

Topic: ASTDR Mortality Study of Marines at Camp Lejeune and Camp Pendleton

Review of: Bove FJ, Ruckart PZ, Maslia M, et.al. Evaluation of mortality among Marines and Navy personnel exposed to contaminated drinking water at USMC base camp LeJeune: a retrospective cohort study. *Environmental Health* 2014, 13:10.

Issue:

- Contaminated drinking water was discovered in the 1980s at Camp Lejeune; there are concerns about long term health effects
- The Department of Veterans Affairs (VA) is responsible for the provision of care for Veterans who lived at Camp Lejeune. Additionally, VA is responsible for payment of care for 15 specific conditions for family members of Veterans who lived at Camp Lejeune.
- On February 19, 2014 the Agency for Toxic Substances and Disease Registry (ASTDR), a branch of the CDC, published a mortality study of Marines and sailors who lived at Camp Lejeune during the time of the water contamination.

Analysis:

- Since 1991, ATSDR has been performing health surveillance of former residents of Camp Lejeune. These studies have been funded by the Navy, totaling more than \$40 million.
- The research question of the mortality study was to determine if exposure of Marine and Navy personnel to contaminated drinking water at Camp Lejeune increased the risk of mortality from cancers and other chronic diseases”.
- The mortality rate of 154,932 Marines at Camp Lejeune was compared to mortality rates of 154,969 Marines at Camp Pendleton. Mortality rates were also compared to the general US population.
- By the end of the study period about 6% (n=9,000) of the Marines in **both** groups died.
- Multiple comparisons were performed on the data, with only three statistically significant findings:
 - Both groups of Marines were significantly healthier than the general population. Both group of Marines had decreased mortality for all causes and for all cancers. It is expected that Marines would be healthier than the general population (healthy soldier effect)
 - The Camp Lejeune Marines had a significant increase in prostate cancer death (18 deaths) compared to the US population, but **NOT** compared to the Camp Pendleton group
 - The Camp Lejeune Marines had a 10% increase in mortality from all cancers, compared to the Camp Pendleton group.

Methodological Flaws

- ATSDR concludes that there were “elevated risks” for several types of cancer and amyotrophic lateral sclerosis. This is misleading, and not supported by data. These results were **NOT** statistically significant.
 - Although risk estimates between two populations may differ from each other in magnitude (i.e., one risk estimated being “elevated” over another), it **does not** mean that they are statistically and meaningfully different from each from an epidemiological perspective. You must use statistical testing to interpret if the difference in magnitude is meaningful. The authors did not use statistical significance testing (p-values testing the null hypothesis of no difference) to interpret these differences, and therefore, there is limited confidence in the conclusions.
 - Another method that is commonly used to test for significance in population statistics is to examine the 95% confidence intervals for the two risk estimates. If the 95% confidence intervals for each of the two risk estimates overlap, it can be deduced that those two risk estimates do not differ significantly (although one may be larger in magnitude). Table 4 demonstrates this.
- The authors state “We did not use statistical significance testing to interpret findings”. It is methodologically suspect that in a study sample this large (N=20,000), statistical testing was not performed, since statistical significance (p-values) is largely a function of sample size.
 - Multiple comparisons were performed (which lead to chance associations) without any corrections for p-values (Bonferroni corrections should have been performed).
 - The 95% confidence intervals for almost all comparisons were unstable and not significant, due to the small number of deaths from each condition.
 - Table 5, which compares the risk of specific cause mortality between Camp Pendleton and Camp Lejeune (which is the best table to assess if cause specific mortality is different between the “exposed” and “unexposed” cohort) reports **all non-significant results**. All p-values are not significant, and all 95% confidence intervals include 1 (which means no association).
 - Data on major confounders was not collected.
 - Data on confounders was limited to administrative data from DMDC, which is known to have errors, namely for race.
 - For example, alcohol consumption and hepatitis C status are greatest predictors of liver cancer, and should have been controlled for in any analysis of liver cancer mortality.
 - Exposure data is based on a theoretical model, which makes several assumptions, years after the exposure occurred. No scientific body, outside of ATSDR, has validated this exposure model. This can result in major bias.
 - Results from one study cannot be considered scientific proof. Replication or concordance with other studies of the same exposure in a different population is needed to make a statement on certainty of results.
 - *Environmental Health* is not a high profile journal--its impact factor is 2.71. It is an open access, online journal. Authors pay to have their studies published in it. It is possible that other journals would have questioned these methodological issues and not selected this paper for publication.

- ATSDR published a similar study of birth defects in the same journal in December of 2013. The same flaws were present in that report and the data did not support the conclusions.

Implications:

- ATSDR will release four more studies in the upcoming year.
- ATSDR has refused to share study results prior to publication with DoD or VA; however, they do share their results with the new media early.
- This study may have direct impact on disability compensation. Congress and Veterans groups are likely to pressure VA for make a presumption of service connection for the diseases in the mortality study and birth defect study, even though the epidemiological/statistical methodology is flawed, producing **potentially** misleading results.

Review by the Office of Public Health, VHA

Reviewer: (b) (6)

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