposure to stress over time causes wear and tear on the body that initiates additional cascades of stress and disease.[31,32] Indirectly, stress might influence CVD-related risk factors as observed in this study and by others.[29,33] Evidence suggesting that stress (eg, discrimination) is linked to disease occurrence and is perhaps intergenerational, places greater stakes on eliminating psychosocial disparities.[34,35]

Missing from the literature is an evaluation of resilience, or the ability to bounce back or recover from stress in the context of black women's cardiovascular health. Resilience is operationalized as the ability to adapt to experiences of stress or adversity and maintain a stable trajectory of healthy psychosocial and physical functioning.[36] Some have demonstrated that higher levels of resilience are linked with longitudinal declines in depressive symptoms among individuals with long-term physical disabilities[37] and overall longevity[38] in study populations inclusive of men and women. In another study, resilience was shown to significantly buffer the association between the co-occurrence of substance abuse, violence, and HIV/AIDS and depressive symptoms among black women.[9] In the current study, we did not observe a direct relationship between resilience and incident CVD, nor did resilience modify the association between stressful life events and incident CVD. We used a shortened version of the Brief Resilience Scale, administered to women during the WHI Extension Study 2. Of note, the women who participated in the WHI Extension Study 2 sub-cohort were women who were alive and motivated to participate, likely culminating in

Table 4. Characteristics of Study Participants according to Resilience, Women's Health Initiative Observational and Clinical Trials, n=2765*

	Resilience			
	Q1 (3–12)	Q2 (13–15)	Q3 (16–17)	Q4 (18)
	(n=604)	(n=766)	(n=500)	(n=895)
Age at WHI entry mean (SD)	59.5 (6.2)	59.2 (6.1)	58.7 (6.1)	58.8 (6)
Age at Extension 2 questionnaire Mean (SD)	75.0 (6.1)	74.6 (6)	74.2 (6)	74.2 (5.9)
Stressful life events				
Q4 (5–22)	232 (38%)	226 (30%)	131 (26%)	143 (16%)
Q3 (3–4)	143 (24%)	191 (25%)	156 (31%)	232 (26%)
Q2 (1–2)	126 (21%)	192 (25%)	122 (24%)	272 (30%)
Q1 (0)	103 (17%)	157 (20%)	91 (18%)	248 (28%)
Education				
Missing	6 (1%)	5 (1%)	5 (1%)	6 (1%)
Less than high school diploma or GED	31 (5%)	25 (3%)	15 (3%)	26 (3%)
High school diploma or GED	83 (14%)	97 (13%)	46 (9%)	83 (9%)
Some college	252 (42%)	296 (39%)	169 (34%)	321 (36%)
College graduate or higher	232 (38%)	343 (45%)	265 (53%)	459 (51%)
Smoking status				
Missing	7 (1%)	12 (2%)	4 (1%)	9 (1%)
Never smoked	287 (48%)	373 (49%)	234 (47%)	449 (50%)
Past smoker	254 (42%)	299 (39%)	205 (41%)	372 (42%)
Current smoker	56 (9%)	82 (11%)	57 (11%)	65 (7%)
BMI				
Missing	11 (2%)	5 (1%)	5 (1%)	9 (1%)
<25 kg/m^2	94 (16%)	140 (18%)	99 (20%)	177 (20%)
25–29 kg/m^2	216 (36%)	270 (35%)	177 (35%)	342 (38%)
≥30 kg/m^2	283 (47%)	351 (46%)	219 (44%)	367 (41%)
Hormone use				
Never	330 (55%)	422 (55%)	267 (53%)	496 (55%)
Past user	90 (15%)	115 (15%)	73 (15%)	118 (13%)
Current user <5 y	76 (13%)	85 (11%)	75 (15%)	94 (11%)
Current user 5 to <10 y	49 (8%)	61 (8%)	38 (8%)	87 (10%)
Current user ≥10 y	59 (10%)	83 (11%)	47 (9%)	100 (11%)
Type of hormone use				
Never user	330 (55%)	422 (55%)	267 (53%)	496 (55%)
Past user of either E alone or E+P	90 (15%)	115 (15%)	73 (15%)	118 (13%)
E alone	134 (22%)	172 (22%)	106 (21%)	194 (22%)
E+P	50 (8%)	57 (7%)	54 (11%)	87 (10%)
Oral contraceptive use	263 (44%)	352 (46%)	258 (52%)	449 (50%)
Diabetes mellitus status				
Missing	2 (<1%)	0	0	1 (<1%)
Yes	35 (6%)	40 (5%)	33 (7%)	45 (5%)
Use of antihyperlipidemia drugs				
Missing	48 (8%)	38 (5%)	37 (7%)	37 (4%)
Yes	71 (12%)	93 (12%)	44 (9%)	74 (8%)
Hypertension history				
Missing	39 (6%)	31 (4%)	36 (7%)	35 (4%)

(*Continued*)

Table 4. Continued

	Resilience			
	Q1 (3–12)	Q2 (13–15)	Q3 (16–17)	Q4 (18)
	(n=604)	(n=766)	(n=500)	(n=895)
Never hypertensive	286 (47%)	395 (52%)	252 (50%)	487 (54%)
Treated hypertensive	217 (36%)	288 (38%)	175 (35%)	299 (33%)
Untreated hypertensive	62 (10%)	52 (7%)	37 (7%)	74 (8%)
Physical activity				
Missing	33 (5%)	27 (4%)	33 (7%)	30 (3%)
None	122 (20%)	158 (21%)	93 (19%)	191 (21%)
>0–3.75 MET-h/wk	95 (16%)	122 (16%)	71 (14%)	113 (13%)
3.75–8.75 MET-h/wk	132 (22%)	142 (19%)	95 (19%)	178 (20%)
8.75–17.5 MET-h/wk	119 (20%)	153 (20%)	95 (19%)	175 (20%)
≥17.5 MET-h/wk	103 (17%)	164 (21%)	113 (23%)	208 (23%)
WHI trial membership				
OS	248 (41%)	342 (45%)	228 (46%)	425 (47%)
E only	37 (6%)	44 (6%)	30 (6%)	55 (6%)
E+P	27 (4%)	33 (4%)	28 (6%)	50 (6%)
DM	236 (39%)	268 (35%)	174 (35%)	293 (33%)
E+P and DM	56 (9%)	79 (10%)	40 (8%)	72 (8%)

*Demographics are restricted to the 2765 participants with available resilience information from Extension Study 2.

BMI, body mass index; DM, dietary modification; E, estrogen; GED, general equivalency diploma; MET, metabolic equivalent; OS, observational study; and P, progestin.

a healthier and nonrepresentative study population. As such, selection bias may underlie the null findings we observed here. In addition, the Brief Resilience Scale is limited to the individual context. Other dimensions, as described by the multisystemic social-ecological theory of resilience, including the quality of the environment[39] and resilience resources[40] might be important considerations for black women. Despite our null findings, future studies should explore these features.

Traditional health behavioral interventions for ideal cardiovascular health include smoking cessation, healthy diet, and physical activity; greatest CVD risk reduction is achieved when such interventions are concurrent.[41] On the other hand, the extent to which interventions to reduce stress result in lower incidence of CVD events is questionable based on limited success when population-wide strategies are implemented.[42] However, intervening on intermediary factors downstream of stress (eg, physical activity) that are also implicated in CVD cause may be a positive strategy to simultaneously reduce stress and CVD risk. Future studies among black women are needed to test these mediation hypotheses and to inform future intervention studies.

Strengths of our study include the large sample size of black women, prospective design, use of previously validated stressful life events and social strain measures, and adjudication of clinical endpoints for all women included in this study. Further, this is the first study to examine the direct and moderating effects of resilience in relation to CVD among black women, which represents an important extension of the current literature.

Limitations of our study center on the scales used to characterize stress and resilience. Specifically, the stressful life events scale queries respondents on the occurrence of certain events during the 1-year interval before questionnaire completion. This one-year duration likely marks an acute as opposed to chronic or cumulative measure of stress. As such, we cannot make conclusions regarding chronic stress, which has been linked with higher CVD.[43] Moreover, we used the stressful life events scale as a composite; however, not all of the individual stressors queried therein are equal. It is possible that some of the stressors may be more impactful and detrimental to CV health (eg, financial stressors) than others, even if the respondent does not endorse worrying about it a great deal. Further, the stressful life events scale does not include discrimination or perceived racism domains, which might be more relevant for black women. We also lacked multiple repeat measurements for our main exposures, preventing an assessment how stress, strain, and resilience change over time and the potential impact on CVD risk. As part of our analytic approach, we chose to categorize stress and strain into quartiles. However, due to the skewed distributions of both stress and strain, the highest quartiles contained a wide range of responses, particularly for stress (range for the highest quartile, 7–30). Our analyses assumed that the relationship between stress/strain and incident

Table 5. Hazard ratios (HRs) and 95% CIs for Associations of Stressful Life Events, Established CVD Risk Factors, and CVD Risk Among Black Women in the Women's Health Initiative, n=2765*

	Events/N	Total Person-Years	Multivariable Model HR (95% CI)†	*P* Value
Stressful life events				0.02
Q4 (5–22)	65/732	2832.8	1.61 (1.04–2.51)	
Q3 (3–4)	49/722	2838.2	1.20 (0.75–1.89)	
Q2 (1–2)	66/712	2733.9	1.83 (1.19–2.82)	
Q1 (0)	35/599	2358.8	1.00	
Resilience				0.66
Q4 (18)	60/895	3536.3	1.00	
Q3 (16–17)	36/500	2015.9	1.04 (0.72–1.51)	
Q2 (13–15)	61/766	2962.8	1.04 (0.72–1.51)	
Q1 (3–12)	58/604	2248.7	0.95 (0.63–1.42)	
Diabetes mellitus status				0.07
No	194/2609	10217.9	1.00	
Yes	21/153	534.0	1.59 (0.97–2.62)	
BMI				0.09
<25 kg/m^2	35/510	2044.3	1.02 (0.66–1.57)	
25–29 kg/m^2	66/1005	3990.3	1.00	
≥30 kg/m^2	111/1220	4614.6	1.40 (1.01–1.95)	
Physical activity				0.20
None	32/564	2210.4	0.70 (0.44–1.13)	
>0–3.75 MET-h/wk	35/401	1516.8	0.92 (0.57–1.49)	
3.75–8.75 MET-h/wk	47/547	2102.9	1.18 (0.77–1.82)	
8.75–17.5 MET-h/wk	44/542	2160.4	1.14 (0.74–1.77)	
≥17.5 MET-h/wk	45/588	2301.9	1.00	
Hypertension history				0.99
Never hypertensive	93/1420	5630.8	1.00	
Treated hypertensive	20/225	861.8	1.01 (0.74–1.38)	
Untreated hypertensive	89/979	3723.3	0.99 (0.59–1.66)	
Use of antihyperlipidemia drugs				0.60
No	176/2323	9072.2	1.00	
Yes	25/282	1070.8	0.89 (0.57–1.39)	
Smoking status				<0.001
Never smoked	82/1343	5314.0	1.00	
Past smoker	102/1130	4338.4	1.48 (1.08–2.02)	
Current smoker	27/260	991.2	2.53 (1.58–4.04)	
Education				0.01
Less than high school diploma or GED	10/97	359.7	1.64 (0.83–3.24)	
High school diploma or GED	22/309	1183.3	1.02 (0.61–1.71)	
Some college	101/1038	3991.5	1.63 (1.19–2.25)	
College graduate or higher	81/1299	5149.5	1.00	

*Analysis is restricted to the 2765 participants with available resilience information from Extension Study 2.

†Adjusted for stressful life events, diabetes mellitus status, BMI, physical activity, hypertension history, use of antihyperlipidemia drugs, smoking status, and education.

BMI indicates body mass index; GED, general equivalency diploma; and MET, metabolic equivalent.

CVD for participants within each quartile was consistent; unfortunately, with so few participants with higher stress and/or strain levels (eg, 95% of the participants had a composite stress sum ≤11), we were not able to verify this assumption.

The Brief Resilience Scale, a validated instrument for resilience, is a 6-item scale.[16] In WHI, a modified version consisting of 3 items was available. It is possible that the modified version does not recapitulate the validated scale, potentially contributing to null findings about resilience and CVD risk. Despite this, our study is the first to examine this novel effect modification hypothesis in a large prospective cohort of black women. Finally, our results are of limited generalizability given the older age distribution and high educational attainment.

In conclusion, we observed age-related associations between stressful life events reported within the previous year and risk of developing CVD among black women. In the overall cohort of women, these associations were attenuated when conventional CVD risk factors were accounted. However, in the sub-cohort of women with updated measures, persistent relationships were observed. Additional studies among black women with diverse education and income levels across a range of ages are needed. In addition, the context of resilience should be further explored as resilience and resilience resources represent novel and potentially more malleable CVD intervention targets.

ARTICLE INFORMATION

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