Reviewer's report

Title: Association between arsenic, cadmium, manganese, and lead levels in private wells and birth defects prevalence in North Carolina: A semi-ecologic study

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Reviewer: Jane Gallagher

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Re MS Association between arsenic, cadmium, manganese, and lead levels in private wells and birth defects prevalence in North Carolina: A semi-ecologic study

Alison P. Sanders1 et al

Sanders et al examined the association between the prevalence of twelve birth defect groups and NC well levels of arsenic, cadmium, manganese, and lead as summarized at the census tract ecologic unit.

Ecological studies are useful because they probe associations between health risk factors in advance of other more classical epidemiological approaches. Appropriately though the authors responsibly point out the potential limitations of this kind of study. This paper is notable because of the rich birth outcome data and extensive well testing measurements which should be of broad interest, to communities and researchers alike.

Comments that need to be addressed

1) Abstract “Statewide, private well metal levels exceeded the EPA Maximum Contaminant Level for arsenic, cadmium, manganese, and lead in 2.4, 0.1, 20.5, and 3.1 percent of Wells tested” …. Mn should not be listed together with the other regulated health based standards ie List Mn last and indicate Mn exceeded secondary guideline level i.e. it is not health based (rather based on taste and odor color).

2) “In North Carolina, 2.3 million residents use private wells for drinking water [27]” What % of the wells in NC wells were tested for metals. Is the extent of testing particularly notable compared to other states? “The analysis included 1,563 census tracts comprising 5,271 block groups across North Carolina” --what was the correlation coefficient between the metal levels at the census tract vs block group. Include a variability measure for each. Since both were looked at separately is there some discussion as to which is the more sensitive indicator (birth defects vs metal concentration ) .any relevant references that might have explored these comparisons of scale ?

3 “Data in this study represent metal analyses from newly constructed private
wells since July 2008 (according to North Carolina rule 15A NCAC 18A.3802) and wells tested between 1998 and 2010 where owners requested testing of existing wells” Results should include any analysis that looked at statistically significant differences between the owner tested vs required testing . b) If owners were not required by the state to test their water yet did so, it is of interest as to whether the owner driven subset had higher higher metal exposures. Ie was the desire to test driven by real or perceived higher well water metal levels.

4“ The resulting 50th and 90th percentiles of block group average levels were 1.24 and 2.75 ppb for arsenic, .50 and 1.90 ppb for cadmium, 41.85 and 163.00 ppb for manganese, and 3.32 and 7.55 ppb for lead vs census tract level i.e. The 50th and 90th percentile of census tract average levels were as follows: 1.29 and 2.54 ppb for arsenic, 0.54 and 1.82 ppb for cadmium, ppb for manganese, and 3.52 and 7.28 ppb for lead”. These are average levels. Was there a statistically significant difference between the block group vs the census tract level ie comparing the individual well measurements for each scale.

5“North Carolina is the fourth largest state population relying on private wells for drinking water; the total number of individuals served is larger only in Pennsylvania,California, and Michigan ---- how many total persons in NC have well water ?

6 “Treatment Technique (TT)” should be defined.

“ exceeded guideline levels” indicate % reported first on exceedances based on the MCL and % exceeding secondary guidelines i.e. Mn which is not health based (not health based).

7 The arsenic data from the current study appears to be the same as arsenic well water data used in the reference. So instead, do you mean that the present study “extends” the findings of reference 20.

8 It is well established that maternal smoking during pregnancy is associated with birth defects especially cleft palates. This point needs to be added to the “limitations” section of the paper. For example, approximately 13 % of NC women smoke during pregnancy (according to a NC state report). Is there an “area” based tobacco use metric that could be considered in future studies linking metals to health outcome measures ?

**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 I have no competing interests