Author's response to reviews

Title: Erosion of the Healthy Soldier Effect in Veterans of U.S. Military Service in Iraq and Afghanistan

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Dear Editor and Reviewers,

Thank you for your very detailed review. The comments of the reviewers resulted in substantial revisions to the paper as was originally submitted. I will answer each issue with reference to where modifications were made to address the reviewers concern.

First Reviewer

1. I think this paper needs some more detail on the groups compared. I think the reader would appreciate some more detail on the non-clinical VHA group. Are all people in this group ex-serving?
   The question of whether these cohorts are former military is not clear cut. The VA data was derived from a file of persons who had separated from the military. However, National Guard and Reserve forces could have been activated again at a later date beyond 2011.

2. It is stated that all those with clinical contact were excluded to remove a confounding effect. This makes some sense, however, by excluding ill people from the cohort is there also potential to bias the results in the other direction? After this exclusion who are you left with? Hopefully a clearer description of the rationale for using this group will address these queries.
   In addition, we updated the cohorts to include all 3 VA cohorts – All VA enrollees, enrollees with VA utilization and enrollees without utilization. We note that veterans who utilize the VA do tend to be less healthy than those veterans who do not use the VA so we expected, and found it to be so, their SMRs to be higher than veterans without VA utilization. The study cohorts are discussed on page 8.

Did the DOD population only include those still serving in the military in 2011 and those who died while they were still serving?
The DOD data includes anyone who was active duty during 2002-2011. These could be persons who are now separated from the military as well as persons who remain on active duty today. Our data do not allow us to make a distinction regarding who remains on active duty and who does not. We have provided clarification of this point in the Methods section (page 7) where we discuss the
cohort. In addition, we excluded persons from the analysis whose deaths were determined to be combat related. (Page 8)

3. **Often in studies like these person-years are used to calculate the expected number of events.** Each person is followed-up from a start date until death or the end of follow-up (whichever comes first). These methods have not been described here in this paper. In the methods section it would be useful to know when did follow-up for each participant begin (was date of return from deployment used?). For the younger group, who joined after 2002, was date of enlistment used in calculations at all? How did you account for people who moved in to an older age group over the course of the study? If more basic methods have been used, please describe these in the methods further and raise possible limitations regarding the techniques in the discussion.

While the date of first deployment and the last day of the last deployment in support of OEF/OIF/OND are known for the VA cohorts, we do not have that data for DOD. We used age at a specific point in time (2010) so age is stationary. It would have been wonderful to have had that data for DOD and we have requested it, but it will be some time before it is received. Given that, we had to use population at risk rather than the time each person was at risk in our SMR calculations. (Page 10) Additionally, we must point out that we have no way of knowing who was actually in a combat zone since the VA data does not have that information.

4. **It would be useful to present the length of follow-up of the study in the abstract, results and discussion. When comparing the results to other research this context is important.**

Study inclusion years have been added to the abstract and Tables have been revised to include dates.

5. **The results section states that mortality was highest for those 24 and younger, in the VHA cohort. This statement is inconsistent with the crude rates in Table 2.**

This point has been clarified. (Page 12)

6. **The abstract is difficult to read due to a large some of abbreviations used. Some of these abbreviations are not defined within the abstract (e.g. VHA, VA). Please consider updating the Methods section of the abstract with this in mind. The abbreviation VA has not been defined anywhere in the**
manuscript. It might also be worth spelling out OEF/OIF/OND at least once in the manuscript. Likewise FY11.
We have corrected this finding.

7. The authors appear to have missed some references in the background section.

"The HSE has been affirmed in military cohorts from Australia, Korea, Norway[10] and New Zealand[11]. In the Australian study the HSE was found to persist up to 30 years following service".

The studies from Australia and Korea have not been referenced. Also it is unclear whether the Korea military cohort mentioned is from the Korean armed forces, or a study of another military deployed to conflict in Korea. We have corrected these obvious errors and have included information from the Australian OEF-OIF study and a French study that while not specifically about this population does cover the years of interest in this study.

8. In the outcomes section the numbers (N=14) and (N=402) appear inconsistent with the numbers in Figure 1.
With the inclusion of all VA cohorts, this figure has been revised and the revisions reflect the change noted above which occurred in VA utilizers.

9. The authors state that no assessment of the HSE has been done in OEF/OIF/OND veterans. An Australian report does document how the mortality of Iraq and Afghanistan veterans compared to the general population (see link). Although not a US study, it may be of interest.
Yes! This study was definitely of interest. We have requested cause of death data and have been following up with the VA to get this data for nearly 2 years. We will examine this issue again in a subsequent paper once cause of death data is received.

10. Instead of saying 'In VHA, crude rates were highest for Army and Marine Veterans'. You could say crude rates were lowest in Navy Veterans - as this is the clearest difference between the categories of Service).
This paragraph has been substantially revised.

Second Reviewer

1. This paper examines the ‘healthy soldier effect’ (HSE) in recent veterans.
HSE is a variant of the healthy worker effect, applied to soldiers, who enter the military based on selection criteria generally ensuring good health and
access to care. Previous studies have examined HSE in veterans of previous wars; I’m not sure any have examined this yet in the recent war.

2. While the topic is interesting, I have a couple of reservations about this paper. First, the multiple samples weren’t clearly described; second, it may be the case that it’s too soon to evaluate the HSE for total mortality and without specific COD, the conclusions are unlikely to hold over time. Yes, we agree that our results may change over time and we fully expect them to do so. This is a first look at this cohort of Veterans, however, and we believe it is an important first step. We have been trying for 2 years to obtain cause of death data from the VA and hope that we can resolve this situation soon. That said, as previously stated, we do believe this is an important first pass at this data. We plan to re-do the analyses once we have obtained cause of death data.

3. The Abstract suggests 3 groups: VHA enrollees (2002-2011), a subset of VHA enrollees who did not use the VA, and a DOD sample. In the paper, it seems the VHA enrollees were divided into 2 groups; those with and without clinical contact (the N’s of each should be reported). In the Figure and the Tables, it seems that the first group, VHA users, were omitted – perhaps they should have been included as a 3rd group? Yes, we agree that the analysis makes more sense with all cohorts included. We initially excluded them because the results confirmed what previous research had shown that Veterans who use the VA are sicker than Veterans who do not. Thus, their mortality is much higher than the mortality for non-utilizers. We have now included them in these analyses.

4. As for the second reservation, it’s likely that the causes of death observed to date are a limited set of possible COD’s, and that over time, it would be interesting to know if, as seemed to be the case for Vietnam vets, the primary causes of early death within the first decade or two of follow-up, were external causes (e.g., MVA, suicide, accidents), whereas after 3 or 4 decades, various disease-related conditions (e.g., heart disease, cancer) came into play differentially between veterans and non-vets, and within veterans depending on deployment. A greater recognition of this limitation would be useful. Thank you for your comment. We have included recognition of this point in our discussion.

5. A number of factors that might alter the relations observed were not fully explored here: e.g., multiple deployments were likely among many troops,
and may have interesting effects on near and long-term mortality. In recent deployments by US armed forces, the use of Guard and Reserve troops has increased, and in many ways they can be quite different from Active duty troops (e.g., older, more likely to be married with children). Thus, it might have been useful to contrast these two subgroups of the military force. While new battlefield technologies have resulted in lower death rates, the number and types of wounds/injuries sustained may have implications for long-term health. These should be considered.

Yes, these are important points. We believe this paper answers the very important question of whether there is an HSE effect. The finding that there is not has led us to explore the topic in a bit more detail and we have begun analyses for second paper examining the HSE by specific population such as in Guard and Reserve forces vs Active Duty.

6. The notion of ‘healthy warrior’ should also be considered. Among troops who are in the military, it’s often the case that some are selected for deployment and others are not. I believe this issue was discussed in several papers in American Journal of Epidemiology in 2008/09, e.g., Jennifer Wilson.

Yes, this is an important point. However, VA OEF/OIF Roster data does not contain information on who was deployed to combat zones vs who was not. All that we know is that the cohort was deployed in support of the Iraq and Afghanistan conflict. That support could have been provided in the combat zone or outside of the combat zone.

7. The age range for VHA is noted (p. 7) as 18 to 72, but what is the range for DOD?

Yes, the age range for DOD data is the same. We have noted the same in our Methods section.

8. Deployment overseas, and deployment to combat zones are important factors to consider in relation to mortality.

See answer to question 6.

9. Page 9, 4th line, should Hispanic be non-Hispanic (see the Table)?

This has been re-worded. See the first page of the Results section.

10. Next para, 5th line, “those 24 and younger” – looks like those 40-72 were also high?

This, too, has been corrected see 2nd paragraph of Results section.
11. **Given that the VA cohort had no VA clinical contact, (a) we don’t know about non-VA clinical contact, and (b) we don’t know about clinical contact among the DOD cohort.**

Yes, we have included all VA cohorts to address earlier points so that data is now available in the results section. We do not know about clinical contact among the DOD cohort. This is one of the reasons we felt that including all VA cohorts made the comparison more meaningful.

12. **Page 11, next to last line, what is the basis for inferring “long-term” military service – is this in reference to the length of an individual’s service?**

Yes, that was the intent. To make this point more clear we have revised the wording.

13. **Page 12, while women might not have had official combat status, the nature of this war was such that any woman deployed was likely to have been exposed to attacks or their aftermath; also, was any consideration given to MST?**

MST was not considered in this paper. However, this data has been used to explore other comorbidities. See the embedded document.

14. **In the Figure, I think the horizontal arrows should go to the right, to indicate as cases move down the chart, these move OUT of the path into exclusions, deaths, etc. Except for the “deaths” added back into the VA cohort.**

Yes, this has been corrected.

15. **Table 1 – why are some entries in bold?**

This has been corrected.

Thank you for your assistance and I look forward to hearing from you.

Sincerely,

Mary Bollinger

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