Reviewer's report

Title: Agricultural Crop Density and Risk of Childhood Cancer in the Midwestern United States: an Ecologic Study

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Reviewer: Susan E Carozza

Reviewer's report:

This well-written paper presents a detailed analysis, using multiple analytic approaches, of an ecological study evaluating potential relationships between agricultural practices (as represented by cropping data) and risk of childhood cancers. As the authors themselves indicate, however, the paper is more a strong demonstration of possible uses of existing data than an addition to the understanding of the role of pesticide exposures in carcinogenesis in children.

Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

1. It is not clear what the rational is for the use of 3 exposure definitions. This approach makes interpretation of different outcomes based on the definition chosen somewhat challenging, and the authors do not attempt to reconcile how these different definitions might result in different RRs. Further, the use of multiple definitions for crop density does not always reflect meaningful differences in potential exposures. For instance, some of the differences in crop density % categories are so slight (eg. oats, sugar beets) that they are unlikely to result in substantially different exposure histories, expect perhaps at a very local spatial scale.

2. Perhaps the most interesting statement in the paper, in terms of interpreting the findings, related to the difference by state in pesticide use for oats “…with as little as 3% treated in Iowa and as much as 61% treated in Michigan.” An examination of supplemental tables 3 and 4 indicates that the risk for CNS tumors associated with oat crops (continuous, any/none) is higher in Michigan than in Iowa. More analysis and interpretation that incorporates additional pesticide use data would greatly strengthen the study.

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

3. The authors highlight the statistically significant positive associations found, but do not also mention the statistically significant negative association seen for the lowest category of crop density for total ag land and risk of total leukemia and ALL. If statistical significance is the criteria for highlighting results, then they should be consistent.

4. The authors note that they were “…not able to evaluate risk of AML and density of dry beans due to the small numbers of cases and counties growing
this crop.” However, there are AML results presented for this crop in Table 3.

5. Sorry to be picky, but Carozza is misspelled on page 13 (“Carroza”). It happens a lot :)

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

6. For clarity, it would help if the authors note that they are using residence at time of diagnosis for the cancer data in the first paragraph describing the cancer incidence data.

7. It would also help the reader to have a justification for selecting only cancers diagnosed under age 5 years.

Level of interest: An article of limited interest

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests.