Manuscript Proposal #1017

PC Reviewed: _06/30/04	**Status: _A__**	**Priority: __2__**
SC Reviewed: __07/01/04__	**Status: _____**	**Priority: _____**

1.a. Full Title: Association between exposure to combat-related stress and predicted risk of CHD and stroke in the Atherosclerosis Risk in Communities (ARIC) Study

b. Abbreviated Title (Length 26 characters): Military Stress & CVD Risk

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

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3. Timeline:

To be completed by December 2005.

4. Rationale:

According to the 2000 U.S. Census, over 26 million or 12.7% of the adult US population served in the military at some time in their lives. Over 90 % are men and 37 percent are over the age of 65 years. [1] In the U.S. 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 psychological, behavioral, and self-reported health symptoms. By contrast, relatively little attention has been given to the long-term cardiovascular effects of military stress. 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 CVD measurements are available, as are behavioral, psychological, and SES 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, this study will make a significant contribution to the extant literature and potentially provide insights for planning subsequent studies on this subject. Also, as a result of the Gulf War in the early 1990s and now the Iraqi occupation, younger cohorts of men and women have and are being exposed to combat related stress. Evidence from studies like the one proposed could be used to help influence public health programs designed for veteran and active service populations and potentially reduce the burden of chronic disease in these populations in middle and older age.

5. Main Hypothesis/Study Questions:

1) Is exposure to combat stress (compared to military service without combat and no military service) associated with less favorable levels of CVD risk factors (higher blood pressure and hypertension, diabetes, smoking, higher LDL and lower HDL cholesterol) and higher predicted risk of CHD and stroke?
   a. Is the association of combat stress with CVD risk factors, carotid atherosclerosis, and predicted CHD and stroke risk in part explained by socioeconomic, psychological, and behavioral risk factor profiles over the life course?
   b. Is the association of combat stress with CVD risk factors, carotid atherosclerosis, and predicted CHD and stroke risk modified by war theater (World War II, Korea, Vietnam), and by pre-exposure socio-economic status?
2) Among those exposed to combat stress, do levels of carotid atherosclerosis and predicted risk of CHD and stroke increase as level of stress exposure increases?

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, as shown in Table 1 below. 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.

Primary study outcomes of predicted 10-year risk of CHD and ischemic stroke will be calculated based on individual baseline (Visit 1) risk factors including blood pressure, carotid artery IMT, cholesterol (total, HDL and LDL), hypertension, and history of CHD, stroke or diabetes. The use of risk prediction equations have become increasingly common in both research and clinical applications [3, 4, 5]. The better known are risk prediction equations based on the Framingham cohort; [3] because of homogeneous, mostly white composition of the Framingham population the applicability of these prediction equations to other populations has been studied extensively [6]. Equations predicting the ten-year incidence of both ischemic stroke and CHD have been optimized for the population we propose to analyze; these have been calibrated against the Framingham Heart Study equations [6, 7].

The following Visit 1 behavioral risk factors, which, considered jointly, provide important information on potential mechanisms through which psychosocial stress affects an individual's risk of CVD [8], will also be included in analysis: pack years of cigarette smoking and current smoking status, alcohol intake, physical activity (assessed using a sports index ranging from 1-5), and overall and central obesity measured by body mass index (kg/m2) and waist circumference (cm), respectively.

We will also examine the relationship of SES prior to military service (based on parental SES) as well as SES in early adulthood and midlife, both at the individual and neighborhood level, to the military stress-CVD associations. Parental and adulthood SES measures will include education, occupation, home ownership, and family income (only available in adulthood). Neighborhood SES will be based on attributes of the county of residence during childhood (lowest level at which data were formerly aggregated) and the census tract where men resided

in early and later adulthood. Area based measures will include: census tract percentage with a high school education, mean family income, and mean housing value, percentage unemployed, and percentage in poverty.

Finally, measures of adverse psychological conditions, particularly depression [6, 9, 10] anger, [7, 8, 9] and low social support [9], which have been associated with higher rates of CVD, will be evaluated for an association with combat exposure, as well as for their contribution to the combat stress-CVD association. The following measures are available from Visit 2 data: the Spielberger Trait Anger Scale [11], the Maastricht Questionnaire of Vital Exhaustion [12], the Lubben Social Network Scale [13] and the Interpersonal Support Evaluation List [14]. The Spielberger Trait Anger Scale has been linked with both stroke and CHD in the ARIC cohort [15], and the Maastricht Questionnaire of Vital Exhaustion includes questions querying depression, hopelessness, and lack of energy and has been associated with stroke [16] and CHD [17]. The Lubben Social Network Scale and the Interpersonal Support Evaluation List measure different aspects of social support.

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

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

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# 611: ARIC CHD risk prediction (Chambless LE)
- MS# 625: Does vital exhaustion increase CHD risk? (Williams JE)
- 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# 1004: ARIC CHD risk prediction from behavioral, psychosocial, and socioeconomic factors (Chambless LE)

References

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15 Williams, J.E., et al., The association between trait anger and incident stroke risk: the Atherosclerosis Risk in Communities (ARIC) Study. *Stroke*, 2002. 33(1): p. 13-19.

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17 Prescott, E., et al., *Vital exhaustion as a risk factor for ischaemic heart disease and all-cause mortality in a community sample. A prospective study of 4084 men and 5479 women in the Copenhagen City Heart Study.* International Journal of Epidemiology, 2003. 32(6): p. 990-997.