Author’s response to reviews

Title: Lung cancer mortality of residents living near petrochemical industrial complexes: a metaanalysis

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Reviewer #2:

The authors assess clearly most of the observations, but one major point remain unclear. It regards the Assessment of data quality. The authors classify six of the selected studies as cohort studies (new table 1) and define the assessment of their quality using the Newcastle-Ottawa quality assessment scale. Nevertheless, reviewing the methods of these studies, it seems that five of them are based on an ecological small-area design. How the authors adapt the Newcastle-Ottawa method, that seems applicable only to case-control and cohort studies, to assess the quality of small-area studies? It is not clear if it is possible and convenient to combine results from studies with case-control, cohort, and small-area design in a formal meta-analysis.

[Authors' Response]

We would like to thank you for reviewing our manuscript again and addressing this point. We agree that the Newcastle-Ottawa method should be applied to comparable estimates. In our selected papers, there is no discrepancy among estimates for this meta-analysis.
First, estimates derived from case-control studies could be considered as those derived from cohort studies under either one of the following two conditions: (1) estimates are obtained from density sampling, or, (2) the disease is rare when under cumulative incidence sampling. Because lung cancer mortalities were usually less than 10-3 per year \( \{1, 2\} \), the OR (only study ID=H) is a reasonable approximation of relative risk/rate ratio (RR) and included in our analysis. We have already clarified the comparability of OR and RR of selected papers in the revision: “Since lung cancer mortalities were less than 10-3 per year \[24\], we could appropriately interpret estimated odds ratios as relative risks \[25, 26\].” (page 7, last paragraph, 1st sentence).

Second, indeed, the ecological studies involving observations of groups may usually be different from studies involving observations at the individual level \[3\]. The estimates derived from the ecological studies should be cautiously interpreted to avoid falling into the ecological fallacy \[3\]. However, if the environmental measurements could be assigned to the individual level, the use of aggregated measures as predictor variables are not ecological study designs but could be regarded as the individual level \[3\]. This condition is frequently encountered in measurements performed for ambient air in a small community. In our analysis, selected studies can link different exposure levels (although it could a binary variable: close to PIC or not) and most importantly, outcome at the individual level. Therefore, potential bias of ecological bias may be minimal, or, they could be regarded as cohort studies. Nevertheless, it should be noted that such an assignment might lead to misclassification bias when limited environmental exposure levels were applied extensively in time and space. We have already clarified the possible limitation in the revision: “First, the definition of exposure varied slightly between studies… Misclassification of exposure and non-exposure might exist and bias the pooled estimates towards the null.” (page 15, last paragraph, last 2 sentence).

In summary, we didn’t find a discrepancy between estimates in selected studies. We believe that the estimates are comparable for meta-analysis and applying the Newcastle-Ottawa method to evaluate those cohort and case-control studies is appropriate.
Reference

