Reviewer's report

Title: Urban air pollution and emergency room admissions for respiratory symptoms: a case-crossover study in Palermo, Italy.

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Reviewer: Dolores Catelan

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The authors have submitted a much improved draft of an earlier version of their manuscript.

I still have some comments.

1) To my comment "The authors say “Because the case and the control were the same person, confounders related to individual factors (e.g. age, gender, smoking habits, nutrition conditions, and so on) as well as time invariant or slowly varying risk factors were controlled by design.[18]” This is correct only when you perform the analysis stratifying by individual. I do not think authors did the analysis in this way." the author answered "We totally agree with the Referee about this topic. In fact, the analyses were conducted by using the “clogit” STATA command, which syntactically include a grouping variable at an individual level (case record + controls records). Thus, the analyses were conducted stratifying by individual." Indeed this seems reassuring but it is not so. The likelihood is equivalent to the Poisson likelihood and the case-crossover fitted to epidemiological time series is equivalent to a Poisson regression model (see Yun LU and Scott L. ZEGER. On the equivalence of case-crossover and time series methods in environmental epidemiology. Biostatistics (2007), 8, 2, pp 337-344). The problem is that there are only aggregate variables and the dataset reduces to a large contingency table. Eventually the case-crossover approach is not superior to Poisson regression. Thus, the analyses were not conducted stratifying by individual. Please change the sentence in the paper.

2) Quoting Stern et al., 2001 the authors say "Furthermore, we totally agree that results of medical research should be interpreted with caution, considering the context of the study and other available evidence. In our opinion (and according to Sterne et al.), the present study “contributes incrementally to an existing body of knowledge”. Our results specifically incremented the evidence of association between air pollution exposure and short-term respiratory health effects in a residential area characterized by the lack of industrial settlements and by a temperate climate (throughout the year) that contribute to the limited use of domestic heating plants. Moreover, the presence of a very active commercial and touristic port, nearly located in the historic centre of the town, further characterize the study area and, consequently, the distribution of air pollutants. In order to avoid making this study a new
“today’s random medical news” particular care was devoted to the “precision of measurement” (as much as possible) being unable to “increase the sample size”. I suggest to report in some way these comments in the Conclusion section both in the paper and in the abstract.

3) Authors reply in this way to my comments on the possible presence of ecological bias: "Different considerations should be formulated about air pollutants exposure. Concerning this topic, we certainly agree with the Reviewer that this study is at an ecological rather than an individual level. It shouldn’t be otherwise considered, as we measured air pollutant levels by fixed monitoring stations instead of passive samplers for personal exposure measurements." My suggestion is indeed to mention the problem in the Discussion section both in the paper and in the abstract. They added also "This because our goal was to study the possible association between trafficrelated air pollution and health effects in general population and not in a selected sample of individuals." This is not connected to the problem of ecological bias, it is just the goal of any statistical inference. 4) the authors say "Thirdly, for each air pollutant, a single value was averaged by a fixed number of monitoring stations instead of individual passive samplers for personal exposure measurements, leading to a possible spatial misalignment between pollutants levels and health data." I suggest to cancel the word "possible" misalignment. It is sure that there is a misalignment since for the nature of the data.

5) to my comment on "statistically significant" results the authors say "We thank the Referee for recalling this interesting paper by Sterne JAC et al. (and, consequently, Biggeri A et al.; Epidemiol Prev. 2010) regarding the use of p-values and significance levels in epidemiological studies. In accordance to the Reviewer’s suggestion, statistical analyses were repeated calculating 90%CI instead of 95%CI. Table 3 (with 95%CI and 90%CI, respectively) is reported below. However, because this gave identical results, for convenience and according to the comments by other Reviewers, Table 3 was included in the manuscript with 95%CI." Since all the uncertainty in the data is addressed by the confidence interval (which could be asymmetric respect to the null value), pvalues in the table should be cancelled otherwise CI are again interpreted only in terms of test of hypothesis. Moreover, highlighting with * the pvalues< 0.05 in Table 3 is absolutely against Stern and Smith suggestions.

I suggest to replace the word "significant association" with "positive association" in the last sentence of the results in the abstract.

Level of interest: An article of importance in its field

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

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.