Reviewer’s report

Title: The association between daily concentrations of air pollution and visits to a psychiatric emergency unit: A case-crossover study

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Reviewer: Marc Weisskopf

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Review of Oudin et al.

This is a generally well done analysis of the association between air pollutants and psychiatric emergency room visits. This is an important topic and one that needs more analyses such as these. I have a few points to address, though:

Major points:

1) In "Materials and Methods: Data": The authors mention that a minority of the psychiatric emergency visits are for things like prescription refills rather than emergencies. This is a very important point as too many of these kinds of visits could raise the possibility that associations are not specific for emergencies. Is there any actual data on how many are this kind of thing? That should be reported, and even possibly a sensitivity analysis done to show what kind of effect size there would be if all the effect was on these kinds of visits rather than true psychiatric emergencies.

2) In the second paragraph of the discussion, there is a section on the possible problems with exposure misclassification. I don't believe the arguments being made are quite correct. The error that is being described is in how well the monitor data predicts the actual personal exposure. In this scenario, the personal exposure is a collider (in Directed Acyclic Graph terminology) between the monitor exposure measure and personal behaviors like how much time one spends indoors vs. outdoors. In this case those personal behaviors cannot confound the estimate of monitor exposure levels. Measurement error (how well the monitor level predicts personal exposure) can lead to a reduction in the effect estimate for the monitor levels (assuming the effect is through personal exposure), but only if there is actually a true association between personal exposure and the outcome, and the bias will be towards the null (see Weisskopf et al., Curr Environ Health Reports, 2015 and Weisskopf and Webster, Epidemiology, 2017 for related issues).

The story is a little different if monitor levels of the pollutants affect behavior. This could then be a "non-biological" way the pollutant affects the outcome. If pollutants are really related to the
outcome, and if high monitor air pollution leads people to stay inside (and so not have as much actual exposure), then the association could flip with higher levels looking protective. But it couldn't create a false positive association since if there was no real association, then how well the monitor levels predict personal exposures is irrelevant as there is no effect of personal exposure. (There is the theoretical possibility that it could inflate a real association, but only if lower monitor pollutant levels made people stay inside more than higher pollutant levels and that seems unlikely).

If the argument is that monitor levels of pollutants affect whether people go to the emergency room, and so become a case (for reasons other than a true effect of the pollutant on biology leading to case status), then one could get a false positive association if high monitor pollution days were associated with people going to the emergency room more than on low pollution days. This could occur by simple confounding of the monitor pollutant level. And the authors have attempted to address this by adjusting for things like temperature and other pollutants. Maybe there are things like that that they have missed, but this falls under the category of residual confounding. If high pollutant levels at the monitor somehow directly led to people going to the emergency room (by some means other than a biological effect of the pollutant leading to mental health issues), then a positive association would be seen. I suppose this could be mentioned, but at the same time pointing out that this seems unlikely would seem warranted to me.

A bias away from the null could occur if there was an overestimate of pollutant levels at the monitor on days with more emergency visits than on days with fewer emergency visits, but that seems very far-fetched.

In sum, I think measurement error could not produce a false association unless somehow monitor pollutant levels were overestimated on emergency room visit days (or underestimated on control days, which seems far-fetched to me). Bias from personal behavior (not driven directly by the monitor level of the pollutant—or something confounding it) should not account for the finding based on arguments similar to those in the papers mentioned above. That residual confounding—perhaps most likely by some other pollutant—could account for the association is certainly possible and should be mentioned (but it would have to be by something that varies on the order of weeks). But I think as this is currently written in the manuscript incorrectly calls more question into the results than is warranted.

Minor points:

1) Abstract, results: In the last sentence, indicate that "during winter" applies to the PM results.

2) Something is wrong with the wording of the third sentence of the "Psychiatric emergency visit (PEV) data" section.
3) Statistical methods: It is stated that four control days per PEV were used, selected as the other same days of the week within the same month. But what if the PEV day was in a month with only four of those days? Wouldn't there be many cases of only 3 control days?

4) Results: Please also show pollutant levels by season, since some of what you do is specific to season.

5) Discussion: the second paragraph is extremely long and contains many points. This could be broken into more paragraphs.

6) Discussion 2nd paragraph: The sentence that begins "A strength of time-series…" later should read: "…, is that the risk OF residual confounding from TIME IN Variant individual…"

7) Same paragraph sentence beginning "However, there could…": Since control days are from within the same month as the PEV day, how could season possibly still confound? Meteorological yes, but only those that vary on a weekly basis.

8) Further down in the same paragraph the discussion of the seasonal differences: another possibility is that the dose-response is not linear and one is at a different place on the dose-response curve in winter and summer. It seems a little unlikely that exposures are higher in the summer, but this is why showing pollutant levels by season in the results is important.

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