Reviewer's report

Title: Assessing Nonresponse Bias in a Large Prospective Cohort of Relatively Young and Mobile Military Service Members

Version: 1 Date: 26 April 2010

Reviewer: Remington Nevin

Reviewer's report:

Major Compulsory Revisions

There are certain issues with this manuscript reflecting methodological concerns that require attention and clarification:

1. This manuscript may inadvertently introduce confusion into the use of the term “combat”. Using the definition in LeardMann et al, BMJ 2009;338:b1273), a “combat” experience was defined based on self-report of combat-related exposures, such as observing refugees, dead bodies, etc. As used in this manuscript, “military combat exposures” appears to imply objective assessment of deployment to a combat zone (as in Table 1) from DMDC-provided data, which is not equivalent, as certain deployments are not associated with such traumatic exposures.

If this error is confirmed, I would consider it essential that the manuscript make it clear that “deployment” and not “combat” is associated with increased response propensity, so as to avoid confusion across other published MCS manuscripts.

2. It is rather difficult for me to accept the hypothesis that self-reported exposures and outcomes that would otherwise be reported on the follow-up survey are not to some significant degree influencing response propensity, and hence invalidating the critical Missing At Random (MAR) assumption and the conclusions of this analysis, particularly in relation to certain critical subgroups.

Assuming the correction noted in (1) above, although the data reassuringly suggest that “deployments” since 2001 are associated with a slight increase in response propensity, it is certainly not clear to me that all deployment experiences result in equal response propensity, particularly in relation to interactions based on frequency of deployment experience, deployment to a “combat” experience (using the definition in LeardMann et al, 2009), and interaction of age, military pay grade, baseline mental health status, and military status at follow-up. It seems reasonable that such differences in propensity must also be assumed to be influenced to some degree by significant differences in exposures and health outcomes.

For example, it is known that young, enlisted personnel, particularly in the Army and Marines, are facing unprecedented deployment pressures, often being deployed on “combat” tours of 12 to 15 months with barely 12 months of
recuperation time between tours. It seems reasonable that these pressures are resulting in significant negative effects on response propensity among this group that may not be experienced by other study participants. Of concern, and contrary to the tone of the conclusion, the findings of this analysis do not inspire confidence that the MCS study design is adequately capturing without bias the unique experiences and outcomes of these members.

An explicit reassurance of this fact supported by data would prove beneficial, but not sufficient, in defending the MAR assumption against this reasonable threat, and would help to alleviate criticism that major findings from the MCS may not, in fact, be heavily influenced by some form of “healthy-responder” bias which would tend to skew many findings towards the null.

Specifically, it would be very helpful to see a table, preferably in the manuscript, revealing response status stratified by both deployment and “combat” experience between 2001 and 2006 among some of the groups seemingly at particularly high-risk for non-response: 17-24 year olds, those with baseline major depressive disorder, and among those no longer in military service.

Current popular concerns related to the cumulative health effects of military service are increasingly focused towards these service members, particularly those among the group with a history of mental health disorders prior to deployment. Such concerns, of course, underscore that there is no substitute for adequate follow-up among these service members to support proper epidemiological inference in this population. A statement to this effect should be prominent in the manuscript, particularly in reference to the results of the requested analysis.

3. Among non-responders, it would be helpful if the authors could confirm the data sources and methods utilized to ascertain contact information among the 3000-large non-responder ancillary study referenced in the Conclusions section. It appears from Reference 10 (Ryan et al, 2007) that taxpayer records, likely referenced by Social Security Number, are utilized to obtain current address. If this is correct, how do the authors explain such a high rate of non-contact?

Additionally, it would be helpful to know whether records available through the Veterans Administration (VA) are utilized at all during contact tracing, and whether varying categories of separation from military service appear to be correlated with certain patterns of response propensity. Are accessing Veterans Administration health benefits or the awarding of a disability rating correlated with response propensity?

4. Related to (3), the results alluded to in the Conclusions section that approximately half of all non-responders could not be located are, contrary to the tone of this section, also not reassuring, and suggest another significant potential source of bias not addressed in this analysis which seriously threatens the MAR assumption.

Given the findings presented, and pending the results of the authors’ response to
(3), it would seem reasonable to entertain the hypothesis that access to health care through the VA system could affect both response propensity and health outcomes to some significant degree, and that exposures and health outcomes as ascertained on the survey may also be significantly contributory to later access to VA care and likelihood of later contact. The implications of these possibilities should be discussed in greater detail in the Conclusions section as they relate to the MAR assumption.

5. Given the previous concerns, the presentation of data in Tables 2 through 4 distracts from a presentation of data more vital in judging the validity of the MAR assumption. Tables 2 through 4, and the corresponding sections devoted to their discussion in the Methods and Results sections, should be reserved for a stronger defense of this assumption, and a more open discussion of the threats to the validity of recent MCS findings, particularly as they relate to outcomes among the “combat” deployed cohort.

Minor Essential Revisions

6. More specifically, I remain somewhat confused as to how so few of the 77,047 enrolled and consenting cohort members prospectively enrolled in Panel 1 seem to be available at follow-up and reporting “combat” experiences (e.g. only 5,410 as reported in LeardMann et al, 2009), given that “combat” experiences would at least by anecdotal reports tend to comprise a significant proportion of recent deployments. As a number of published MCS manuscripts focus primarily or secondarily on the experiences of this “combat” deployed cohort, it is worthwhile to focus additional commentary on this area as it may relate to the potential for bias. Is information available to compare these cohort proportions against the entire force, so as to confirm representativeness? At face value, Panel 1 of the MCS appears increasingly non-representative of the current military force, particularly the portion of the military force at greatest concern in regards to health outcomes. Is so, this should be explicitly commented on.

7. It is not clear to me where the figure of N=76,775 comes from. I am attempting to reconcile this figure with the N=77,047 reported as comprising the Panel 1 population in Reference 10 (Ryan et al, 2007). The discrepancy appears to be due to ascertainment of death among some study members, but is not clear to me how the authors determined whether a cohort member remained alive at the time of the analysis. Could detailed clarification please be provided? Also, is it correct to say that some deaths may not be ascertained? If so, it may be more correct to state “76,861 individuals thought to be alive” on page 6.

Discretionary Revisions

8. This is a minor point, but Figure 1 could be significantly improved in appearance through the use of an alternative software package; as it appears currently it resembles the raw output of Stata. A properly formatted histogram consisting of solid bars (not asterisks), with a clear white background, variable-width font for labels, and a formatted box-plot would be well worth the effort for publication.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I report the following conflict of interest:

I have been a staff member at a U.S. military public health activity which competes indirectly with the Naval Medical Research Center in performing public health surveillance and research studies relating to the U.S. military population. In this capacity, while I have endorsed the quality, methodological rigor, and public health relevance that generally characterizes Millennium Cohort Study (MCS) publications; I have, and remain, an outspoken critic of the MCS, in regards to the manner in which it is executed.

Specifically, I am on record as stating that I believe the funding, expert staffing, and attention focused on what is in retrospect, a significantly under-powered prospective cohort, detracts from the broader goal of obtaining systematic improvements in long-term public health surveillance of the entire active and reserve component cohorts, and of those separated from military service. I am also on record as stating that the goals of the MCS could all be more effectively pursued through the systematic administration of MCS survey instruments (particularly the standardized and validated instruments PRIME-MD, PHQ, PCL-C, and SF-36V) to the entire 2.2M-plus military cohort, and by devoting significantly increased attention towards improvements in standardized longitudinal outcome and exposure data and biospecimen collection across the active and reserve components, and particularly among those separated from the military whether in Veterans Administration (VA) or in private care, via federal insurance mandates and improved funded health outreach programs.

These are purely professional criticisms which express nothing more than a basic underlying difference in opinion about what the priorities for U.S. military public health surveillance efforts should be, and perhaps also the extent to which U.S. military public health leaders should advocate openly for definitive improvements, over incremental and less effective solutions.

However reasonable these disagreements might be, they might also reasonably be perceived as creating a conflict of interest where I might seek to accentuate perceived weaknesses in work derived from the MCS, and therefore be potentially more critical than the typical reviewer.

Should the editors believe an objective review of this manuscript is possible
given these disclaimers, it may prove helpful to exercise flexibility and discretion where compulsory revisions are marked as such.