Reviewer’s report

Title: Pancreatic Cancer Clusters and Arsenic-Contaminated Drinking Water Wells in Florida

Version: 1 Date: 25 February 2012

Reviewer: How-Ran Guo

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This study evaluated if there were any pancreatic cancer clusters in Florida and tried to identify socio-demographic and behavioral correlates associated with these clusters. In particular, the authors aimed to determine that, after controlling for these factors, if the cancer cluster membership was associated with proximity to identified arsenic-contaminated drinking well water. As the result, the authors found that cases living within 1 mile of known arsenic-contaminated wells were significantly more likely to be diagnosed within a cluster of pancreatic cancers relative to cases living more than 3 miles from known sites and concluded that exposure to arsenic-contaminated drinking water wells may be associated with an increased risk of pancreatic cancer. The topic is a relevant public health issue, and the finding is interesting.

Major Compulsory Revisions

1. The research question is well defined, but the authors should provide more information to support the hypothesis of an association between arsenic and pancreatic cancer. Reference 23 was cited to support the argument “there is some suggestion of a possible connection of arsenic-contaminated drinking water and pancreatic cancer” in the Background and the statement “There was one study in the literature that reported a non-significant association between arsenic and pancreatic carcinogenicity (23).” in the Discussion. However, the meta-risk ratio in that study was in fact 1.0 (95% confidence interval 0.6 to 1.5), which is equal to the null value, indicating no (neither a positive nor a negative) association at all. Are there any other epidemiological evidences besides a previous finding of an association between bladder cancer and proximity to known arsenic-contaminated drinking water wells using the similar study design (Reference 22)?

2. A brief description of the cancer registry should be provided, so that the readers can learn about the strengths and limitations of the data.

3. The logistic regression model used to generate the major results (Table 2) should be given in mathematical formula. The dependent variable was described as “a patient with pancreatic cancer living in a cluster versus being diagnosed outside of a cluster,” which is confusing because logistic regressions generally model the probability of an event occurring versus that of an event not occurring. Since the authors used residence at the time of diagnosis as the indicator, they seemed to model the probability of a patient living in a cluster versus living outside of a cluster. A more direct approach is to model the probability of a
disease occurring in a participant versus not occurring, such as in a case-control study. There is a gap between a patient occurring and a patient being diagnosed in a cluster. The authors should discuss briefly the issues involved in extrapolating the model used in this study to the model corresponding to the research question directly.

4. Given that most studies which evaluated the associations between arsenic ingestion and the whole spectrum of cancers did not observe such an association on pancreatic cancer, the authors should discuss other potential explanations for the association observed in this study.

5. The biological plausibility of an association between arsenic and pancreatic cancer should be discussed further.

6. In comparison with people who never smoke, current smokers had a higher risk (OR=1.1) whereas former smokers had a lower risk (OR=0.9), both with marginal statistical significance (95% CI with 1.0 as the upper or lower bound). Please discuss it.

Minor Essential Revisions

1. Report the percentages in Table 1 to the same number of digits below the decimal point.

2. Report the odds ratios in Table 2 to the same number of digits below the decimal point.

3. Please indicate in the legend the meaning of green spots in Figure 1.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests'.