Author's response to reviews

Title: Certified causes of death in patients with mesothelioma in South East England

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Author's response to reviews:

Dear Mr Dunckley,

I am happy to provide a revised version of our manuscript ‘Certified causes of death in patients with mesothelioma in South East England’.

In revising the manuscript we have taken account of the suggestions from the two reviewers and we have formatted the manuscript according to your guidelines.

Reviewer 1

1. The results for the whole of England refer to the coded causes of death, as reported in official mortality statistics. For the analysis of the data from South East England we used the multiple causes of death as listed on the death certificate. These are subsequently coded to the single, underlying cause of death that is used in mortality statistics. The cancer registry has routine access to the information that is written on the death certificate, but not to the coded, underlying cause of death. We are, therefore, not able to analyse these data by the underlying cause of death, as suggested by the referee. It is evident from the consistent findings at England and South East England levels that a mention of mesothelioma on the death certificate almost always leads to coding of the mesothelioma as the underlying cause of death.

2. We have considered the layout of Table 1 and decided not to change its format. More complicated table layouts could be attempted, but we prefer the simple one. We have improved the paragraph about age-specific results.

3. We are happy to include reference to the articles on reliability of death certification, as suggested.

4. We have modified the text as suggested by the referee.

Reviewer 2
1. In the UK and many other countries, the occurrence of mesothelioma (the incidence of mesothelioma) is measured by the occurrence of mesothelioma deaths. The study question is about the validity of this approach, i.e. ‘What proportion of incidence cases of mesothelioma can be identified from death certificates?’ We have revised the first sentence in the abstract to make this clearer.

2. The information on asbestos use is in the cited reference (3).

3. In the analysis of classification and misclassification, there is no need to compute rates. Of course, population denominators can be applied to each count, but all the information relevant to classification is in the numerator of the rate, in the count of events. This is similar to the standard computation of sensitivity and specificity, which are proportions of frequency counts, not proportions of rates. There is no information gained from analysing a temporal trend over a four-year period. The time trends of mesothelioma incidence and mortality have been explored and published, e.g. references (2) and (3).

4. The point has been addressed above, reviewer no. 1, point 1.

5. The point has been addressed above.

6. The second paragraph of the Discussion section is necessary for the following paragraph about the study from Scotland. We prefer the two paragraphs to stay together in the Discussion section.

7. The misclassification between histopathological diagnoses of mesothelioma, lung carcinoma and other relevant tumours is likely to be small. The entire paragraph, including references (7) and (8), support this statement. The Cury study provides diagnostic sensitivities and specificities for several antibodies, but we are not aware of any general assessment of the sensitivity and specificity of a routine pathological diagnosis of mesothelioma.

8. We have made a very robust conclusion that information from death certificates underascertains mesothelioma occurrence by around 10%, and we have shown that the remaining deaths are classified as lung cancer deaths or unspecified cancer deaths. We are not offering an explicit ‘recommendation’, but it is obvious that more accurate death certification would be helpful. If we knew of a practical way of achieving this, it would be our recommendation.

Best regards,

Henrik Møller
Director and Professor of Cancer Epidemiology