Reviewer’s report

Title: Short-term effects of ambient particulates and gaseous pollutants on the incidence of transient ischaemic attack and minor stroke: a case-crossover study

Version: 1 Date: 25 January 2012

Reviewer: Julie Johnson

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Major Compulsory Revisions

• A line or two discussing the clinical difference between TIA and ischemic stroke in the Introduction section is needed for those unfamiliar with stroke classification.

• References 4 and 5 specifically reported results on the short-term effects of ambient pollution on TIA and mild stroke. These results should be mentioned in the Introduction section and used to compare/contrast against this study’s results in the Discussion section.

• If the patient database does permit identification of recurrent strokes, it is advisable to remove them.

• In the 1st paragraph of the Methods section, does “emergency unit” patients refer to those who presented to hospital emergency departments with stroke? Were “stroke unit” patients transferred from an ED? What needs to be clarified is: Could the same individual be included once as an ED patient and again as a stroke unit patient?

  o Similarly, if a TIA patient has been admitted to a stroke unit, is it possible they could also be enrolled in a TIA clinic? Are the databases compatible in the sense that they would allow you to identify duplicate entries for the same individual? If so, and if there are duplicate entries, they should be removed.

• Was there only one monitoring station in each city? Was everyone in the city, regardless of their postal address assigned the same pollutant level on case and control days if their stroke admission date or onset date were the same? If so, this should be noted in the Discussion section as a considerable limitation due to the inability to capture the spatial variability of some pollutants.

• The differences in mean and distribution of pollutant levels are commonly reported in this field, but as Kunzli and Schindler pointed out (J Epidemiol Community Health, 2005; 59:527-530), these are merely indications of the levels over the whole study time period, which is not the unit of comparison in case-crossover studies. What matters in the case-crossover study is the average and distribution of the differences between case and control periods. In the Discussion section of this study, the authors comment on the differences in baseline pollution between the 2 cities (which is interesting and could potentially be a valid reason for conducting separate analyses); however, it is imprecise and possibly incorrect to suggest, even indirectly, that this might be due to the higher
baseline level of NO in Manchester. If the mean and distribution of the

differences between case and control days are shown in the Results section and

are, in fact, greater in Manchester than they are in Liverpool, then you have a

stronger argument.

• Although the OR in lag 3 shown in Table 4 for PM10 was marginally

non-significant, it is interesting and noteworthy that the percent increase in risk

(12%) is actually twice that of NO (6%). Given a slightly larger sample size, one

might see this become a more important finding. (According to Witte et al, the

increase in sample size required to maintain sufficient power in analyses with

additional comparisons is not as much as you might think {Stat Med, 2000;

19:369-372})

• Exact p values used along with criteria for statistical significance at # = 0.05 are

not as informative as the point estimate of the OR and the 95% CI, which reflect

the magnitude of association. In Table 4, the p values detract from the

information presented and can mislead the reader. (See Chapter 10, Modern

Epidemiology, 3rd Edition, Rothman, Greenland, Lash, 2008; Lippincott Williams

and Wilkins)

• The Discussion section statement “In the main model, a total of 48 regressions

were performed and with a conventional 5% significance level, one would expect

2 to 3 effect estimates that would have occurred by chance” needs to be clarified.

Minor Essential Revisions

• Reference 2 is not a study of short-term effect. Reference 9 is specifically

looking at effects on stroke recurrence, which is based on a defined population

(more susceptible to stroke) that is different than a first-stroke population and

should be removed.

• The first sentence of the 3rd paragraph in the Introduction section does not read

smoothly. Perhaps, if consistent with the intention of the original sentence, the

following would be better: “There have been a number of studies that have

suggested an association between ambient air pollutants and stroke morbidity

and mortality [], while others have suggested this association does not exist []

More importantly, there are more recent studies in less-polluted regions than the

studies included in the citations listed. For example, Ren et al. (Env Health, 2010;

9:3) and O’Donnell et al. (Epidemiol, 2011; 22:422-431).

• What is meant by “accident and emergency and stroke units” in the first

paragraph in the Methods section? Why would accident patients be included in

this study? Is this confusion simply due to the label – if so, please clarify.

• Diagnostic criteria or clinical guidelines used by the stroke neurologists to

classify TIA in the study would be informative in the Methods section.

• Caution against citing studies of long-term effects in the Discussion section.

The present study is one of short-term effects. There are physiological and

epidemiological differences between long and short term effects. These studies,

therefore, should not be pooled without distinguishing them.

• There are inconsistencies in the formatting used in the reference list.
Discretionary Revisions

• If the authors are aware of reasons for why air pollution effects on TIA has been apparently ignored in the scientific literature (relative to acute ischemic strokes), the reasons might be of value to the reader of the Introduction section.

**Level of interest:** An article of importance in its field

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

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.