Reviewer’s report

Title: Changes in triggering of ST-elevation myocardial infarction by particulate air pollution in Monroe County, New York over time: a case-crossover study

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Reviewer: Michela Baccini

Reviewer's report:

The paper presents the results of a case-crossover analysis aimed to compare the effect of exposure to particles and other air pollutants on ST-elevation myocardial infarction before, during, and after air quality policies and economic changes.

The topic is of interest, the paper is well written, but the design of the study and the methods used for the analysis are quite weak. This has consequences on the results that should be interpreted in a descriptive way.

Major revisions:

1) The air quality policies and economic changes cited in the title are not well defined, and simple time windows are used as a proxy of the interventions. This is a clear limitation of this study, which should be discussed by the authors and accounted for in interpreting the results of the analyses. I think that also the title should be more adherent to the actual analysis performed in the paper: a comparison between time-periods characterized by different levels of air pollution/particles composition.

2) Due to fact that the authors perform a large number of analyses, selecting the "significant" results on the basis of the p-value can be misleading (Figure 1). In fact, one can argue that the "significant" results could be false positives. This point should be discussed in the paper and the results interpreted accounting for this problem.

3) In the analysis of epidemiological time series, influenza epidemics are usually considered a confounder of the air pollution effect. Did the authors include this term in the model? Was information about influenza available at the individual level?

Similarly, the potential confounding effect of holidays should be accounted for.

4) The authors write that the characteristics of the patients are not well balanced among time periods. Thus, the estimated interaction between time period and air pollution could be indicative
of a different association between exposure and outcome in patients with different clinical/individual characteristics (frailer/aged people could be more susceptible to high exposures than less frail/younger ones), rather than of a difference among periods. In the supplemental material, the authors show that there are not "significant" interactions between patients' characteristics and exposure. I think that this analysis is not sufficient. Did they try to include in the main models interaction terms between patients' characteristics and exposure? Sensitivity analyses should be conducted to evaluate if the results are robust to the introduction of these terms in the model.

5) I suppose that a problem in including terms involving personal characteristics in the main model is related to the presence of missing values. Did the authors consider the opportunity to perform some kind of imputation of the missing values?

6) Is a linear term sufficient to describe the effect of temperature? I would expect an excess of events during both very cold and very hot days. I suggest to include the results of the preliminary analysis on the temperature-outcome relationship in the supplemental material. Moreover, the sensitivity of the results when changing the shape of the temperature-outcome relationship should be evaluated as well as the presence of possible interactions between temperature and patient's characteristics.

7) In Table 4, the interaction tests are not reported. Is there a reason to report such tests for the confounders but not for the exposures?

Minor comments

1) pag 7. "If a patient experienced multiple STEMIs during the study period, we only included STEMI that occurred at least 72 hours after a previous STEMI, resulting in 921 STEMI events in 912 patients available for analyses". The correlation arising from considering multiple episodes for the same patient is likely negligible (the number of multiple events is very low), but this point should be discussed in the paper. In particular, did the authors account for within subject correlation or not?

2) pag 8. "Case periods of this study were defined as the 1, 3, 12, 24, 48, and 72-hour periods prior to the time of STEMI symptom onset, with control periods (3-4 per case, depending on the number of days in calendar month) matched by calendar year, month, weekday, and hour of the day". This description is not completely clear. It seems to me that it confounds the definition of the exposure with the definition of the control periods.
3) pag. 10. Defining the average concentrations of the pollutant in the 1 hours prior to each symptom "lag hour 0" seems to me misleading.

4) pag. 10. "The IQRs used to scale effect estimates were the IQRs of the pollutant specific lag times, from the control periods during the entire study years (2005-2016)". This statement is not clear. Did the authors use only the control periods to calculate the IQRs? Is there a reason for this?

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