# Air Pollution Exposures and Respiratory Health in 5-Year-Old Children

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**Abstract**
Background: Growing evidence indicates that respiratory health in children is related to air pollution. Most of previous studies rely on residential air pollution estimates to represent individual exposure; however, there is evidence that residential estimates tend to misclassify exposure. Aim: This study aims to assess the relations between air pollution exposures and respiratory health (asthma, wheezing and lung function) by applying a sophisticated exposure assessment technique. Methods: The study relies on a Dutch cohort and includes 733 children. The prevalence of asthma and wheezing and the spirometry measurements were determined at the age of 5. The annual average concentration maps of Particulate Matters and Nitrogen Oxides that we used in the study were derived from the European Study of Cohorts for Air Pollution Effects. To assess individualized air pollution exposures an updated exposure assessment technique was applied. Results: This study did not show significant associations between air pollution exposures and the studied health outcomes in the 5-year olds. For example, after adjusting for possible confounders, the ORs were 1.2 (95% CI: 0.86, 1.61) and 1.2 (95% CI: 0.87, 1.64) for wheezing prevalence for $NO_x$ and $PM_{2.5}$ respectively.
**Keywords:** air pollution, exposure assessment, asthma, wheezing, lung function, children

## 1. Introduction

Air pollution may be related to as many as 4.2 million premature deaths globally in 2016 (World Health Organization, 2018). Many studies suggest an association between air pollution and respiratory health (Bowatte et al., 2015). Often the methodology applied to estimate air pollution exposures is based on air pollution (point) estimates at the front door of individuals' home locations. However, this cannot be representative for the true exposure because humans are not static and do not spend their entire day at a fixed location (Dijst, 2009). We set out to determine the relation between air pollution exposures and respiratory health by applying a novel methodology which incorporates the daily activities of the 5-year old children.

## 2. Title Subjects and Methods

### *2.1. TitleStudy Population*

We used The Wheezing Illness Study Leidsche Rijn (WHISTLER) which is an ongoing population based, prospective birth cohort (Katier et al., 2004). The study participants mainly live in Leidsche Rijn, which is a 25 $km^2$ residential area in Utrecht Municipality, the Netherlands. The markers we used are: wheezing at any point in life (ever), wheezing the last 12 months, asthma at any point in life (ever), asthma the last 12 months, forced expiratory volume in 0.5 sec ($FEV_{0.5}$), peak expiratory flow (PEF) and forced vital capacity (FVC).

### *2.2. Individualized air pollution exposures*

To assess long-term air pollution levels we used land use regression (LUR) models which were originally developed in the European Study of Cohorts for Air Pollution Effects (ESCAPE) project (Eeftens et al., 2012). The models enable to retrieve the annual average concentrations of the air pollutants at any location in the study area, including $PM_{10}$, $PM_{2.5}$, $PM_{2.5absorbance}$, $NO_x$ and $NO_2$ for the year 2009.

Instead of using the conventional residential air pollution concentration we applied a novel technique to calculate the individualized exposures. The technique defines individual air pollution exposure as the time-weighted air pollution concentration for each activity place visited by each child as described in a previous study (Ntarladima, et al., 2019). As primary activities we used: being at home, playing in the neighbourhood, travelling to/from school or other destinations, and being at school.

*2.3. Statistical analyses*

We fitted models for all dependent variables (asthma, wheezing, $FEV_{0.5}$, PEF, and FVC) and for all individualized exposures ($PM_{10}$, $PM_{2.5}$, $PM_{2.5absorbance}$, $NO_x$ and $NO_2$). We applied logistic regression to obtain odds ratios (OR) and the 95% confidence interval (CI) of the associations between the air pollutants and the dichotomous health variables (asthma, wheezing) and linear regression to obtain the associations between the air pollutants and the continuous health variables ($FEV_{0.5}$, PEF, FVC). We adjusted for possible confounders (sex, age, height, mother smoking during pregnancy, exposure to second hand smoke, parental asthma and parental SES) in an increasing way.

**Table 1.** Whistler cohort characteristics

| Child Characteristic | n(%) or mean (SD) | NA* |
|---|---|---|
| Sex = girllrs | 376(51.3) | 0 |
| Age (years) | 5.42 (0.35) | 0 |
| Height (cm) | 115.0 (4.8) | 117 |
| Asthma, ever | 72 ( 9.8) | 0 |
| Asthma, last 12 months | 45 ( 6.3) | 23 |
| Wheezing, ever | 200 (27.2) | 0 |
| Wheezing, last 12 months | 61 (19.1) | 415 |
| $FEV_{0.5}$ ($L^{-1}$/0.5sec) | 1.01 (0.28) | 37 |
| PEF (L/sec) | 2.84 (0.67) | 37 |
| FVC (L) | 1.36 (0.44) | 37 |
| **Air Pollution Exposures** | | |
| $NO_2$ ($\mu g/m^3$) | 29.47 (2.08) | 0 |
| $NO_x$ ($\mu g/m^3$) | 35.34 (6.17) | 0 |
| $PM_{2.5}$ ($\mu g/m^3$) | 16.71 (0.24) | 0 |
| $PM_{10}$ ($\mu g/m^3$) | 25.03 (0.60) | 0 |
| $PM_{2.5\ absorbance}$ ($10^{-5}$/m) | 1.32 (0.09) | 0 |

*NA: Not Available

## 3. Results

The characteristics of the children included in the WHISTLER cohort are presented in Table 1. Nearly all studied air pollution exposures were not associated with the health variables neither before nor after adjustment for individual confounders. For example, the odds ratios for the wheezing the last 12 months were between 1.00 and 1.20 but not significantly associated; (95% CI: 0.87, 1.64).

## 4. Discussions and Conclusions

Although a large body of studies observed associations between respiratory health and either all or some of the tested air pollutants (Bowatte et al., 2015), in this study we do not observe associations. Similarly to our findings more studies did not find associations between air pollution and asthma/wheezing (Hirsch et al., 1999; Mölter et al., 2014). Additionally, we have also found associations with cardiovascular outcomes (carotid distensibility) by using the aforementioned methodology in the same cohort (Ntarladima, et al., 2019).

The overall insignificant associations can be attributed to the moderate levels of exposures compared to other European countries (Eeftens et al., 2012) and the young age of the children (5-years). Finally, there was low spatial variation of exposures especially for $PM_{2.5}$ and $PM_{10}$ within the study area.

**References**

Bowatte, G., Lodge, C., Lowe, A. J., Erbas, B., Perret, J., Abramson, M. J., … Dharmage, S. C. (2015). The influence of childhood traffic-related air pollution exposure on asthma, allergy and sensitization: a systematic review and a meta-analysis of birth cohort studies. *Allergy*, *70*(3), 245–256. https://doi.org/10.1111/all.12561

Dijst, M. (2009). Time Geographic Analysis. *International Encyclopedia of Human Geography*, 266–278. https://doi.org/10.1016/B978-008044910-4.00548-4

Eeftens, M., Tsai, M. Y., Ampe, C., Anwander, B., Beelen, R., Bellander, T., … Hoek, G. (2012). Spatial variation of PM2.5, PM10, PM2.5 absorbance and PMcoarse concentrations between and within 20 European study areas and the relationship with NO2 - Results of the ESCAPE project. *Atmospheric Environment*, *62*, 303–317. https://doi.org/10.1016/j.atmosenv.2012.08.038

Hirsch, T., Weiland, S. K., von Mutius, E., Safeca, A. F., Gräfe, H., Csaplovics, E., … Leupold, W. (1999). Inner city air pollution and respiratory health and atopy in children. *The European Respiratory Journal*, *14*(3), 669–677. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10543291

Katier, N., Uiterwaal, C. S. P. M., De Jong, B. M., Kimpen, J. L. L., Verheij, T. J., Grobbee, D. E., … Van Der Ent, C. K. (2004). The Wheezing Illnesses Study Leidsche Rijn (WHISTLER): Rationale and design. *European Journal of Epidemiology*, *19*(9), 895–903. https://doi.org/10.1023/B:EJEP.0000040530.98310.0c

Mölter, A., Agius, R., de Vocht, F., Lindley, S., Gerrard, W., Custovic, A., & Simpson, A. (2014). Effects of long-term exposure to PM10 and NO2 on asthma and wheeze in a prospective birth cohort. *Journal of Epidemiology and Community Health*, *68*(1), 21–28. https://doi.org/10.1136/jech-2013-202681

Ntarladima, A.-M., Vaartjes, I., Grobbee, D. E., Dijst, M., Schmitz, O., Uiterwaal, C., … Karssenberg, D. (2019). Relations between air pollution and vascular development in 5-year old children: a cross-sectional study in the Netherlands. *Environmental Health*, *18*(1), 50. https://doi.org/10.1186/s12940-019-0487-1

World Health Organization. (2018). *Burden of disease from ambient air pollution for 2016* (Vol. Version 2). Geneva. Retrieved from https://www.who.int/airpollution/data/AAP_BoD_results_May2018_final.pdf