Reviewer's report

Title: Arsenic in drinking water and cerebrovascular disease, chronic airways obstruction, diabetes mellitus, and kidney disease in Michigan: a standardized mortality ratio analysis

Version: 1 Date: 18 September 2006

Reviewer: Kenneth Cantor

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General
The authors present an ecological analysis of 23 selected mortality outcomes with respect to arsenic levels in a six county study area in Southern Michigan. SMRs for these outcomes, by sex, in the six counties (with somewhat elevated arsenic in drinking water) were calculated, using statewide race, and age-specific rates. The report requires a more detailed description of exposure assessment, as well as addressing the issue that one county of the six (Genesee) has more than half the total study-area population. More details may be found below.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
A. One county of the six - Genesee County - represents almost 60% of the total study population - yet the exposure figures are presented for the whole of the six county area. It is not clear from the text how representative the exposure scenario in Genesee county is of the full study area. This may or may not be a fundamental flaw in the approach and analysis. At any rate, the issue must be addressed. In addition, the demographics of Genesee County are somewhat different from the other counties, and this could influence study findings. (For example, in 2000, Genesee Co. was 75.3% white, implying that most of the non-white population in the 6 county area resided in Genesee.) The authors could address these related problems by the following:
1. Present a table showing exposure & total population statistics for each of the six counties in the study area. This could be an expansion of the current Table 1.
2. Present separate analyses for Genesee and the other five counties.
B. Estimates of exposure need further clarification. The paper cites "9,251 analyses of water samples from the six-county area." Presumably, these analyses are the basis for the exposure estimate of an arithmetic mean of 17.7 ug/L, with 10% of the samples exceeding 43.0 ug/L. It appears that the arithmetic mean is not a population-mean exposure (which is what is needed), and that the great majority of water sample analyses are from private wells. What is really needed - if county-wide mortality statistics are used in the analyses - are county-wide estimates of arsenic exposures, including weighted estimates of arsenic levels in public water supplies. The authors should make the best attempt possible to estimate population-wide average exposures, not only exposures from individual well water supplies.
C. A weakness of all ecologic studies is the possibility that in- or out-migration could distort the findings. Migration statistics should be presented, to assist readers in interpreting the findings.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)
A. The authors cite reference 17 (Lewis et al.) liberally throughout the discussion. A close look at this reference reveals a high likelihood of extensive misclassification of exposure, throwing great doubt on its findings. The authors may wish to rethink how they compare their own findings with those of Lewis et al.
B. Would it be helpful to mention which counties are in the Detroit metro area?
C. To help avoid the possible pitfall arising from multiple comparisons, the authors used 99% CIs instead of the usual 95% CIs. In principle, this is an informal application of the Bonferroni approach to statistical significance, and quite appropriate in some settings. In my opinion, this is not necessary here, and the standard 95% CIs would be quite sufficient. This is an exploratory exercise, not a hypothesis-testing study.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions
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.