Author's response to reviews

Title: Mortality study of civilian employees exposed to contaminated drinking water at USMC Base Camp Lejeune: A retrospective cohort study

Authors:

Frank J Bove (fbove@cdc.gov)
Perri Z Ruckart (pruckart@cdc.gov)
Morris Maslia (mmaslia@cdc.gov)
Theodore C Larson (tlarson@cdc.gov)

Version: 2
Date: 4 August 2014

Author's response to reviews: see over
Author’s response to reviewers:

Dear EH staff,

Thank you for your review of the manuscript, “Mortality study of civilian employees exposed to contaminated drinking water at U.S. Marine Corps Base Camp Lejeune: A retrospective cohort study”.

We have carefully considered the reviewers’ excellent comments and revised the manuscript. Changes made to the manuscript include stating that long-term follow-up is necessary to provide a comprehensive assessment of the effects of the drinking water exposures at Camp Lejeune, adding text discussing the use of the commercial tracking service and the possible impact of confounding by alcohol consumption, and added confidence bands to the spline figures.

Responses to all the peer reviewer comments can be found below.

We feel that we have addressed all of the reviewers’ comments and hope that you will consider the manuscript acceptable for publication in your journal.

Sincerely

Frank J. Bove, Sc. D
Senior Epidemiologist, ATSDR
Mortality study of civilian employees exposed to contaminated drinking water at USMC Base Camp Lejeune: A retrospective cohort study.

Responses to Reviewer #1

Specific Comments:

-Page 6, last paragraph – Might also include emphysema in the smoking outcomes not known to be linked with these solvents.

Response: The cause of death, COPD, combines emphysema and chronic bronchitis. The Life Table Analysis System (LTAS) used to obtain SMRs combines these two outcomes into COPD. We decided to be consistent with the LTAS grouping of these two outcomes. We have revised the text to mention that COPD includes both emphysema and chronic bronchitis.

-Page 7 – I assume that these cohort members were civilians working at the bases, although I did not see where the manuscript indicated that in the initial description of the cohort.

Response: We have added the word “civilian” to the first two sentences in the section on “Study Population and Eligibility” to make it clear that the study focused on civilian employees. The abstract does state that the study is focused on civilian employees.

Page 7 - Most civilians employed at government installations provide a history of previous jobs
on the application form. Was this done for these two bases? This information is available in base files or personnel record centers.

Response: This information was not available in the DMDC database during the time period under study.

-Might provide a little more information about use of “commercial tracking service,” i.e., how were they selected for tracking, how many were tracked, and success rate.

Response: The text states that the tracing service was used for those whose vital status remained unknown after the search through the SSA databases. In actuality, the tracing service was used if the search through the SSA’s ORES database was not successful, i.e., either there was not a perfect match for Social Security Number, name and date of birth, or the ORES database indicated that the vital status was “unknown”. Almost 49% (N=4,540) of the cohort members either did not have a perfect match with the ORES database (41.4%, N=3,866) or did match but the vital status was listed as “unknown” (7.2%, N=674). Of the 4,540 sent to tracing, information on vital status was obtained for 4,383, so the success rate was 96.5%. Some of this information will be added to the manuscript in the methods section.

-For Table 4, it would be useful to include the number of deaths from Lejeune and Pendleton for each cause of death. –

Response: We have added the number of deaths to this table.

Page 15, should mention the SMR for liver cancer from Lejeune.

Response: We did not mention the SMR for liver cancer at Lejeune because we were only indicating SMRs above 1.00. The SMR for liver cancer at Lejeune was 0.42.

-Page 16, I would put the SMRs for lung cancer for Lejeune in the text. Although it is elevated, the excess is small (SMR=1.09). This would have to be the upper SMR that would be cause by smoking confounding. So any SMRs for nonsmoking outcomes larger than this would not likely be entirely due to smoking confounding.

Response: We did not include the SMRs in the text for those diseases of secondary interest such as lung cancer because the SMR analyses were not the primary focus of the study. The primary focus was on the comparisons between Lejeune and Pendleton and within the Lejeune cohort. For the Lejeune vs Pendleton comparisons, we used the HR for COPD to provide an upper bound on the possible confounding effects of smoking. The HRs for COPD and for lung cancer were very similar, 1.21 and 1.25, respectively. Since lung cancer has been associated with occupational exposures to PCE, we based our assessment of the possible confounding effects of smoking on the HR for COPD. For the within-Lejeune comparisons, there was no association between the cumulative exposures and the smoking-related solvent-unrelated diseases or for lung cancer.
Responses to Reviewer #2

The only issue that I have is that the conclusion should mention the need for continued follow-up of this and similarly exposed cohorts so that future mortality analyses can be based on a larger number of deaths.

Response: Text has been added to the abstract and conclusion section stating that: “Additional follow-up would be necessary to comprehensively assess effects of drinking water exposures at the base.”

Background Section

It would be useful to give the reader more information on the manner in which the underground storage tanks and waste disposal practices contaminated the drinking water

Response: The reference provided in the text describes the contamination sources in more detail. We have added some text to the background section as well.

More information should also be provided on the years and pattern of operation of the contaminated wells at Hadnot Point.

Response: A reference was added to the paragraph mentioning the supply wells serving the Hadnot Point treatment plant. This reference provides details on the operation of the supply wells. We have added text to the paragraph indicating that between 20 and 30 supply wells were in use during the study period.

Methods Section

The exposure assessment section should provide any available information on the residences of the workers and whether or not their residential drinking water was contaminated.

Response: Virtually all the civilian employees resided off-base. The contamination at the base did not affect off-base drinking water supplies. We are unaware of any contamination of the public water systems in the areas near the base. We have added text to clarify these points.

The frequency distribution of the length of employment should be provided.
Response: Table 2 is too large to include additional information. Therefore, we added information on the distribution of the length of employment of the cohort members during the period 1973-1985 in the results section of the text.

Similar to the analyses for residual confounding by cigarette smoking, it would be useful to present analyses evaluating possible residual confounding by alcohol consumption using alcohol-related deaths. These analyses would address criticisms regarding the interpretation of some of the findings.

Response: Kidney cancer and the hematopoietic cancers are not known to be associated with alcohol consumption. A recent study also indicated that Parkinson’s disease is unrelated to alcohol consumption. On the other hand, several of the diseases that were elevated in the Camp Lejeune cohort compared to the Camp Pendleton cohort have been associated with alcohol consumption: cancers of the oral cavity, breast, and rectum. Other diseases that have been associated with alcohol consumption were not elevated in the Camp Lejeune cohort compared to the Camp Pendleton cohort: cancers of the liver, esophagus, and colon, cardiovascular diseases and liver diseases. Therefore it does not appear that alcohol was a confounder for the comparisons between Camp Lejeune and Camp Pendleton. Within the Camp Lejeune cohort, cumulative exposures were related to esophageal and rectal cancers but not for other alcohol-related cancers or diseases. Therefore, it does not appear that alcohol was a confounder for these comparisons internal to the Camp Lejeune cohort. We have added text to the discussion section on these points.

Conclusion section

A statement should be made that follow-up of this civilian cohort should continue and that updated mortality analyses should be conducted in five or so years. It is particularly important that this be done because many cohort members are entering the age of increased cancer incidence (i.e. 60+ years).

Response: We agree and have added text to the abstract and conclusion to address this comment.

Supplementary Figures: These figures should include confidence bands.

Response: The original splines did not include confidence bands because the bands are so wide that the shape of the curve is obliterated. However, we have added spline curves with 95% confidence intervals so that the reader can observe the width of these bands around the curve.