Reviewer’s report

Title: Systematic review and meta-analysis of case-crossover and time-series studies of short term outdoor nitrogen dioxide exposure and ischemic heart disease morbidity

Version: 0 Date: 20 Dec 2019

Reviewer: Lidia Casas

Reviewer's report:

Overall, this systematic review is well written and summarizes results of the associations between NO2 and ischemic heart disease. I only have some minor comments.

Introduction: There is already one review on the effects of NO2 on IHD (ref #9). Why do we need a second review? I am not saying it is not needed, but it would be good to justify. The results of both reviews are compared and discussed in the discussion sections, and the added value of the review presented in this manuscript is highlighted. However, it would be nice to read about the added value of this review and meta-analyses already in the introduction: what did the previous review not cover that the current review will add?

Methods: In the results section it is mentioned that the review is part of a broader review including cardiovascular and respiratory health effects of NO2. The reference provided indicates that it is registered in PROSPERO. This should be explained in the methods section. When looking at the search terms provided at the additional file 1, one realizes that the search includes respiratory and cardiovascular terms. Thus, there was one common search. How did you select the articles to be included in this specific review on IHD? Also, the registration in the PROSPERO dataset should be mentioned in the methods.

Results:

In the first paragraph, providing percentages next to the n of papers would help contextualize.

It would be good to mention the lags included in the analyses. On what exposure lags are the results of the meta-analyses based?

"Risk estimates", I prefer to call them effect/association estimates. Risk is for incidence proportions and therefore RR. You also report OR here.

The authors specify that they finally included 66 studies in the meta-analyses. How many case-crossovers and how many time-series?

Discussion: First sentence: "based on an analysis of 85 case-crossover and time-series studies, we found that short term exposure..." According to the results section and the flowchart, only 66 studies were included in the meta-analyses. Please, correct this.
Figure 1: in line with my comment on the methods, it would be nice to show here how the data for this specific study on IHD is collected. What are the numbers included in the identification part of the flowchart? Are they based on all search terms described in the additional file 1? When does the study on IHD start? Also, when records and full articles are excluded, is it possible to show n of excluded records by reason (or groups of reasons if too many different reasons) for exclusion?

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