Author's response to reviews

Title: A Systematic Review of Post-Deployment Injury-Related Mortality Among Military Personnel Deployed to Conflict Zones

Authors:

Joseph J Knapik (joseph.knapik@us.army.mil)
Roberto E Marin (roberto.estaban.marin@us.army.mil)
Tyson L Grier (tyson.grier@us.army.mil)
Bruce H Jones (bruce.h.jones@us.army.mil)

Version: 4 Date: 2 March 2009

Author's response to reviews: see over
Dear Sir or Madam:

We would like to thank the reviewers for their very helpful comments on our paper entitled “A Systematic Review of Post-Deployment Injury-Related Mortality among Military Personnel Deployed to Conflict Zones” (MS 1694140932240521) that we submitted for possible publication in *BMC Public Health*. We have provided our replies to the reviewer’s comments and made appropriate changes in the manuscript, as required.

This work is original and is not under consideration by any other journal. No author has a financial or other relationship in this paper that might be perceived as leading to a conflict of interest. The manuscript has been read by and approved by all authors.

Please direct correspondence regarding this manuscript to me as follows:

Dr Joseph Knapik  
US Army Center for Health Promotion and Preventive Medicine  
Directorate of Epidemiology and Disease Surveillance  
Aberdeen Proving Ground (Edgewood Area), MD 21010  
My phone number is (410) 436-1328, my FAX number is (410) 436-5449, and my e-mail address is joseph.knapik@apg.amedd.army.mil.

We look forward to your final decision and the possibility of having our work published in *BMC Public Health*.

Respectfully,

Joseph Knapik, ScD  
Research Physiologist
MAJOR REVISIONS

1. The reviewer states that the methodology for the systematic review is severely lacking and suggests we include additional information she has listed. As BMC Public Health suggests in their Information for Authors, we generally followed the MOOSE (Meta-analysis of Observational Studies in Epidemiology) guidelines in our review. The MOOSE guidelines do not call for the information that the reviewer has suggested we include (See the Table in Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, and Thacker SB (2000). Meta-analysis of observational studies in epidemiology. JAMA, 283: 2008-2012). We understand that this information is often included in systematic analyses but in our experience, it is not very useful. However, we did retain much of this information and have, in deference to the reviewer included what we could in the Methods section. We now note that 5,144 unique studies were identified in the initial search, that two investigators examined the titles of these studies, and that these two investigators examined abstracts from 156 investigations that appeared to meet the review criteria. The two reviewers concurred on 20 original studies that fully met the review criteria.

2. The reviewer has correctly identified that, with regard to the in the proportionate mortality studies, it was inappropriate to say that injury-related mortality of the in-country Vietnam veterans was elevated relative to Vietnam veterans who did not serve in-country. We did not mean to imply this and our wording in this regard was unfortunate. As the reviewer suggested, we have now corrected this. The second and third paragraphs of the section entitled “Injury-Related Mortality among Vietnam Veterans” now separately discuss the proportionate mortality and retrospective cohort investigations.

3. The reviewer is correct in that we tend to concentrate on the point estimates in our description of the results. However, we do not ignore the confidence intervals as they are readily available for the readers to see in Tables 3 and 4. Our goal in the text is to note the general trends in the data. Confidence intervals indicate the precision of the point estimate. A confidence interval that crosses the 1.0 level means that the differences between the groups are smaller, not that these differences do not exist. The meta-analyses allowed us to combine the data from all appropriate investigations and, in effect, increase the sample size. The conclusions from the meta-analyses were similar to those when we performed the descriptive examination of each study. That is, injury-related mortality was elevated in conflict-zone service members and much of that elevated mortality appears to be due to vehicle-related events.

4. As the reviewer has suggested, we have now included the fact that we could not combine the proportionate mortality studies and the retrospective cohort studies in the meta-analysis because with the proportionate mortality investigations we only know the number of deaths as a proportion to the total deaths and do not have denominators. This is now included in the first paragraph of the section entitled “Meta-Analyses”.

Reply to Hollie Thomas
5. The reviewer is correct in that in 3 of the 4 meta-analyses there are only two studies. In the other case there are 3 studies. However, this is all the data that are available and that can be reasonably combined for the reasons provided in the third paragraph of the section entitled “Meta-Analysis”. Combining the all Vietnam studies and/or all Gulf War studies into a single meta-analysis would not be appropriate given the facts that 1) long and short-term follow-up results differ in individual investigations, as discussed earlier in the paper, and 2) some of the studies involve the same (or similar) cohorts of Service Members. The power of combining even two or three studies is readily apparent in Table 7: the point estimates decline from the short-term to the long-term follow-up for all external causes and motor vehicle events as suggested by individual studies. Further, the confidence intervals are smaller than for the individual studies.

6. As the reviewer has suggested, we have included the fact that our short-term results on Vietnam veterans agree with the short-term results cited by Boyle 1989. This also reminded us that Kang et al. had performed a similar review of first Gulf War veterans and we have also included this in the first paragraph of the Discussion (Kang HK, Bullman TA, Macfarlane GJ, and Gray GC (2002). Mortality among US and UK veterans of the Persian Gulf War: a review. Occupational and Environmental Medicine, 59: 794-799). For these changes, see the last sentence of the first paragraph of the Discussion.

DISCRETIONARY REVISIONS

1. The issue here is what group might be appropriate as a “control” group for deployed service members. The Kang and Bullman study was cited to address the possibility that those who deployed were healthier than those who did not deploy. If deployed service members were healthier, there would be a selection bias in favor of those deployed. In the Kang and Bullman study, two groups of service members were compared, one who deployed to a non-conflict zone and another who did not deploy. There was no difference between the 2 groups in injury-related mortality. This suggested little selection bias in the major outcome variable of interest and thus we selected as a “control” group non-deployed service members serving in the military at the same time as the deployed service members.

2. As the reviewer suggested, we have stated how many studies related to the Vietnam War and how many related to the First Gulf War. We have provided a summary of how many studies involved US, UK, and Australian service members. We have provided information on the number of studies involving extended follow-up. We have also included more details on the WWII and Korean studies and why these investigations were not included in the review. These changes were integrated throughout the first three paragraphs of the Results.

3. As the reviewer suggested, we have highlighted in the last sentence of the section entitled “Methodological Quality Score” the fact that the retrospective cohort studies scored higher on methodology quality than the proportionate mortality studies. The
average±SD for the proportionate mortality studies was 79±4 and that for the retrospective cohort studies was 89±5. The 10 point difference is larger than that would be expected based on the additional 5 points given for study design alone.

4. As the reviewer suggested, we have included the fact that although all external cause mortality of conflict-zone women is only slightly elevated compared to men, motor vehicle-related mortality of conflict-zone is considerably elevated. This was added as the last two sentences of the last paragraph of the section entitled “Injury-Related Mortality among Vietnam Veterans”

5. We did not calculate the number of excess deaths from external causes that might be expected from deployment.
a. The reviewer suggested we perform a sensitivity analysis on our methodological quality scoring system. Sensitivity analysis is a technique that determines how different values of an independent variable will impact a particular dependent variable under a given set of assumptions. It is more used in mathematical modeling. In our case, we are evaluating several important criteria (study design and accuracy of veteran status, conflict zone status, vital status, and cause of death coding) to arrive at an overall quality score that reflects the accuracy of the data sources and adequacy of the study design. The maximum total points listed in the last column of Table 2 shows how much each criterion contributes to the maximum score, and reflects the sensitivity of each criterion. The greatest weight is put on vital status and veteran status and the least weight on study design.

b. The reviewer raised a good point. We have suggested several hypotheses in our conclusions but we have not specifically tested any of these. We did carefully note in the Discussion the literature supporting these hypotheses. We have now modified the Conclusion to state that “Although the reasons for this elevated mortality cannot be determined from the data analyzed here, several hypotheses can be derived from the literature.”

c. The reviewer notes that she would like to see the data in more graphic form. However, the latest recommendations in our field suggest minimal use of graphs and more data in numeric form. Numeric data provides a somewhat more precise form of information (compared to graphs) and makes secondary analysis much easier. If readers would like to plot the data, the information is readily available for this. See: Hopkins WG, Marshall SW, Batterham AM, and Hanin J (2009). Progressive statistics in sports medicine and exercise science. *Medicine and Science in Sports and Exercise, 41*; 3-12.