Reviewer's report

Title: Epidemiological patterns of asbestos exposure and spatial clusters of incident cases of malignant mesothelioma from the Italian national registry

Version: 2 Date: 23 November 2014

Reviewer: Bruce W Case

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This is a well-done study by an experienced group of authors which attempts to use advanced statistical techniques to integrate actual individual exposure data with spatial mesothelioma incidence data. This is meant to overcome ecological bias, although that is not explicitly stated.

1. Minor Essential Revisions:

A. Lines 119-123 are misleading and should be replaced or reworded. Specifically, the attributable risk for mesothelioma to exposure is given for the United Kingdom (95%, from reference 1) and it is implied that this is true generally. In fact this is the HIGHEST attributable risk anywhere. Possible solutions include rewording to say one of the following:

- "most cases of MM are attributable" without a reference
- "Attributable risk for MM has been reported to be as high as 95%" (and retain the reference
- Expand the statement to include other references and percentages (i.e. "between x per cent and y per cent" (refs)).

B. There are many instances in the paper in which there are very minor errors due to the fact that the MS has not been written by a native English-speaker. Most commonly these are small mistakes in the use of articles and prepositions (especially using "the" where it does not belong and omitting it where it does belong). Rather the produce a line by line list of these I have made the corrections on a word document version of the MS with the changes, deletions, and insertions marked.

C. Despite the extensive reference to interview data, this does remain an ecological study with the problems inherent in such studies. This should be acknowledged and to the extent possible the authors should show how their approach deals with the problems that have been identified for such studies for this type of data. Reference can be made to the following articles which show the inherent problems with such approaches:

Chang ET, Adami HO, Bailey WH, Boffetta P, Krieger RI, Moolgavkar SH, Mandel


Cox and Berman have also provided a specific example of how the ecological type of approach even when paired with individual exposure level data may be misleading, but this is controversial and disputed: See the Author's reply to their critique of the Pan et al. study of proximity to asbestos sources and MM in California as well as their reply to the authors:


It is not necessary to go into this in great detail, but it is necessary to acknowledge the debate and to determine to what degree this study avoids the potential pitfalls which have been identified.

D. In several places speculation about the sources of exposure has been included in relation to specific point sources (e.g., types of factory). This is speculation and has to be identified as such, which is done most simply by using language like "This may be explained by...". I have made these changes where they are needed in the attached word document.

2. Discretionary Revisions

On page 8, it is noted that 78% of cases had pathologically proven diagnoses and exposure was "defined by direct or indirect interview" in 77.3% of cases. It would be of interest to know if there is any change in results if only the 78% and
the 77.3% were included in the analysis. However, this should be done only if the authors are interested in doing it and if it is a non-trivial amount of work. It would buttress their main arguments but it is not absolutely necessary.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I have acted and/or am currently acting as an expert witness or consultant for law firms representing defendants and plaintiffs in asbestos litigation and compensation board proceedings, and I have been a paid and unpaid consultant to regulatory and medical agencies and compensation boards in North America, including but not limited to the U.S. EPA, ATSDR, ATS, nongovernmental organizations (NGOs), and individual and collective citizen groups concerned with asbestos exposure and disease. I have also received (and may apply in the future for) competitive-funding research grants from European, U.S., and Canadian publicly financed, peer-reviewed grant approval process agencies concerning asbestos exposure and disease, including topics covered in this article, including but not limited to research support from EPA, NCI of Canada, Canadian Institutes of Health Research (formerly Medical Research Council of Canada), Quebec and American Lung Associations, and the Quebec National Institute for Public Health (INSPQ).