ARIC Manuscript Proposal # 1260

PC Reviewed: _6_/_8_/07 **Status: __A_** **Priority: _2___**
SC Reviewed: _____ **Status: _____** **Priority: _____**

1.a. Full Title: Association between exposure to combat-related stress and psychological health in aging men: the Atherosclerosis Risk in Communities (ARIC) Study

b. Abbreviated Title (Length 26 characters): Military Stress & Psychological Health

2. Writing Group (list individual with lead responsibility first):

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I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. _JEW_ **[please confirm with your initials electronically or in writing]**

3. Timeline:

To be completed by December 2008.

4. Rationale:

According to the 2000 US Census, over 26 million or 12.7% of the adult US population served in the military at some time in their lives. [1] In the US, coronary heart disease (CHD) and stroke are the first and the third leading causes of death, respectively, [2] and as the proportion of the population over the age of 65 increases, the public health burden due to morbidity and mortality from these conditions will be considerable. Most studies of the deleterious health effects of combat-related stress focus on short-term outcomes and self-reported health symptoms. By contrast, relatively little attention has been given to the long-term cardiovascular effects of military stress.

The specific psychosocial stress experienced by veterans who have engaged in active combat is a unique stressor that includes both psychological and physical components. [3] One of the primary mechanisms through which exposure to combat is thought to be associated with increased risk of cardiovascular disease (CVD) is through psychological mechanisms. Although little research has been done in this area, combat stress has been found to be associated with higher rates of psychological distress. [4,5] Two measures of psychological distress will be investigated in this study in particular: *trait anger*, a measure of how prone an individual is to experience anger often, intensely and for long periods of time and *vital exhaustion*, defined by symptoms of unusual fatigue, loss of energy, increased irritability and feelings of demoralization.

There is a growing body of literature supporting the association between anger/hostility [6,7,8] and vital exhaustion [9] and CVD. Trait anger has been positively associated with CVD incidence [10] and mortality [11,12], clinical [13,14,15] and subclinical [16] atherosclerosis, atrial fibrillation [17], incident coronary heart disease [18], incident stroke [19], and behavioral risk factors [20,21]. Vital exhaustion has been found to be associated with incident myocardial infarction [22,23,24,25], incident stroke [26, 27, 28] and subclinical atherosclerosis [29]. The symptoms that collectively define vital exhaustion are very similar to those that define depression [30,31]; however, vital exhaustion is a construct that has been specifically developed to predict future myocardial infarction. [32].

In this analysis, we propose to investigate whether exposure to such combat stress (compared to military service without combat and no military service) is associated with higher levels of trait anger and vital exhaustion among men in middle to later life. The military service and combat exposure data collected as part of the ARIC ancillary study “Life Course SES, Social Context and Cardiovascular Disease (LC-SES) Study” provide an extraordinary opportunity to address this issue. Standardized, extensive cardiovascular measurements are available, as are behavioral, psychological, and socioeconomic measures. Furthermore, in contrast to most studies, ARIC includes both veteran and population “controls” and men from birth cohorts with military service including World War II and the Korean and Vietnam conflicts. Given these advantages, and the small and inconclusive extant literature, findings from this analysis will make a significant contribution to our knowledge regarding the role of psychological mechanisms that may mediate combat stress and cardiovascular outcomes.

One concern with these analyses that merits mentioning is the potential for survivorship bias, in that combat exposure was not assessed until 12-14 years after baseline, at which time 17% of male baseline participants had expired. In order to address concerns about the potential for differential survival among veterans and non-veterans between baseline and ascertainment of military history, we took two steps. First, we conducted a pilot study on a subset of decedents from North Carolina for whom veteran status was recorded on death certificates. Briefly, we found a small (2%) but not statistically significant excess mortality among veterans, even after adjustment for age, race and education. Second, we conducted a crude sensitivity analysis to estimate the extent to which differential survival, if extant, may influence observed results. To do this, we applied the adjusted mortality rates obtained from the pilot study to some hypothetical data with incident CHD as the outcome. Liberally assuming that those who eventually had a CHD event were 1.5 times more likely to die before providing data on military history than those who do not go on to develop a CHD event, our odds ratio was underestimated by only 1.5%. Even under a more extreme scenario, assuming both a substantially larger difference in mortality between veterans and non-veterans and that those who eventually go on to develop CHD were two times more likely to die prior to providing their military history, our observed effect estimate only differed from the corrected estimate by 7%. These results were reassuring that both the potential magnitude of survivorship bias and the possible effect of such bias, if extant, may be expected to be small in these data.

5. Main Hypothesis/Study Questions:

Is exposure to combat stress (compared to military service without combat and no military service) associated with less favorable psychological health?

a. Does this association vary by conflict era/war theater (World War II, Korea, Vietnam)?

6. Data (variables, time window, source, inclusions/exclusions):

The subset of participants included in the current study will consist of 5,368 men (1,097 black and 4,271 white) who were queried about military service and a variety of combat exposures during the LC-SES Study (2001-2002). Only 48 of all ARIC women in the LC-SES study indicated that they had served in the armed services. Of these only four had been exposed to military stress. Because of the small numbers we will restrict our study to men. A breakdown of the male participants by sociodemographic and military exposures can be found in Table 1. Individuals who have specified that they do not give consent for non-cardiovascular research will be excluded from the analysis dataset.

The following series of seven questions on the LC-SES questionnaire detailing military experience will be analyzed: (1) age at entry into the service, (2) length of service, and whether (3) served overseas, (4) in a combat zone, (5) under fire or fired at the enemy, (6) had seen others wounded or killed, or (7) had been wounded or missing in action.

Measures of adverse psychological conditions, particularly vital exhaustion [33, 34, 35] and trait anger, [33, 36, 37] which have been associated with higher rates of cardiovascular disease, will be evaluated for an association with combat exposure, as well as for their contribution to the combat stress-cardiovascular disease association. The following measures are available from Visit 1 data: the Spielberger Trait Anger Scale [38] and the Maastricht Questionnaire of Vital Exhaustion [39].The Spielberger Trait Anger Scale has been linked with both stroke and CHD in the ARIC cohort [34, 35], and the Maastricht Questionnaire of Vital Exhaustion includes questions querying depression, hopelessness, and lack of energy and has been associated with stroke [40] and CHD [41].

Attributes considered as potentially confounding or modifying the hypothesized associations will be indicators of socioeconomic position prior to (parental SEP) and following exposure to military stress (individual and area-based life course SEP), social support, comorbidity and access to care.

7a. Will the data be used for non-CVD analysis in this manuscript? __X__ Yes ____ No

b. If Yes, is the author aware that the file ICTDER02 must be used to exclude persons with a value RES_OTH = "CVD Research" for non-DNA analysis, and for DNA analysis RES_DNA = "CVD Research" would be used? __X__ Yes ____ No
(This file ICTDER02 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8. Will the DNA data be used in this manuscript? ____ Yes __X__ No

9. The lead author of this manuscript proposal has reviewed the list of existing FHS Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status.

___X___ Yes _____ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

- MS#:1017: Association between exposure to combat-related stress and predicted risk of CHD and stroke (Johnson AM)
- MS# 626: Differential prediction of CHD risk by trait anger subtype (Williams JE)

- MS# 640: The convergence of acute and chronic psychological factors and its impact on CHD risk (Williams JE)
- MS# 920: Psychosocial factors as predictors of ABI change (Wattanakit K)

Table 1. Characteristics of ARIC Participants by Socio-demographic Characteristics and Reported History of Military Service

Questionnaire Item	N	Mean (SD) / %
Responded to Questions re military service	5368	100%
History of military service (%)	3312	62
Age Group (%)		
45-49	648	44
50-54	772	54
55-59	988	72
60-64	906	81
RACE (%)		
Black	442	40
White	2872	67
EDUCATION (%)		
<12 years	456	42
12 years or equivalent	1282	65
12+ years	1570	68
Respondents with history of military service	3304	100%
Age when entered armed forces (mean, years)	3304	19.6 (2.4)
Years served in active duty (mean years)	3312	3.7 (4.3)
Served overseas in armed services (%)	2199	66
Served in combat zone (%)	980	30
Under enemy fire or fired at enemy (%)	704	21
See others wounded or killed during the war (%)	858	26
Ever wounded /MIA during war (%)	155	5
Era of Service (%)		
World War II (1941-1945)	745	22
Korean conflict (1950-1953)	1013	30
Vietnam war (1961-1975)	705	21
Multiple conflicts/wars	137	4
Between conflicts	714	22
Military Service Summary Variable (%)	5386	
No reported military service	2064	22
Military Service, no reported combat exposures	2118	40
Military Service, with 1+ combat exposures	1184	38

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