Author's response to reviews

Title: Incidence of cancer in the area around Amsterdam Airport Schiphol in 1988-2003: a population-based ecological study

Authors:

Otto Visser (o.visser@ikca.nl)
Joop H van Wijnen (jvwijnen@ggd.amsterdam.nl)
Flora E van Leeuwen (f.v.leeuwen@nki.nl)

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Author's response to reviews: see over
Major compulsory revisions

1. We were able to extend the period of our investigation to 2003, as reference incidence rates of the Netherlands covering 2001, 2002 and, very recently, 2003 have become available. We have redone all our analyses and, as suggested by the reviewer we now report in table 3 in three time periods (1988-1993, 1994-1998 and 1999-2003), instead of the original two time periods. As, inevitably, the SIRs slightly changed because of the extension of the study period, we have adjusted all rates in table 3 and 4 as well as in the text (abstract and results).

2. 95% confidence intervals have been included in the results section, wherever they were missing.

3. In the Discussion we have inserted in the paragraph discussing the incidence of cancer of the respiratory tract the following sentence, in order to emphasize the overall decreased incidence of these cancers: ‘As the overall incidence of cancer of the respiratory tract was decreased (SIR 0.94), this observation does not support a positive association between the airport and the occurrence of cancer of the respiratory tract.’

4. We have inserted a sentence in the Results section regarding the relatively low incidence of Hodgkin lymphoma: ‘A relatively low rate was observed for Hodgkin lymphoma (SIR 0.78, 95% CI: 0.58, 1.04)’. We have also added this observation in the discussion, but as the decreased incidence was not statistically significant this observation did not justify an extensive discussion.

5. In the Methods section, we have added several sentences explaining the core and ring zone as depicted in figure 1. In this figure we have also added the locations of the three air quality monitoring stations.

6. A sentence explaining the purpose of data on per capita income has been included in the Methods section.

Minor essential revisions

7. As the third version of ICD-O was introduced in the Netherlands Cancer Registry in 2001 and the study period was extended to 2003, the mentioning of ICD-O-3 is no longer superfluous. The sentences regarding the classification on NHL might still be confusing and we have deleted these two sentences in the Methods section.

SP

Major compulsory revisions

1. We agree with the reviewer that the definition of the study area based on noise contours may be a bit questionable, but as the available data of the air quality network did not allow us to define a study area based on elevated ambient air pollution levels, in our opinion the noise contours are the second-best solution for defining the area around the airport. We have included the following sentences in the methods section: ‘However, it is possible that exposure to aircraft emissions has been greater in the past when aircraft engines used to be technologically and ecologically less advanced. Also, we cannot exclude that certain carcinogenic compounds specific to aviation combustion have not been monitored. Since most cancers have a long induction period and the noise contours are thought to reflect best the historical exposure of the surrounding population to aircraft emissions, we continued to use the levels of aircraft noise to define our study area.’ As suggested by the reviewer, we have included a table (table 1) presenting a summary of the results of the three monitoring stations in the Schiphol area. The locations of the stations have also been indicated in figure 1.
2. We did not calculate CIs of RR values using a Poisson distribution. The way we calculated CIs of RR values has now been included in the methods section. As suggested by the reviewer, we have also included SIRs by subzone in table 4.
3. The number of cancer cases in children has been included in table 4.
4. Risk values for the specific sites of female genital organs have been added in the results section (‘cancer incidence in the core zone’).
5. Unfortunately, RR estimates adjusted for socio-economic status cannot be calculated as socio-economic levels according to postal code areas are not available. Moreover, socio-economic status is not defined by Statistics Netherlands as it is in for example the United Kingdom. A detailed analysis of the lung cancer incidence according to postal code area revealed large differences between postal code areas, but the numbers in the smaller areas were quite small. Generally only a weak association between per capita income and lung cancer incidence in males was observed within the Schiphol area. Of the larger areas, postal code area 1161 (per capita income below the average) was the main contributor to the relatively high incidence in the core zone, while in postal code areas 1082, 1181 and 2131 (per capita income above the average) the lowest incidence rates were observed (but not in 1171). As a detailed description of the results of this analysis does not shed new light upon the research question whether a relation exists between cancer incidence and residence in the Schiphol area and the results may be prone to chance findings due to small numbers, we prefer not to include this detailed information in the manuscript. In the discussion we have included the following sentence: ‘However, within the Schiphol area only a weak association was observed between the incidence of lung cancer and per capita income by postal code area (data not shown).’

Minor essential revisions
1. The bibliographic reference regarding the emissions of aircraft engines has been included.
2. Risk estimates by gender have been included in tables 3 and 4 for all selected cancer sites.

TT

Major compulsory revisions
Based on the comments of the reviewer we made a number of changes:
- We have revised the discussion according to the suggestions of the reviewer (see ‘minor essential revisions’ for the details).
- In the methods section a phrase has been added regarding the definition of the core zone and levels of air pollution. ‘We also defined a core zone for the 4-digit postal code areas within the 45 Ku contour ……. although we do not have empirical data showing that this zone corresponds to a zone with increased levels of ambient air pollution.’
- We agree with the reviewer’s comment that there was no overall excess risk and that the sites specific excess risk could not be explained by high levels of ambient air pollution. We have changed the conclusions accordingly.
- We agree with the reviewer’s conclusions regarding NHL and we have added the following sentence: ‘It therefore seems unlikely that the increased incidence of hematological malignancies is specifically related to ambient air pollution caused by aircraft emissions.’

Minor essential revisions
- Abstract
The aim of the study has been added to the background: ‘We investigated whether residents of the area around Schiphol are at higher risk of developing cancer than the general Dutch population.’
The phrase ‘, since historical data on ambient air pollution were not available and recent emission data did not differ from the background urban air quality.’ has been added to the Methods.
We agree with the conclusion as formulated by the reviewer and changed the conclusion if the abstract accordingly.

- **Background**
  A sentence addressing the aims of the study has been added at the end of the background section.

- **Methods**
  *Definition of study population and the study area*

  We have revised the methods section describing the definition of the study as follows: ‘Since 1994, the ambient air quality outside Schiphol has been monitored and no differences with the background urban air quality have been reported for the compounds that were measured [9]. Table 1 summarizes the results of the three monitoring locations in the Schiphol area. However, it is possible that exposure to aircraft emissions has been greater in the past when aircraft engines used to be technologically and ecologically less advanced. Also, we cannot exclude that certain carcinogenic compounds specific to aviation combustion have not been monitored. Since most cancers have a long induction period and the noise contours are thought to reflect best the historical exposure of the surrounding population to aircraft emissions, we continued to use the levels of aircraft noise to define our study area.’

  *Statistical methods*

  The phrase as suggested by the reviewer does not completely cover the analysis as we performed it. We have modified the phrase into:
  ‘In our analysis, the incidence of cancer among the national population of the Netherlands served as a reference entity. The expected numbers of cancer (E) for the Schiphol area were calculated for three periods (1988-1993, 1994-1998 and 1999-2003), based on the population data of the Schiphol area (according to 5-year age category and sex) and the 5-year age category and sex-specific cancer incidence rates from the Netherlands Cancer Registry. For the period 1988-1993 we used the average incidence rates of the NCR covering the period 1989-1993 [11], because data for 1988 were not available from the NCR. For the periods 1994-1998 and 1999-2003 we used NCR-data covering 1994-1998 and 1999-2003, respectively [12].’

- **Discussion**

  We have modified the first paragraph of the discussion as suggested by the reviewer. The paragraph discussing cancer of the respiratory tract has been rewritten. However, as one of the other reviewers suggested to report on cancer of the respiratory tract in more detail, we only slightly shortened the paragraph on this subject.

  Regarding the findings on hematological malignancies the following conclusion has been added: “It therefore seems more likely that the increased incidence of hematological malignancies is related to urban ambient air pollution in general than to ambient air pollution caused by aircraft emissions.”

- **Conclusion**

  The conclusion was modified in agreement with the conclusion of the abstract.