Reviewer’s report

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

Version: 1 Date: 26 February 2012

Reviewer: Melissa Slotnick

Reviewer’s report:

Major Revisions

This manuscript is fairly well-written and reads easily, and the methods are well documented. However, I am hesitant to recommend this paper for publication based on many weaknesses in the methodology; the fact that a fairly substantial odds ratio is reported seems unusual and I suspect it’s artificial. It would be unusual to see such strong results for an ecological study when the exposure level is relatively low (10 ppb, but not exactly specified) and the exposure-disease relationship has not been previously demonstrated. Specifically, because this is an ecologic study, no individual-level data on exposure were collected, resulting in a high degree of exposure misclassification (especially over the lifetime). Because an individual lives near a contaminated well does not mean that they are exposed to that drinking water. In fact, if many of the contaminated wells were in urban areas it might be likely that the patients were drinking city water as opposed to private well water. The results may have been more convincing if a stratification of exposure supported the association. I would be surprised to see a true association for 10ppb, but might be more convinced if the exposures were much higher. Furthermore, lifetime exposure was in no way addressed or calculated. In a state like FL where a high percentage of the population may have migrated there later in life, residential stability must at least be considered.

There is the potential for geographic bias, which the authors touch upon, but which seems significant. If the wells sampled were only sampled based on complaints or industrial contamination, it seems as though there would be a disproportionate number of wells sampled in urban areas. If this is the case, you may see false clustering in high population areas. This potential bias deserves further analyses and exploration. Lastly, there is little support throughout the document for the suspected relationship between pancreatic cancer and arsenic exposure. The discussion of this association is very general and unconvincing. More of an argument needs to be developed throughout the manuscript, and the reader is left feeling as though this is a very exploratory analysis. If the authors wish to examine the association further, I would suggest fully assessing the geographic bias, working towards individual-level exposure estimates through geographic modeling and model validation using random well water sampling. Most importantly, the source of drinking water needs to be incorporated into the analyses, even if an attempt is made based by municipality boundaries.
Minor Revisions

Abstract
- concentration of arsenic should be defined

Background
- original articles should be cited when discussing association between pancreatic cancer and arsenic
- the significant findings seem like an afterthought give the way the last paragraph is written

Methods
- Should mention population calculation methods here as were reported in limitations. Why was the population multiplied by 5? Is this a standard way of extrapolating population data?
- Why was the 3-mile distance selected? What happens if you change the distance slightly? Do the results hold?

Discussion
- see major revisions
- I’m not sure the statement “… well water may serve as a proxy for environmental arsenic contamination in the soil and air” is true. Citations should be added.

Figures and Tables
- Because of the geographic nature of analysis, I would like to see more figures. The Figure is lacking and needs more description. Is this showing all of the wells?

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.