A pproximately 2.6 million troops have served or are serving overseas as part of Operation Iraqi Freedom/Operation New Dawn in Iraq and Operation Enduring Freedom in Afghanistan, as of September 2013.¹ There have been 6664 casualties and 51 904 wounded as of February 2014.² Although definitions of combat experience vary, 30% of veterans with service in Afghanistan and 71% to 86% of those serving in Iraq have participated in a firefight.³ The rising mental health problems of returning veterans are well documented,⁴ with ≤20% of returning veterans meeting diagnostic criteria for posttraumatic stress disorder (PTSD)⁵ and up to 17% meeting criteria for depression, anxiety, or PTSD.³ These mental health problems stem directly from combat, with a dose-response relationship—the more firefighters the soldiers had experienced, the higher the rate of PTSD and depression.³

However, evidence is emerging for a role in combat in exerting not just a psychological but also a physiologic toll. Previous studies of the long-term physical consequences of combat have shown mixed results. In one prospective longitudinal study enrolling veterans shortly after World War II, those who had experienced combat were more likely to die or report physical decline over a 15-year period.⁶ In the Atherosclerotic Risk in Communities study, however, no increase in coronary heart disease (CHD) was seen in combat-exposed veterans compared with those who had not seen combat or who had not served in the military.⁷ Both studies included limited numbers of combat veterans, however, and in the Atherosclerotic Risk in Communities study, combat experience had occurred more than 30 years earlier, in World War II or Korea.

In this issue of Circulation, Crum-Cianflone et al⁸ use the Millennium Cohort Study, which enrolled >60 000 military personnel, including active duty, Reserve, and National Guard from all branches of the military, starting in 2001, to provide a definitive answer to the question. All were free of CHD at the onset of the study. Overall, approximately one quarter of the troops reported exposure to combat before (N=900) or during (n=13 000) the study period. Self-reported CHD was evaluated in all, and record-confirmed diagnoses were evaluated in a subset of approximately one third, who remained on active duty (in whom records were thus accessible). Among the entire cohort, in a model adjusting only for demographic variables, combat exposure increased the odds of self-reported cardiovascular disease by 1.8. In the final longitudinal model adjusting for clinical and psychological variables, the odds ratio was 1.63. PTSD was associated with CHD in unadjusted analysis but lost significance after adjustment for depression and anxiety, with which it was moderately associated. Among the continuing active duty participants, results were similar, with combat doubling the likelihood of development of CHD. The addition of PTSD along with other health- and behavior-related variables attenuated the magnitude of the effect of combat, although combat remained highly significantly associated with CHD even after this adjustment. These data have some limitations, which do not detract from the validity. Less than one third of those invited to participate agreed, but demographic and military variables were only minimally different, suggesting that the results are generalizable. Also, concordance between self-report and record-diagnosed CHD was only moderate; however, the 2 types of analyses showed very similar results. The large size and prospective nature of the study, as well as longitudinal analyses with control for appropriate covariates, strongly support the definitive nature of the results.

The findings raise interesting questions about the pathophysio logic links among combat, PTSD, and cardiovascular disease. This study shows combat experience to be more important than PTSD. In other studies, however, PTSD prospectively predicted the development of clinical CHD, as well as perfusion abnormalities, in a rigorous twin-design study of Vietnam veterans⁹ and was more predictive of development of coronary disease than combat alone.¹⁰ The truth is likely not either-or/combat-versus-PTSD, but, rather, is more complex. The stress of combat has been described from World War I to the present day, with variations in the technology of combat but not the psychological impact.¹¹,¹² Acutely, psychological stress increases sympathetic¹³ and decreases vagal¹⁴ activity, and ongoing stressors have longer-term effects on the body¹⁵ through the wear and tear of recurrent sympathetic activation.¹⁶ These autonomic changes have, in turn, been linked with inflammation,¹⁷ well known to be associated with the development of CHD. PTSD perpetuates the physiologic stress response through reminiscences of the trauma triggered by external stimuli and has also been associated with long-term autonomic changes.¹⁸ For some individuals, the physiologic damage wrought by the initial stressor may be enough; for others, the amplification and repetition of this response attributed to PTSD may mediate some of the effects of the initial combat-related stress, as suggested by the data here showing

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some attenuation of the combat effect when PTSD is added to the model.

Differences in the relative importance of combat and PTSD between this and previous studies may also in part be explained by the fact that those studies examined veterans many years after their active service, when the prolonged stress of PTSD may be more important than combat years earlier. Recall bias may also play a role in studies conducted long after the sentinel time period. Other differences between returning veterans of the current wars compared with previous wars have also been noted, such as the all-volunteer force deployed to Iraq and Afghanistan compared with previous drafts and the type of warfare conducted in the regions.

The role of health-related behaviors is uncertain. Although adverse health behaviors such as smoking were more common with combat exposure in the present study and with PTSD in the Vietnam veterans twins study above, in both cases, controlling for these factors did not impact the significance of combat or PTSD. Although there may be some mediating role, health behaviors do not appear to be a large part of the explanation. These data suggest that combat experience should be considered a risk factor for CHD. Although past combat experience is not modifiable, like family history, presence of this risk factor should draw attention to surveillance and treatment of other, modifiable, risk factors, such as hypertension, cholesterol, and smoking. This is particularly important, because both hypertension and hyperlipidemia have been associated with PTSD. Although PTSD did not explain the entire impact of combat on cardiovascular risk, it does appear to have at least some mediating role. Several modalities for PTSD treatment have been shown to reduce symptoms. The most effective of these is prolonged exposure, in which patients relive and confront trauma-related stimuli to extinguish conditioned fear responses. Veterans Administration hospitals are required to offer either this therapy or cognitive processing therapy. Whether PTSD screening and treatment will reduce cardiovascular risk is unknown, but treatment of other stressors has shown cardiovascular benefits. The findings of Crum-Cianflone et al emphasize the importance of cardiovascular health as a priority for returning veterans who are at increased risk.

Disclosures
None.

References

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Veterans of Combat: Still at Risk When the Battle Is Over
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