Author's response to reviews

Title: Meteorologically estimated exposure but not distance predicts asthma symptoms in schoolchildren in the environs of a petrochemical refinery: a cross-sectional study

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Author's response to reviews: see over
Reviewer: Nilsa I Loyo-Berrios

Major Compulsory Revisions

1. There is need for discussion on the cross-sectional nature of the study and how it limits the interpretation of the study results.

The point is taken. Since the exposures and outcomes are being measured at the same time, over-reporting is a likely bias in a “sensitised” community. This is dealt with in the Discussion.

2. Children spend most of the time at school. A discussion as to why residence was used instead of school location is also needed.

In fact, we calculate that they spend 35 hours a week over approximately 40 weeks in the year, i.e. only about 16% of the annual hours at school.

3. A high proportion of smoking is reported among adults (64.2%) and among the kids themselves (53.8%). Was the prevalence of smoking in the comparison area as high? Paper needs to include more detailed discussion as to how smoking prevalence, not only among adults in the households, but also among the kids, affect the study results.

Active smoking at this age is most likely to be “trying it out” rather than serious smoking. However, we have analysed active smoking as a potential confounder of the associations in Table 3 and found no associations with the symptom outcomes. We do not have comparable active smoking prevalences from control areas. We have stated that some of the difference between the study area and control areas could be due to confounding.

4. Authors state it was not possible to measure pollutants for the study, yet later on include in the discussion air pollution data (SO2 and PM) from a station nearby the refinery. Why were these data (actual measurements of pollutants) not included in the analysis?

These are area data which cannot be used for personal exposure assignment. Citywide data are too sparse to permit of small area population comparisons. We have included some illustrative monthly means in the discussion.

5. A statement of public health practice is needed. They conclude the study provide evidence that correlates the exposure measure with the outcome, yet no recommendations as to what should be done to protect the children from having recurrent symptoms is not provided.

Over the past two decades, there have many processes involving residents, the refinery in question and the local air quality authorities aimed at improving air quality in this area. This study was designed to ask the question about whether health effects could be identified and measured. This we believe the paper has done within the limitations of the available resources. Discussion of local control activities, of which there are many, is we believe beyond the scope of the paper. However, the concept of wind adjusted distance as a measure could be of value to epidemiological practice.

Minor Essential Revisions

There are several typos that need to be corrected. We have gone through the manuscript carefully to remove typos.
Reviewer: Fernando A Wichmann

Reviewer's report:

This paper provides an interesting report on environmental exposure in a city in South Africa, and shows that meteorologically exposure but not distance predicts asthma symptoms in schoolchildren near petrochemical refinery.

Although the study was well performed and is consistent in itself, there are a few issues that require further attention, as follows:

Discretionary Revisions

1. In the Abstract the background is not clear and in results, can you include more data? For example how much symptoms, etc.

We have adjusted the last sentence of the Background paragraph in the abstract, which we hope will make it clearer.

We have included more data in the Results section of the abstract.

2. Discussion: What was the definition of “Proximity to a busy road” A standard definition is living within 50 meters of a busy highway, but this is not specified.

We analysed distance as a numeric variable. We thus did not specify a cut-off.
Reviewer: Joachim Heinrich

Reviewer's report:

Obviously there is severe public concern about whether emissions from petrol chemical refinery might cause asthma exacerbation and asthma development in particular in children in Cape town, South Africa. This study is an attempt to collect data which could be used to support or reject this public health concern.

The authors used GIS based distance data to the point source of the petrochemical refinery and in additional meteorological trajectories which are mainly based on wind direction and wind speed. These two approaches lead to individualized exposure assessment although they have clear limitations. However, these exposure surrogates have the great advantage to be intuitive, easily feasible and cheap compared to a large spatial measurement program. This paper has a limitation that no air pollution data was used. Nevertheless, the results of this study could be used to reject or to support the idea, that emissions from a petrochemical refinery might be harmful for respiratory tract in children. The paper is well written, but has several severe limitations which could be avoided by a modified data analyses.

Major

1. The title of the paper and the key finding seems to support the notion that the meteorological derived trajectories are more important than a simple distance to the point source. This notion is mainly derived from the results of table 3. This conclusion from table 3 is not correct because the effect sizes in table 3 are related to an increment of one for each of the two exposure metrics. This is not fair to compare an increment of one mile or one km with an increment of a unit of 1 for the meteorologically estimated exposure. The effect estimates should be expressed here as inter-quartile range effects. This might have a strong effect of the general conclusion of the paper and also the title needs to be eventually rephrased.

This point is well taken and we have re-analysed after standardising by interquartile range. The conclusions are unchanged.

2. A second major concern is related that the results are not adjusted for socio economic status. This potential confounding factor is extremely important and needs to be included in the study and if the authors do not have data on the socio economic status their finding is strongly devaluated and this needs a cautious discussion.

This is now clarified in the paper. Of the 17 schools, 15 were high (in South African terms) SES (formerly “white” schools) and two were low SES (children from informal settlements or low income formal housing area). Given the homogeneity of SES across this sample, it is highly unlikely that the findings in Table 3 could be explained by confounding by SES. Nevertheless, the analysis in that table was repeated omitting the two low SES schools, with no change in the results. This is stated in the text rather than repeated as a table.

Regarding the comparison with the control areas, only the higher SES areas were included in the control group, effectively “matching” the study population with the control population on this variable.
3. Although no spatial data on ambient air pollution is obviously available, the reader wants to know first which specific air pollutants might be emitted by petrochemical refinery on the bases of the literature and the current knowledge.

This section has been moved from the Discussion to the Introduction.

Further more, any data on the annual average of the criteria air pollutants in that area might help the reader to evaluate the health problem. The given exceedance fraction of certain limits of ambient air pollutants is not sufficient. The reader wants to know at least a few annual means of ambient air pollutants.

We have now provided monthly means (only these are available) for SO$_2$ and PM$_{10}$ in the discussion. Given the low average values for SO$_2$, which was the pollutant of concern, we have suggested that it is short term peaks that may be the source of the complaints in the area. We have commented on particulates.

4. The paper contains data on three questions in the current version. One is related to the question whether living close to the petrochemical refinery is associated with an increased risk of asthma, the second question whether children of the refinery area have a similar prevalence of asthma compared to other areas of Cape Town, and the third question is related to temporal changes of asthma prevalence in that area. The paper would be strengthened if the authors could restrict themselves to the first question. This would also improve the readability of this paper. Time trends in prevalence of asthma are not an issue here, so far the emissions of the petrochemical refinery is constant over the time. The data to answer question 2 seems to be poor because the data are not adjusted (see table 4).

Only the first two questions mentioned by the reviewer are the subject of the paper. We considered the reviewer’s recommendation to drop the cross-Cape Town comparison. However, later in the review, the reviewer suggests including some comparative data from elsewhere in South Africa. Comparison with other areas of Cape Town was a question of importance to the community representatives as a first step in deciding whether the community concern was real. We also believe that dropping the cross-Cape Town comparison weakens the inference that the refinery is the point source, limiting the argument to a purely “internal” comparison of those pupils living downwind from the refinery with those not. We have thus retained the cross-Cape Town objective and comparison. The comparison is inherently adjusted for age and socioeconomic status which we believe is sufficient to make inferences.

**Minor**

5. Abstract

The abstract needs a revision recording to the previous major comments.

Done.

6. The background could provide at least a few data on those ambient air pollutants which are probably highly emitted by a petrochemical refinery.

The description of possible refinery emissions has been moved from the Discussion to the Introduction.
Also some data on the area in terms of the size, the geography and average ambient air pollution levels including meteorological data would be informative.

Data on size and a sense of geography can be obtained from Figure 1. We have added a description of meteorology to the Methods text. Some mean ambient levels are now included in the Discussion.

The last part of the section three and the section 4 would be better placed in the methods chapter. The last section of ‘background’ is mostly a repetition of that what was written before.

These paragraphs have been trimmed or moved to Methods.

The background chapter could be started with a reference of several other epidemiological studies which analysed potential health effects of industrial emissions by living close to point source with epidemiological methods. There are several studies published in the peer reviewed literature which are ignored.

A number of studies related to point sources/industrial emissions are now included and referenced.

The author also could draw conclusion whether their approach revealed as a promising approach in previously published papers.

The particular model used here is novel. There is one study we could find of children in relation to point sources that adjusted for wind (Loyo-Berrios 2007) - this is now mentioned and referenced in the Discussion.

7. Methods

Last sentence on p. 4: In how many cases a GIS match could not be made? The numbers should be given here.

86 could not be geocoded. This is now reflected in the text.

P. 5, 2nd section: meteorological data which were used for deriving the trajectories are based to the year prior the study. Is there any temporal variation of meteorological data from year to year in the study area? If this is the case, the authors should have better used average of meteorological data for more than 1 year.

While there is month to month variation, wind patterns are generally stable from year to year in Cape Town. The point is taken regarding annual variation which is a feature of all weather patterns. It should be noted that such variation would have introduced non-differential misclassification in exposure which would have reduced any observed association between MEE and symptom prevalences.

The entire methods chapter should be more strictly organised following the following substructure: study subjects and design, outcome measures, exposure assessment approaches, and statistics.

Subheadings have been inserted.
8. Results

_1st section of the chapter results contains data on inclusion/exclusion criteria. This criteria needs to be mentioned in the method section._

As the exclusion criteria follow logically from the study design, we believe it would be repetitive to mention them in the Methods section as well as under Results.

_P. 7, 2nd section:_ Obviously the association with several health outcomes are rather inconsistent. Do the authors have any idea about the reasons for these inconsistencies? These inconsistencies should also be discussed.

There is reasonable consistency (at least in direction) with regard to the ISAAC video outcomes (Table 3), which we believe are less susceptible to reporting bias than outcomes based on the written questionnaire such as wheezing and asthma. This point is now made in the Discussion.

_P. 8, 1st section:_ What was the reason to combine objective and subjective measure for living close to a busy road?

We have dropped the subjective variable as it did not add anything to the findings.

_How do both estimates correlate?_

(The Spearman correlation coefficient was 0.19).

_Are there any associations between living close to major road estimated by questionnaire or a GIS based distances with any of the health outcomes?_

A few symptoms were related to distance from a major road as now indicated in the text on the univariate analysis.

_Traffic as a potential further source of the exposure of ambient air pollutants needs a much more cautious analyses and data needs also to be presented here._

Traffic related pollution, particularly particulates, is citywide and not localised. We have now adjusted the multivariate analysis for objective distance from a major road. A previous source apportionment study did not find elevated PM2.5 levels in the study area. This is now stated and referenced in the Discussion.

_Section 2 and 3 on p. 8 need a revision according to the revised statistical analyses using the inter-quartile range increments._

This has been done as stated above.

_Section 4 and 5 on p. 8 and 1 and 2 on p. 9 were suggested to be cancelled._

As above.

_Did the authors make any attempt to study the type of the association? Are the reported associations between the exposure estimates and the health outcomes linear?_
We did, via LOESS smoothing, which showed a non-linear association between the video symptom outcomes and MEE. However, this technique does not adjust for confounding and we believe that the extra description and figure(s) would complicate and lengthen the paper beyond what is desirable.

9. Discussion

The 3rd section on p. 9 together with the last section on p. 9 could be summarized and shortened.

Since we have elected to retain the analysis comparing the study area to other areas in Cape Town, these paragraphs are needed to discuss the limitations of this comparison.

The 4th section on p. 9 could be deleted because it is a very general statement and did not substantially add to understand and to interpret the results.

Especially in light of the reviewer’s concerns about the wind adjustment formula, we feel that a more “ordinary language” explanation of the formula would be of assistance to readers and we have thus retained it.

2nd section on p. 10 needs a revision.

The reviewer has not specified what needs revision.

3rd section on p. 10 did not reference recent papers on ambient air pollution and the development on asthma.

This has been done.

4th section on p. 10: Atopy was considered as a potential confounding factor ignoring that the onset of parental atopy might be also associated with living close to the refinery. In addition parental atopy is a strong risk factor for the onset of asthma in the off-spring and is part of the causal chain. It needs a more cautious analyses. A sensitivity analyses stratifying for those children whose parents have and have not an atopy would be one option.

We can’t see how family (parental) atopy could be a mediator. The causal chain would be refinery exposure → expression of parental atopy, but parental genotype → expression of atopy in offspring. This is not a complete causal chain. Parental atopy might be an effect measure modifier, but that is a separate (although not uninteresting) question which we did not pursue within the limited space available. It would not alter the conclusions.

In addition, as written previously the socio-economic status is a potentially major confounder.

This is dealt with above.

P. 11, 1st section could be substantially shortened.

This paragraph is needed to explain the potentially important role of pollen as an aeroallergen.

2nd section needs to be moved to the beginning.
Done.

3rd and 4th section could be better placed together with a few annual data on ambient air pollutants in the background chapter.

The 3rd paragraph has been moved to the Introduction and some data on ambient air pollutants are included later in the Discussion.

P. 12, 1st section: Instead of exceedance frequencies a few annual means of ambient air pollutants might be more informative.

The above has been done for SO₂ and PM₁₀.

The 2nd section is more related to potential short-term effects of air pollutants which is not an issue for this paper.

On the contrary, we would argue that potential short-term effects are very much an issue for the paper.

A section on strength and limitations of the study could be added.

These are stated at various points in the Discussion and we felt it would be repetitive to restate these, lengthening the paper unnecessarily. Points already made include the possibility of over reporting, lack of direct measurements of pollutants and therefore inability to identify specific mechanisms of effect, and possible confounding by pollen. Strengths are dealt with in the Conclusion.

10. The references are not appropriate because several studies which are performed in vicinity to industrial emission sources were ignored. Also the most recent papers on the association between ambient air pollutants and the development of asthma are missing.

We have included a number of studies of asthma or respiratory symptoms in children in relation to industrial emission sources. We are aware that there is a very large literature on ambient air pollution and asthma, although asthma exacerbation rather than development of asthma has been easier to show (the latter being still controversial), as we state in the Discussion. We have included some of latest papers on this subject.

11. Table 1 and 2: the prevalence of hay fever of more than 60% seems to be extremely high. Are there other data showing that hay fever is so common in South Africa. This is also the case for the category ‘family atopy’. Also the prevalence of asthma is extremely high. Are there any prevalence data from other areas in South Africa which could be used for comparison purpose.

There are other studies from South Africa, but these differ in a number of important characteristics, such as socioeconomic status and we believe the 2002 Cape Town ISAAC study provides the most useful comparator for purposes of our hypothesis. Also, the focus was on lower and not upper respiratory symptoms.

A footnote explaining what is ever recent and frequent would be helpful.
This has been added.

Table 3: Table 3 did not report any association for hay fever and physician diagnosed asthma or use of inhalers. What is the reason for that?

Asthma inhaler use is now included. There were no association between self-reported asthma, hayfever and either MEE or distance

As previously mentioned these effect estimates should be expressed per inter-quartile range.

Done.

A footnote on recent and frequent might help the readability because each of the table should stand by itself.

Done.

Table 4 presents crude odds ratios? However, table 4 was a candidate for deletion as commented previously. A footnote on recent and frequent might help the readability because each of the table should stand by itself.

Not entirely crude, as the age and socioeconomic status ranges are the same. However, a caution regarded unmeasured has been added to the Discussion (first paragraph).

Also, a footnote has been added to the tables.

12. The formula on page 5 is not clear to me. The authors should double check whether the denominators are correct. The denominators v could be possibly better replaced with 1/v? The unit of the current formula would be s/m2, which looks strange to me.

The formula is correct. The unit expressed as s/m² (or hr/km²) is somewhat unintuitive but can be conceived of as the time that one is exposed downwind of the refinery (numerator) with the wind spread over a two-dimensional area (denominator). This measure was designed as a product of the three factors that represented the neighbourhood exposure to the refinery: wind blowing in your direction (or not) as a binary variable, distance from the refinery inversely (the closer to the refinery, the greater the exposure), and wind speed inversely (the slower the speed the less the dilution). Using time per cubed distance gave a weaker but still significant fit.

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