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Beyond the Runway: Respiratory health effects of ultrafine particles from aviation in children

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ABSTRACT

Aviation has been shown to cause high particle number concentrations (PNC) in areas surrounding major airports. Particle size distribution and composition differ from motorized traffic. The objective was to study short-term effects of aviation-related UFP on respiratory health in children.

In 2017–2018 a study was conducted in a school panel of 7–11 year old children (n = 161) living North and South of Schiphol Airport. Weekly supervised spirometry and exhaled nitric oxide (eNO) measurements were executed. The school panel, and an additional group of asthmatic children (n = 19), performed daily spirometry tests at home and recorded respiratory symptoms. Hourly concentrations of various size fractions of PNC and black carbon (BC) were measured at three school yards. Concentrations of aviation-related particles were estimated at the residential addresses using a dispersion model. Linear and logistic mixed models were used to investigate associations between daily air pollutant concentrations and respiratory health.

PNC20, a proxy for aviation-related UFP, was virtually uncorrelated with BC and PNC50-100 (reflecting primarily motorized traffic), supporting the feasibility of separating PNC from aviation and other combustion sources. No consistent associations were found between various pollutants and supervised spirometry and eNO. Major air pollutants were significantly associated with an increase in various respiratory symptoms. Odds Ratios for previous day PNC20 per 3,598pt/cm³ were 1.13 (95%CI 1.02; 1.24) for bronchodilator use and 1.14 (95%CI 1.03; 1.26) for wheeze. Modelled aviation-related UFP at the residential addresses was also positively associated with these symptoms, corroborating the PNC20 findings. PNC20 was not associated with daily lung function, but PNC50-100 and BC were negatively associated with FEV1.

PNC of different sizes indicative of aviation and other combustion sources were independently associated with an increase of respiratory symptoms and bronchodilator use in children living near a major airport. No consistent associations between aviation-related UFP with lung function was observed.

1. Introduction

Numerous studies have found associations between exposure to atmospheric aerosols and adverse health effects (Juginović, 2021; Yazdi, 2021; Kappos, 2004; Kurt et al., 2016). Particulate matter (PM) is often classified by its aerodynamic diameter. Health effects associated with mass concentrations have been well characterized. However, particles with an aerodynamic diameter <100 nm, also known as PM0.1 or ultrafine particles (UFP), are not well represented by the mass measurements of fine (<2.5 μ m; PM2.5) and coarse (<10 μ m; PM10) PM. Moreover, UFP have a higher surface area-to-mass ratio, exacerbating potential carrier-effects, they can penetrate deeper into the lungs and

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some studies found them able to cross the lung-blood barrier (Schraufnagel, 2020; Lammers, 2020; Geiser, 2005).

UFP can be generated from (incomplete) combustion, including sources such as road traffic, shipping, industrial sources, and aircrafts (Geiser, 2005). Previously, many studies focused on roadway vehicle emissions as a major source of UFP exposure. Recent studies have shown that aircrafts form a significant source of UFP as well (Keuken, 2015; Keuken et al., 2015; Keuken et al., 2010; Bezemer, et al., 2015; Hsu, 2013; Hudda, 2014; Hudda, 2018; Westerdahl, 2008; Austin, 2021; Zhu, 2011; Choi, 2013; Abdillah and Wang, 2022; Stacey et al., 2021; Stacey, 2019). Airports are often built in the vicinities of cities and both the number of passengers and the number of total flights have been increasing steadily over the past 25 years (period before COVID-19; 1993 – 2018) (Maandelijkse Verkeer Vervoer cijfers, 1992).

Multiple studies observed and confirmed elevated levels of UFP in the vicinity of Amsterdam's Schiphol Airport, up to 7 km downwind, with an average increase in UFP from Schiphol of 4,500pt/cm³ (Keuken, 2015; Keuken et al., 2015; Bezemer, et al., 2015). Monitoring campaigns near other airports have also found increased UFP levels due to aircraft engine exhaust emissions even at longer distances and wider areas (Hsu, 2013; Hudda, 2014; Hudda, 2018; Westerdahl, 2008). Airport emissions seem to affect a larger area compared with traffic-exhaust sources, with less sharp gradients with distance to the source. Both traffic and aircraft emissions are characterized by local increases in carbon dioxide (CO₂), nitrogen oxides (NO_x), volatile organic compounds and (PM bound) polycyclic-aromatic hydrocarbons. Aircraft emissions are further characterized by increased levels of sulfuric acid and relatively low levels of black carbon (BC), compared to road traffic particles (Westerdahl, 2008; Austin, 2021; Zhu, 2011; Choi, 2013; Kapadia, 2016). Moreover, both Keuken et al. (2015) and Austin et al. (2021) concluded that UFP released from aviation are dominated by particles between 10 - 20 nm, whereas e.g. road traffic particle sizes are predominantly >50 nm (Keuken et al., 2015; Austin, 2021). This distinction in particle size has also been concluded in a review by Stacey et al. (2019) (Stacey, 2019).

The significance of these elevated UFP levels for the health of local residents remains unclear, as little is yet known about the health effects of aviation-related UFP. A study executed by Habre et al. (2018) observed short-term increased levels of systemic inflammation in healthy adults following mild walking activity inside a high aviationrelated UFP zone, compared with outside the high UFP zone (Habre, 2018). In a study by Lammers et al. (2020) healthy volunteers were repeatedly exposed for 5 hr. to ambient air near Schiphol Airport, which resulted in a short-term decrease in lung function and prolonged QTc interval associated with UFP <20 nm, but not particles >50 nm (Lammers, 2020). Moreover, He et al. (2020) exposed human bronchial epithelial cells for 24 hrs. to low dose UFPs collected from mainly aviation- or road traffic emissions and an aircraft turbine engine. All exposures were related with a decrease in cell viability and the release of inflammatory markers. This was also observed by an earlier study, during which human bronchial epithelial cells were exposed for 4 hrs. to PM_{0.25} collected at Los Angeles International Airport, a central Los Angeles site (campus) and PM2.5 directly from turbine and diesel engines. All samples were related to an increase in relative reactive oxygen species (ROS) activity, but turbine samples showed overall a greater effect on ROS induction compared to diesel samples (He, 2018).

Using a dispersion model, Keuken et al. (2015) assessed that in total more than 555,000 addresses were exposed to elevated UFP levels, with over 60,000 addresses exposed to an additional short-term particle number concentration (PNC) of 10,000–15,000pt/cm³, originating from Schiphol Airport (Keuken, 2015). Therefore, additional research is needed to get more insight into the extent to which aviation-related UFP contribute to health effects, taking into account other urban sources of UFP, especially motorized road traffic (Bezemer, et al., 2015). The objective of the current study was to investigate daily changes in spirometry, exhaled nitric oxide (eNO), a variety of respiratory symptoms and bronchodilator medication use in association with daily UFP

concentrations in general and UFP from airplane emissions specifically, in children aged 7–11 year. The study was conducted as part of an integrated research program on the health effects of UFP around Schiphol Airport.

2. Methods

2.1. Study design

We conducted a panel study with repeated measurements of respiratory health in two panels of primary school children living in the vicinity of Schiphol Airport. The study was conducted with children, because children are a sensitive subgroup of the population with respect to air pollution effects. Increased sensitivity compared to adults is due to a combination of increased time spent exercising outside, high ventilation rates per body weight, developing lungs and immature metabolic pathways (Guarnieri and Balmes, 2014; Goldizen et al., 2016; Heinzerling et al., 2016). Moreover, a large societal interest exists in the potential health effects within children. Children are also a very suitable research group because there are less potential confounding factors, such as active smoking and occupational exposure. Finally, school age children have more predictable time activity patterns, allowing for accurate exposure assessment based on outdoor monitors.

The first panel consisted of 161 children selected from three primary schools, located either on the North or South side of the airport. Each child participated for 8 – 9 weeks in the schoolyear between Dec. 2017–May 2018. The second panel was added to increase the overall number of asthmatic children. This included 19 children with asthma complaints from the wider Schiphol area, participating between September and December 2018. The school panel participants performed weekly supervised spirometry and eNO tests at their schools. Additionally, children from both panels performed daily home spirometry and recorded respiratory symptoms and bronchodilator use.

Throughout the study period, hourly concentrations of the particle size distribution (focusing on UFP) and BC were measured at the schoolyards of the participating schools. Particles smaller than 20 nm (PNC20) were considered as particles deriving primarily from aviation. Particles larger than 50 nm(PNC50-100) and BC were considered as deriving primarily from motorized road traffic sources.

This study has been approved by the Utrecht Medical Ethics review committee (METC 17/576).

2.2. Study population

2.2.1. School panel

The area in which schools are affected substantially by Schiphol Airport emissions was previously established using dispersion modelling (Bezemer, et al., 2015). Primary schools with children (7–11 years old) from the villages to the North (Badhoevedorp) and South (Aalsmeer) of Schiphol Airport were selected in such a way that on most days, either one of the schools was exposed- while the other school was not exposed to UFP from Schiphol (Fig. 1). Furthermore, criteria for the selection of the schools included modelled aviation-related UFP exposure >5000pt/ cm³, >500 m distance from highways, >100 m distance from major roads, school size, regular school attracting predominantly children living in close distance to the school and no planned reconstruction during the schoolyear 2017–2018.

The schools within the affected area were contacted in consultation with the public health services in the region, specifically Amsterdam and Kennemerland. A short presentation was given at each school for pupils, teachers and parents to explain the study. Information letters were emailed to the children in the selected classes. Parents and children decided at home whether they wanted to participate. An informed consent form was filled in, signed and sent to the Utrecht University researchers.

The first period of the fieldwork started mid December 2017 in



Fig. 1. Locations of the schools (S1-3) and asthma (A) panel in relation to the airport. Location of the volunteer study and in vitro study (V) reported previously from Lammers et al. (2020) and He et al. (2020) also added.

Badhoevedorp (School 1) and in Aalsmeer (School 2). A total of 64 children of grade 7 in both schools participated for nine weeks. The second period started the beginning of March 2018 in Badhoevedorp (School 1) and Aalsmeer (School 3) with a total of 54 children of grade 6 in both schools for eight weeks. The third period started the end of May 2018 in Badhoevedorp (School 1) and Aalsmeer (School 3) with a total of 43 children of grade 5 of both schools with a duration of nine weeks. In total 161 different primary schoolchildren, respectively from grade seven (10–11 years old), six (9–10 years old) and five (7–8 years old) participated in the study. The specific choices for time periods and grades were made together with the schools in order to reduce disturbance for the schools as much as possible. In Aalsmeer the first school agreed to participate a priori in only one study period, so a second school was included. Air monitoring equipment was moved when the second school was included in the study.

2.2.2. Asthma panel

Additional to the school panel, 19 children (7–11 yr. old) living in the wider Schiphol region with current symptomatic asthma were recruited for the asthma panel. The asthma definition was based on the PIAMA birth cohort study and a large international collaboration among birth cohort studies: Mechanisms of the Development of Allergy (Medall). The asthma definition in these studies was based on three criteria: (1) asthma diagnosis by a physician ever, (2) current wheeze, and (3) current asthma medication. If at least two of the three questions were answered positively, we included the child as having current asthma. A screening questionnaire was used to evaluate whether a child met the inclusion criteria. The target population included children living in Aalsmeer, Amstelveen, Badhoevedorp and parts of Amsterdam: communities with a modelled average UFP concentration contribution from aviation larger than 5,000pt/cm³ (Bezemer, et al., 2015). The schools in the relevant communities had approximately 8,000 7–11 yr. old children. According to the PIAMA cohort study conducted in the Netherlands, 12.6 % of the children have asthma when they are 8 years old (Scholtens, 2009). Using this percentage, the total number of children with asthma between 7–11 years old and living in the Schiphol region was estimated at about 1,000 children.

Children were recruited using advertorials in local newspapers in the wider Schiphol region, social media, relevant websites and home delivery of information folders to more than 10,000 homes within 1,000 m from primary schools. Finally, school physicians brought the study to the attention of parents and children during vaccination sessions, part of the Dutch National Immunization Program. Interested parents were asked to complete a screening questionnaire. If the screening criteria were met, a first house visit was planned, which included signing first the informed consent form.

2.3. Health outcomes

2.3.1. General characteristics

General characteristics of the participants were obtained using a baseline questionnaire at the start of the study, adapted from the PIAMA birth cohort study (Scholtens, 2009). These included characteristics such as gender, medication use, social-economic status and potential indoor exposure. The baseline questionnaire was used for population characterization and definition of potential confounders and effect modifiers. Information on age was obtained through the screening questionnaire. Height and weight were measured on each participant's first day of the supervised measurements at the schools, and for the asthma panel at home during the first home visit.

2.3.2. Weekly exhaled nitric oxide and spirometry

Weekly eNO and spirometry were executed on the same day and at the same time for each school, during three periods of 8–9 weeks. The school in Aalsmeer was measured in the morning (between 10:00 AM – 12:00 PM), whereas the school in Badhoevedorp was measured in the afternoon (between 1:00 PM and 3:00 PM). eNO was measured before spirometry measurements were done. All measurements were executed by the same team of 5 trained research assistants with the same two instruments for eNO and the same four calibrated instruments for spirometry.

eNO was measured using a NIOX VERO (Aerocrine AB, Solna, Sweden) following the 2017 standardized procedures of the European Respiratory Society (Horváth, 2017). Spirometry was measured using an EASY ON-PC spirometer (NDD Medical Technologies, Zurich, Switzerland), in a sitting position with a nose clip on. A minimal of four maneuvers was performed per person.

The best values from the technically-correct maneuvers were selected according to the ATS/ERS criteria. As children that age sometimes have difficulty maintaining the 3 s forces exhalation, we added a second end of test criterion, defined as ≤ 25 mL change in volume for at least 1 s at the end of the expiration. For the start of test the following criteria were monitored: BEV <150 mL or <5 % of FVC, PEFT <0.15 sec. The spirometer complied with the ATS/ERS requirements (Miller, 2005). We analyzed FVC, FEV1, PEF and MMEF. All tests were checked by a certified research nurse and assigned a quality grade. We only accepted the highest two quality grades (~85 % of the tests). The other measurements were excluded from further analysis.

2.3.3. Daily home spirometry

Daily spirometry, including forced expiratory volume in 1-second (FEV1) and peak expiratory flow (PEF), were performed at home by the children, using a Vitalograph Asma-1 monitor for both panels. The instrument is used extensively in asthma care. It automatically stores date, time and measured spirometry, performing automatic quality checks with feedback to the participant e.g. on a too short maneuver or hesitant start. Children performed morning and evening spirometry at home, unsupervised by study staff. Morning was defined as between 6:00 - 10:00 AM, whereas evening spirometry was between 6:00 - 10:00 PM. Instructions were given to measure around the same time every day, in the same position (sitting or standing), to perform at least three attempts and take potential respiratory medication after the measurements. At every measurement time point (morning/evening), the best result out of three attempts was automatically recorded.

In the school panel, children practiced performing the tests at school under supervision of study staff before the start of the 8 - 9 weeks measurement period. Several times during the measurement period, the children were asked to bring their devices to school to monitor the process. Technical recommendations and encouragement was provided when necessary. The asthma panel participants were visited at home three times: at the start of the 3-month study period, after 1.5 months, and at the end of the study period. During the first visit, the study was explained to the child and parent(s) and instructions for filling out the daily diary was given. After 1.5 months the research assistant visited the participants at home to keep up motivation, answer potential questions and monitor general progress. At the end of the study period, the devices were collected.

2.3.4. Daily symptom diary

In the school and asthma panel the same daily diary was used. Instructions took place at home for the asthma panel and at school for the school panel. During the study periods, children filled out an electronic diary every evening, under the supervision of a parent.

The diary included questions about the occurrence and severity of different symptoms and use of on-demand/ relief airway medication. The symptoms were selected based upon previous studies in asthmatic and non-asthmatic children (Roemer et al., 1993; Van der Zee, 1999; van

der Zee, 2000). Symptoms included: wheeze, shortness of breath (SOB) at rest, SOB after exercise, coughing, coughing up phlegm, nose complaints and waking up during the night because of breathing problems. The asthmatic symptoms SOB at rest and after exercise, wheeze and woken up with breathing problems were combined into one additional symptom: lower respiratory symptoms (LRS). The severity was recorded using a 3-point scale, with 0 for no symptoms, 1 for low degree symptoms and 2 for moderate/ severe symptoms. Appendix A.1 presents the diary in the native language, in Dutch (Table A.1).

2.4. Exposure assessment

Our primary exposure assessment was based upon real-time air pollution measurements at the schools of the participating children of the school panel. We used these measurements to represent 24-hour average exposure of the children, based on earlier research documenting high temporal correlations between central site UFP and residential outdoor concentrations across an urban area (Puustinen, 2007). Children in urban areas generally live within ~ 1 km from their school, based upon a time survey data (Ntarladima et al. 2019) and spend about 6.5 h per day at primary schools (8.30 to 15 hr.). To address limitations of the school measurements to represent 24-hour average exposures, we additionally modelled the concentration of aviation-related emissions at the residential addresses of all children on a daily basis using the Stacks + dispersion model from Voogt et al. (2023) (Voogt, 2023).

2.4.1. Exposure measurements at the schools

Measurements were performed by the Public Health Service of Amsterdam and TNO, between December 2017 and December 2018, with an interruption during the 2018 summer holidays when no health observations were obtained. Air monitoring equipment was moved within Aalsmeer from the second to the third school, the moment the third school was included in the study. Measurements included particle number concentration (PNC) in different size classes (consolidated as 10–20 nm, 20–30 nm, 30–50 nm, 50–70 nm, 70–100 nm, 100–200 nm and 200–1180 nm) and BC, to distinguish between potential health effects of UFP from Schiphol Airports emission and from other sources. Only particles larger than 10 nm were measured, as particles below 10 nm could not be measured using the available equipment. Table 1 gives an overview of the exposure variables and the rationale of monitoring them to investigate UFP predominantly from aviation and other combustion sources.

PNC measurements were conducted with two identical Scanning Mobility Particle Spectrometers (GRIMM SMPS model 5420). Sampling took place with use of a sample dryer according to manufacturer's instructions. The SMPS measured a combination of non-volatile and (semi-)volatile UFP, as is common in ambient concentration monitoring near

Table 1

Overview monitored air pollutants at the school and source indication.

Pollutants	Explanation	Rationale
PNC20	Particle number concentration of particles between 10 and 20 nm (pt/cm ³)	Predominantly from aircraft emissions
PNC50- 100	Particle number concentration of particles larger than 50 and smaller than 100 nm (pt/cm ³)	Predominantly from non-aircraft emissions (road traffic, wood burning, industry)
PNC100	Particle number concentration of particles smaller than 100 nm (pt/cm ³)	To address health effects of UFP in general irrespective of source
BC	Black Carbon (μg/m ³)	Predominantly from non-aircraft emissions (road traffic, wood burning, industry)
PNCMOD	Particle number concentration of particles from aircraft emissions modelled at home addresses, truncated at the P99	Modelled data specific for aircraft

airports (Stacey, 2019). As aviation can also release e.g. various (semi-) volatile organic compounds and ammonium-nitrate these will partly be reflected by the concentrations measured by the SMPS monitor. The contribution however, will be small compared to the non-volatile fraction, dependent on the atmospheric conditions leading to particle formation and condensation from the exhaust containing a complex mixture of particles. Continuous measurements of BC were done using the Multi Angle Absorption Photometry (MAAP).

We tested the assumption based on previous studies (Stacy, 2019), that PNC20 represents predominantly aviation emissions in this study area near the airport, by developing wind roses and comparing the differences in distribution with wind direction. Particles smaller than 20 nm measured in the atmospheric can also reflect particle new formation events, unrelated to aviation emissions. We additionally assessed the correlation with other pollutants, reflective of traffic emissions including BC.

2.4.2. Routine monitoring data

Furthermore, hourly concentration data from the National Air Quality monitoring network for key pollutants ozone (O₃), PM10 and nitrogen dioxide (NO₂) was collected (http://www.luchtmeetnet.nl), from two sites within the study area, including Badhoevedorp-Sloterweg and Oude Meer-Aalsmeerderdijk. Hourly O₃ data was obtained from the nearest urban background measurement site in Amsterdam, located in the Vondelpark, approximately 10 km Northeast from Schiphol. Because of very high correlations (R > 0.85) between simultaneous measurements from the two stations we averaged the data to represent the Schiphol region. In this way, the same data was used in both the school and asthma panel. We selected PM10 instead of PM2.5 as PM2.5 is not monitored at the Aalsmeer location.

Furthermore, weather data from the weather station at Schiphol was obtained from the Royal Netherlands Meteorological Institute (Koninklijk Nederlands Meteorologisch Instituut, KNMI), including hourly values for temperature, humidity, wind speed, wind direction, precipitation, radiation and air pressure (KNMI, 2016). Daily pollen data were obtained through the pollen count data from the hospital in Leiden, including Corylus, Alnus, Betula, Quercus, Fraxinus, Poaceae, Artemisia, Rumex, Plantago and Chenopodiaceae, based on their allergenicity). Leiden is located about 30 km south-west of the Schiphol Airport region. Because of the highly skewed nature of the pollen counts (with many zeros), we dichotomized the variable indicating high pollen counts in the analysis based upon the 95th percentile in an earlier study (Brunekreef and Holgate, 2002).

2.4.3. Modelling of aviation-related particles

Dispersion modelling of hourly UFP concentrations from air traffic at the home and school address of the children was performed with the Stacks + model (Voogt, 2023). Stacks + is a Gaussian plume model thatis used as a National Model in the Netherlands and that has been widely used to model the dispersion of aircraft emissions and other sources. The dispersion modelling used hourly-specific actual flight data from the FANOMOS database from the Netherlands Aerospace Centre (NLR), meteorological data from the Royal Netherlands Meteorological Institute (KNMI) station Schiphol and generic emission figures to estimate hourly PNC levels. Hourly PNC levels were used to calculate 24-hr average exposures. The models were calculated for receptor points of all geo-coded residential addresses and schools of the school and asthma panels. The model predictions were calibrated based on measurements of total PNC using an EPC with a lower particle size of 7 nm at multiple sites across the study area (Voogt, 2023). The average model predictions correlated well with the average concentration at the seven sites (R = 0.91). For the present study, 24-hour average concentrations were used, the hourly mean concentrations were considered too uncertain. The model also sometimes generated hourly estimates that, compared to the measurements, were clearly too high, possibly related to low wind speed conditions. Therefore, the 24-hour averages were calculated after

truncation of the hourly values at their 99th percentile. A comparison between measured and modelled concentrations at the schools is presented in section 3.1.

We used the modeled aviation-related particle concentration as an additional exposure metric and did not calculate a weighted average with the measured particle concentration at the school. We considered a combined exposure difficult to interpret because of the differences in assessment (modelled vs measured) and the metric (total aviationrelated PNC vs particles less than 20 nm).

2.5. Quality assurance and quality control

Daily quality control checks were executed to assure quality of the data, including checks on alarms and flag modes, necessary trouble shooting and interference of the data. For the MAAP ambient temperature was crosschecked with measurement stations nearby. Furthermore, periodical checks were executed on locations where maintenance was carried out on the equipment. Monthly sample lines, flows, fittings and air dryers were checked and compared to standard criteria. Zero checks were performed and the butanol of the CPC was drained and refilled. Yearly the SMPS was maintained and calibrated by the manufacturer (GRIMM). Every 3 months relevant checks were achieved according to maintenance instruction MMK-O-023.8. A zero and span check was performed with standard slides, reflection at 165° and 135°, transmission and Reference Diode was compared to standard criteria. Furthermore sample gas flow, temperature, pressure as well as sample gas leakage were checked and compared to standard criteria. Finally measurement chamber, sample hoses and sampling hat were periodically cleaned. The measurement equipment was at all times kept in climatized high-end shelters at a constant temperature of 20 °C using air conditioning.

Two measurement campaigns were carried out at the school yards in order to ensure that the measurements of BC and particle size distributions at the two locations were intercomparable. The first measurement took place before the equipment was installed at the schools (in between 7–11-2017 and 28–11-2017). The second measurement campaign took place after all measurements at the schools where carried out (in between 10–12-2018 and 3–1-2019). In both these campaigns correction factors where obtained for the MAAP and SMPS measurements. These factors were interpolated over time in order to apply the correction factors to the measurements at the school. More detailed information about the comparison campaigns can be found in the **appendix** (Figures A.1 and A.2 and Table A.2).

2.6. Statistical analysis

The individual observations were used to investigate associations between air pollution exposure and health, adjusting for potential confounders. We used the generalized estimating equations (GEE) approach to account for repeated measurements within subjects and autocorrelation (Janes et al., 2008). Associations were evaluated between average concentrations of the same day and lagged concentrations to allow for delayed effects for all endpoints, including previous day (Lag), two days ago (Lag2) and average of the same day, previous day and two days ago (Mean). Development of inflammation (a major mechanism of air pollution effects) is not immediate, but following human controlled exposure studies typically occurs within 24 h after exposure. In the RAPTES study by Steenhof et al. (2014), inflammatory biomarkers returned back to baseline within 24 hrs. post exposure (Steenhof, 2014). We used two days prior to the health outcome to represent delayed effects. Our final evaluation is based on consistency of the associations between the various lags and statistical models. We interpreted an association between a pollutant and health outcome as consistent, when one of the four evaluated lags or average had a p value <0.05, and at least one other lag had an effect estimate in a similar direction, with no significant associations in the opposite direction. Effect estimates are

presented for interquartile range (IQR) increments for the full study period of the school and asthma panel. Specifically, increments were 3,598pt/cm³ for PNC20, 6,460pt/cm³ for PNC100, 994pt/cm³ for PNC50-100, 7,445pt/cm³ for modelled aviation PNC and 0.71 μ g/m³ for BC. All analysis were performed in the Statistical Analysis Software (SAS) version 9.4 Proc Genmod.

2.6.1. Supervised spirometry

In all spirometry and eNO models we a priori adjusted for covariates gender, height, weight and age to describe differences between subjects (minimal adjustment models). In the main model we additionally included temperature, relative humidity, time trend and reporting a cold during the spirometry test day.

Spirometry and eNO were measured on a continuous scale. Linear mixed models were used to investigate the associations between air pollutants and supervised spirometry and eNO, accounting for differences between subjects and confounders. An exchangeable correlation structure was specified, which assumes that observations are clustered within individuals and that there is no pattern to the order of the observations, supported by the weekly frequency of measurements. We analyzed each of the three study periods (Lags) separately to relax assumptions about the relationship between confounders such as time trends and weather with health. A *meta*-analysis of the three periods including the covariates was performed to obtain the association of interest. Due to the relative small group size in the three individual periods, we only interpreted the combined association.

As the hour of measurement was known, we additionally assessed associations between hourly averaged air pollution and supervised spirometry, including the previous hour, same hour and average of same- and previous three hours (4 h in total). Weighted hourly exposure levels were assigned to the children, that is if a test was conducted at 9.30 AM, 30 min of the 9–10 and 30 min of the 8–9 hourly average was used. Sensitivity analysis included assessing associations between supervised spirometry and the various pollutants, adjusting for the first measurement day due to a potential learning curve (Hoek and Brunekreef, 1992). Additionally, we adjusted for pollen, technician and spirometry device.

For daily spirometry an AR-1 correlation structure was specified, assuming clustering of observations within individuals and correlation of observations of subsequent days. Daily spirometry included morning and evening collection, which were analyzed separately. A small fraction of observations fell outside the defined time windows and was not used for further analysis. Observations where both the PEF and FEV1 were 3 individual standard deviations higher or lower compared with the individual mean PEF, were deleted (<1% of observations).

2.6.2. Daily symptoms

For the daily symptom data, logistic regression models were used to investigate relationships between air pollution concentrations and daily symptoms, accounting for differences between subjects and confounders with an AR-1 correlation structure. In the analysis of daily symptom data, we adjusted for gender, age, temperature, relative humidity and time trend. The main model used linear terms. We assessed the impact of adding quadratic terms in the weather variables, to evaluate the linearity assumption. As no differences were found, we will only show the results of the linear model.

Again, each study period was first analyzed separately, after which a combined fixed effects *meta*-analyses of the three study periods was executed. The school panel and asthma panel were first analyzed separately. As similar tools and procedures were used, and combination of the panels was planned a priori, we additionally combined effect estimates from the two panels using fixed effects *meta*-analysis for the daily spirometry and symptom measurements (pooled).

2.6.3. Two pollutant models

In addition to single pollutant models for the above pollutants, we

also specified two pollutant models adjusting the PNC20 association for respectively BC, PNC50-100, PM10, O_3 and NO_2 . If the coefficient for UFP changed substantially upon adjustment for BC or the fraction between 50–100 nm, this would be an indication that the association was mostly due to non-aircraft emissions.

2.6.4. Stratification

As the school panel included children both with and without asthma, we additionally performed stratified analyses for all health outcomes, comparing asthmatic versus non-asthmatic children.

3. Results

3.1. Exposure patterns

Distribution of 24-hr average concentrations of analyzed pollutants at the spirometry days of the entire study period can be found in Table 2. Daily average PNC20 levels, which we assumed reflected predominantly aviation-related UFP, ranged between 669 and 16,242pt/cm³, indicating a large temporal contrast between days. A large contrast was also observed for the motorized road-traffic-related exposure levels (PNC50-100 and BC) and generic UFP (PNC100). Modelled PNC from aviation at the residential address varied more than measured concentrations, with a max concentration of 51,075pt/cm³. For 18% of the days, a concentration of zero was modelled. The measurements contain particles from other sources as well. The mean modelled PNC from aviation was slightly higher than measured PNC20 at school. Similar exposure levels were observed for the daily diary days for the whole research period, which is relevant for interpretation of the daily spirometry and respiratory symptoms (Table A.3).

Table 3 shows the correlations between the air pollutants and weather. PNC100 was highly correlated with PNC20 (Pearson r: 0.96). Both pollutants were weakly correlated with the other pollutants and weather characteristics. The low correlation between PNC20 and PNC50-100 and BC of respectively 0.21 and -0.05, supports the feasibility of disentangling different UFP sources using particle size. Modelled PNC from aviation at the residences was moderately correlated with PNC20 and PNC100 at school (R = 0.62 and 0.66) and weakly with the other pollutants (R <0.2). PNC20 and PNC100 had a low correlation with PM10 and NO₂. For the Badhoevedorp location, the correlation of the 24-hour average PM2.5 and PM10 concentrations in the study period was 0.92, illustrating that the choice for PM10 instead of PM2.5 in further analyses would likely not have made a difference. The correlation between PNC20 with PM10 was -0.23 and -0.28 for PM2.5.

Low correlations between PNC20 and PNC50-100, PM_{10} and BC, were also found for the daily diary periods of specifically the school panel (Table A.4). Modelled PNC from aviation at the residences was moderately correlated with PNC20 and PNC100 at school (R = 0.68 and

Table 2

Distribution of 24-hr average measured air pollution concentrations and modelled PNC from aviation at the residences on spirometry days during entire study period.

	Unit	Mean	SD	Min	Max
PNC20	pt/cm ³	4,005	3,361	669	16,242
PNC100	pt/cm ³	8,425	5,143	2,442	24,381
PNC50-100	pt/cm ³	1,381	730	465	3,680
BC	µg∕m ³	0.9	0.5	0.2	2.3
PNCmodelled	pt/cm ³	4,340	6,959	0.0	51,075
O ₃	µg∕m³	53.0	21.5	8.1	98.2
PM10	µg∕m³	21.9	8.9	11.8	39.2
NO ₂	µg∕m ³	26.5	11.1	10.7	58.1
Temperature	°C	9.8	6.8	0.9	23.0
Relative humidity	%	79.2	10.8	51.3	98.3

	PNC20	PNC 100	PNC 50–100	BC	Temp.	Rel. hum	O ₃	PM10	NO ₂
PNC20 PNC100	1.00	0.96	0.21	-0.05	0.12	0.12	-0.08	-0.18	0.15
PNC50-100		1.00	1.00	0.67	0.35	-0.24	0.02	0.52	0.30
BC				1.00	-0.15	0.08	-0.48	0.81	0.83
TEMP					1.00	-0.61	0.67	0.15	-0.15
REL. HUM						1.00	-0.75	0.02	0.25
O ₃							1.00	-0.20	-0.44
PM10								1.00	0.59
NO ₂									1.00

<u>Abbreviations</u>: PNC = particle number concentration; BC = black carbon; Temp. = Temperature; Rel. hum = relative humidity; $O_3 = Ozone$; PM10 = particulate matter with aerodynamic diameter <10 μ m; NO₂ = nitrogen di-oxide.

0.69) and weakly with the other pollutants (R <0.2). A correlation of 0.94 between PNC20 and total PNC was found for the entire study period. The correlation between PNC100 and total PNC was 0.99.

Overall, the mean PNCtotal concentration was about 10 % higher than PNC100 (mean 10,221 vs 9,246pt/cm³).

Hourly measured particle number concentrations, per size class,



Fig. 2. Wind roses of hourly measured particle number concentrations (PNC; total and in various size classes) and black carbon (BC). Collection periods were for Badhoevedorp between 07/12/2017-09/12/2018, for Aalsmeer school 2 between 01/12/2017-27/02/2018 and for school 3 between 01/03/2018-05/12/2018. Distance between the schools and airport was 2 km for Badhoevedorp and Aalsmeer school 2, and 3 km for school 3. PNC is expressed per $1000pt/cm^3$ and BC per 1.0 µg/m³. Left panels: PNC20 in blue, PNC20-30 nm in red, PNC total in black. Right panels: BC in black, PNC30-50 nm in red, PNC50-100 nm in blue, PNC > 100 in purple. (Please note the difference in the scales between the left and right panels). School 1 was located North of the airport; schools 2 and 3 were located South of the airport (see Fig. 1). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

classified by wind direction can be found in Fig. 2. The left panels of the wind roses showed higher concentrations for PNC with smaller size classes (20 and 20–30 nm) and generic UFP (PNC100), when the wind direction was from Schiphol Airport for all three schools. This was not the case for the BC concentrations and the higher size classes of UFP (right panels), which showed a more general distribution pattern.

Our assumptions that in this study area, close to a major airport, PNC20 is predominantly affected by aviation-related emissions, is supported by the wind roses showing that PNC20 at the two schools are substantially higher when the wind is from the airport. The wind direction with the highest PNC20 concentrations differs per school, consistent with their location relative to the airport. If particle new formation was the dominant contributor to PNC20, we would expect high concentrations from the same wind sector, as the schools are located within 10 km from each other. Consistently, we observed that on days that the PNC20 exposure at Badhoevedorp was increased, the PNC20 exposure levels at Aalsmeer were substantially lower (and vice versa) (figure A.3). This was however not the case for pollutants BC and PNC50-100 (figures A.4 and A.5). The correlation between simultaneous 24-hour average measurements at the Badhoevedorp and Aalsmeer school sites was -0.20 for PNC20 versus +0.94 for BC and +0.87for PNC50-100 (all statistically significant). A linear regression model with the difference in PNC20 between the two schools and two indicator variables for the daily percentage of north $(290^{\circ} - 60^{\circ})$ and south (150°) - 240°) wind direction, explained 74 % of the difference. The slope (standard error) for North was + 9216 (607) pt/cm³, indicating that if the wind is from the North 24 h, in Aalsmeer (located south of the airport) PNC20 was 9,000pt/cm³ higher than in Badhoevedorp. The slope for South was -9,204 (677) pt/cm³ showing the opposite. The intercept was 423 (350) pt/cm³, indicating that for other wind directions, there was no difference between the schools.

Furthermore, the correlation between modelled PNC from aviation at the schools with PNC20 was 0.78 (affected by both limitations in the model and the extent to which PNC20 reflects aviation emissions), versus 0.27 for PNC50-100 and 0.06 for BC. Figure A.6 shows the difference between Badhoevedorp and Aalsmeer PNC20 concentrations as percentage of Northern wind, measured at the schools. The correlation between modelled PNC from aviation at individual residential addresses with measured PNC20 at the schools was 0.68 versus 0.18 for PNC50-100 and 0.07 for BC. This was consistent with our assumption that the measured concentrations at the schools also reflect residential exposures.

3.2. Descriptives of the panels

The overview of the baseline characteristics for the two panels can be found in Table 4. In the school panel 161 children in total participated, whereas in the asthma panel 19 children were included. The children from the asthma panel lived in 4 communities, of which 9 children in the villages Aalsmeer and Badhoevedorp. The other children of the asthma panel lived in South-West parts of Amsterdam or Amstelveen. Mean age was comparable between the two panel groups (9–10 yrs), whereas respiratory symptoms e.g. wheezing, shortness of breath and hay fever symptoms were between 36 and 78 percent points higher in the asthma

Table 4

Characteristics	s of study	participants	(T = 0)	; 2017–2018:	baseline).
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Characteristic	School panel	Asthma panel
Ν	161	19
Age (yr. \pm SD)	10.0 ± 0.7	9.2 (6.7 – 11.6)
Sex (female)	49.1 % (79)	42.1 % (8)
Asthma diagnosis ever	8.1 % (13)	57.9 % (11)
Hay fever	18.6 % (30)	52.6 % (10)
Shortness of breath past 12 months	13.0 % (21)	89.5 % (17)
Wheezing	9.9 % (16)	79.5 % (15)
Asthma medication past 12 months	NA	94.7 % (18)

panel, compared to the school panel. Moreover, asthma prevalence and intake of asthma medication were by design much higher in the asthma panel. More than half of the asthma panel reported a doctor diagnosis of asthma and only one child did not take asthma medication throughout the study period.

The distribution of the successful spirometry tests, eNO and the prevalence of a selection of the symptoms in the two panels over the entire study period, is shown in Table 5. Daily pulmonary function was overall lower for the asthma panel, whereas the prevalence of daily symptoms was overall higher compared with the school panel.

3.3. Associations between air pollution and supervised spirometry and exhaled NO measurements

Adjusted associations for the combined effect estimates of the different schools between various lags of air pollutants and the supervised spirometry measurements, can be found in Table 6, including adjustment for a potential learning effect. No clear pattern of associations was found. Only a consistent negative association between BC and PEF, and a positive association with FVC, was noticeable. Before adjustment for the first measurement days, several positive and negative associations were observed (Table A.5).

3.3.1. Sensitivity analyses

We additionally analyzed data using one hour or 4 h prior to the spirometry tests (Table A.6). PNC20 and PNC100 were generally significantly associated with an increase in FEV1 and MMEF and a decrease in PEF. PNC50-100 and BC were both negatively associated with all spirometry parameters, but only PNC50-100 was statistically significantly associated with a decrease in FVC.

Stratified analyses by asthma status showed slightly larger negative associations of PNC20 with FEV1, FVC and MMEF for the 36 asthmatic children, compared with the 121 children without asthma from the school panel (Tables A.7 and A.8). PNC20 was generally positively associated with eNO in the non-asthmatic and negatively in the asthmatic group, though with overlapping confidence intervals. Overall, associations between children with and without asthma showed no consistent differences.

The two-pollutant model, subsequently adjusting the PNC20

Table 5

Average respiratory function and eNO measurements over study period.

	School J	panel	Asthma panel		
Variable	N	Mean (SD)	N	Mean (SD)	
Supervised spirometry	1,329		NA	NA	
FEV1 (mL)		1,935 (306)			
PEF (mL/s)		4,692 (787)			
FVC (mL)		2,289 (356)			
MMEF (mL/s)		2,153 (572)			
eNO (ppb)	1,295	20 (23)			
Daily spirometry (morning)	5,006		976		
FEV1 (mL)		1,721 (329)		1,545 (502)	
PEF (mL/s)		3,989 (892)		3,577 (1,339)	
Daily spirometry (evening)	5,651		1,112		
FEV1 (mL)		1,719 (342)		1,602 (477)	
PEF (mL/s)		4,125 (929)		3,756 (1,299)	
Prevalence symptoms (%)	7,382		1,498		
Cough		22.3		33.0	
Bronchodilator use		1.6		11.7	
LRS		8.8		32.1	
Wheeze		1.9		10.6	
Phlegm		8.4		11.7	
SOB rest		3.3		9.1	
SOB exercise		4.3		18.8	
Woken up		3.1		9.9	

Abbreviations: SD = standard deviation; eNO = exhaled nitric oxide; ppb = parts per billion; LRS = lower respiratory symptoms; SOB = shortness of breath. NA = not available.

Adjusted associations between 24-hr average exposure to air pollution and supervised spirometry, additionally adjusted for first measurement day (school panel, n = 161). Effect estimates and 95 % CI expressed per 3,598pt/cm³ for PNC20, 6,460pt/cm³ for PNC100, 994pt/cm³ for PNC50-100, 0.7 μ g/m³ for BC and 7,455pt/cm³ for PNCMOD.

Exposure	FEV1 (ml)	PEF (ml/s)	FVC (ml)	MMEF (ml/s)
PNC20	1.2 (-7.5;	-14.6 (-45.6;	-1.9 (-9.5;	-0.8 (-23.0;
	9.8)	16.4)	5.6)	21.4)
LAG	1.2 (-6.9;	-6.7 (-35.4;	-4.1 (-11.6;	3.4 (-18.3;
	9.2)	22.1)	3.5)	25.1)
LAG2	-0.9 (-6.2;	11.4 (-6.2;	-2.7 (-8.2;	-0.7 (-12.7;
	4.3)	28.9)	2.8)	11.3)
MEAN	-2.3 (-10.9;	2.8 (-25.9;	-4.6 (-13.2;	-5.3 (-25.3;
	6.4)	31.5)	4.1)	14.7)
PNC100	0.9 (-7.8;	-17.1 (-48.7;	-2.3 (-10.0;	0.3 (-22.4;
	9.6)	14.5)	5.6)	22.9)
LAG	3.7 (-5.4;	0.1 (-32.1; 32.2)	-1.1 (-9.6;	6.4 (-17.4;
	12.7)		7.4)	30.2)
LAG2	-1.0 (-6.1;	10.9 (-5.6;	-1.8 (-7.1;	-2.5 (-13.9;
	3.9)	27.3)	3.4)	8.9)
MEAN	-1.7 (-10.6;	6.8 (-22.3; 35.9)	-3.2(-12.1;	-4.8 (-25.4;
	7.0)		5.7)	15.8)
PNC50-	-0.9 (-9.4;	-21.2 (-49.9;	-3.0 (-10.5;	2.4 (-18.6;
100	7.7)	7.6)	4.6)	23.3)
LAG	8.6 (-2.4;	21.2 (-20.7;	8.4 (-2.2;	1.6 (-26.5;
	19.8)	62.9)	19.2)	29.7)
LAG2	1.3 (-6.0;	9.8 (-17.3;	6.9 (-0.3;	-9.4 (-27.6;
	8.5)	37.1)	13.9)	8.6)
MEAN	3.2 (-7.5;	-0.3 (-39.9;	7.4 (-3.4;	-1.4 (-29.4;
	13.9)	39.4)	18.1)	26.6)
BC	-6.8 (-15.8;	-44.5 (-72.1;	-4.8 (-11.9;	-8.4 (-31.8;
	2.3)	-17.0)	2.4)	14.9)
LAG	1.2 (-6.0;	-42.3 (-75.5;	7.3 (-0.1;	-11.3 (-32.2;
	8.4)	-9.2)	14.8)	9.6)
LAG2	1.0 (-5.0;	-4.5 (-31.0;	8.7 (2.3;	-13.7
	7.0)	22.0)	15.1)	(-28.5; 1.0)
MEAN	-1.6 (-9.1;	-34.7 (-69.0;	6.7 (-1.2;	-17.5
	5.9)	-0.4)	14.7)	(-38.3; 3.3)
PNCMOD	0.3 (-3.4;	1.4 (-11.9;	-0.4 (-4.1;	-0.4 (-8.4;
	4.1)	14.8)	3.1)	7.6)
LAG	1.4 (-3.8;	8.1 (-7.4; 23.6)	-0.3 (-4.9;	2.8 (-8.2;
	6.6)		4.4)	13.7)
LAG2	-1.0 (-4.2;	5.3 (-7.1; 17.7)	-2.2 (-5.6;	-1.1 (-9.2;
	2.1)		1.3)	7.0)
MEAN	-0.1 (-5.0;	7.5 (-9.3; 24.4)	-1.3 (-6.0;	-0.1 (-11.6;
	4.9)		3.4)	11.3)

associations for PNC50-100, BC, O₃, PM10 and lastly NO₂, can be found in **Table A.9**. Additional adjustment for the air pollutants resulted in no major changes in either the direction or the magnitude of the effect estimates.

3.4. Daily spirometry

The effect estimates of the main model between the various lags of the air pollutants and the daily FEV1 and PEF (morning and afternoon) conducted at the homes of children from both panels, can be found in Table 7. PNC20 was only associated with a decrease in FEV1 in the evening and no associations were observed for PNC100 with any of the spirometry parameters. PNC50-100 and BC were negatively associated with FEV1 in the morning in both panels. Furthermore, PNC50-100 had a negative association with PEF in the morning in the school panel, and BC with morning and evening PEF in the asthma panel. Modelled PNC from aviation was positively associated with evening PEF in the school panel, but both positive and negative associations were observed within the asthma panel for the various lags. Next, daily spirometry measurements in the morning and afternoon were assessed for the combined school and asthma panel (Table A.10; pooled panel). No consistent associations were found between PNC20 and PNC100 with FEV1 and PEF. PNC50-100 had a consistent negative association with FEV1 and PEF, but only in the morning. BC was consistently associated with a decrease in FEV1 in the morning. Modelled PNC from aviation was not consistently associated with lung function either. Two positive associations were found of lag2 and mean exposure with PEF in the evening, not supported by lag 0 and 1.

3.4.1. Sensitivity analysis

The daily at home spirometry measurements from the school panel, were additionally stratified into a non-asthmatic group and an asthmatic group (Table A.11). In the non-asthmatic strata (n = 125), only PNC50-100 had consistent negative associations with morning FEV1. All other pollutants were not consistently associated with changes in either FEV1 or PEF, in the morning or evening. The asthma strata however, resulted in multiple consistent associations in both directions. PNC20 was associated with an increase in evening FEV1 and PEF. PNC100 was consistently positively associated with FEV1 in the morning and evening. PNC50-100 and BC on the other hand, had negative associations with FEV1 in the morning, and PNC50-100 was also negatively associated with PEF in the morning.

3.5. Daily diary symptoms and bronchodilator use

Associations between 24 h average air pollutants and a selection of the daily symptoms and bronchodilator use (main analysis), assessed both in the school and asthma panel, are displayed in Table 8. The associations of all other symptoms using the main model, can be found in the **appendix** (Table A.12: school and asthma panel). In the school panel, PNC20 and PNC100 were both positively associated with bronchodilator use, wheeze, phlegm and Shortness Of Breath (SOB) at rest, with a significant associated with an increase in the combined Lower Respiratory Symptom (LRS) variable. Modelled PNC from aviation was consistently associated with LRS, bronchodilator use, SOB at rest and wheeze. PNC50-100 and BC were consistently and positively associated with an increase in wheeze, SOB at rest and LRS. Associations with cough were close to unity for all pollutants.

In the asthma panel PNC20 and PNC100 and modelled PNC from aviation were significantly and consistently associated with increased reporting of cough, decreased SOB at rest, but not with any of the other symptoms. Most ORs were <1, with the exception of wheeze, though not statistically significant. Overall, PNC50-100 was not consistently associated with any of the symptoms. BC and LRS and phlegm were negatively associated.

Appendix Table A.13 records the associations between the air pollutants and daily symptoms, assessed using the combined school and asthma panel (pooled panel, main analysis). Several consistently significant increased ORs were observed, particularly for wheeze. Specifically, PNC20 and PNC100 were both significantly associated with an increase in cough, bronchodilator use and wheeze. PNC20 was additionally consistently associated with phlegm and PNC100 with SOB in rest. PNC50-100 and BC had a positive association with wheeze and SOB at rest, and PNC50-100 was additionally associated with an increase in bronchodilator use. None of the ORs <1 were statistically significant

3.5.1. Sensitivity analysis

Further adjustment for self-reported 'flu' did not result in changes in the effect estimates for both panels, compared with estimates from the main model. Flu was positively associated with most symptoms. We additionally performed sensitivity analyses for the asthmatic children in the school panel. We did not perform analyses for the non-asthmatic children because of low prevalence of most of the evaluated acute respiratory symptoms. Associations in the group of children with asthma

Adjusted associations between 24-hour average exposure to air pollution and daily spirometry in the morning and afternoon, school and asthma panel. Effect estimates and 95 % CI expressed as change in ml for FEV1 or ml/s for PEF per 3,598pt/cm³ for PNC20, 6,460pt/cm³ for PNC100, 994pt/cm³ for PNC50-100, 0.7 μ g/m³ for BC and 7,455pt/cm³ for PNCMOD.

Exposure	School panel (n =	161)		Asthma panel (n $=$ 19)				
	FEV1 (ml)		PEF (ml/s)		FEV1 (ml)		PEF (ml/s)	
	Morning	Evening	Morning	Evening	Morning	Evening	Morning	Evening
PNC20	-1.2 (-7.4; 5.1)	4.0 (-2.3; 10.3)	-2.0 (-18.2; 14.1)	-6.5 (-19.9; 6.9)	-0.2 (-14.3; 13.9)	7.2 (–3.4; 17.8)	-12.9 (-45.7; 19.9)	-11 (-47.2; 25.2)
LAG	-2.6 (-9.3; 4.0)	-6.6 (-13.0; -0.3)	5.8 (-9.2; 20.7)	-1.4 (-15.0; 12.2)	5.2 (-2.3; 12.7)	3.8 (-3.2; 10.8)	-2.0 (-28.6; 24.6)	26.9 (0.9; 52.9)
LAG2	-1.7 (-8.1; 4.7)	4.1 (-1.8; 10.1)	-10.2 (-25.0; 4.7)	13.7 (–1.3; 28.7)	1.6 (-12.0; 15.1)	-3.3 (-12.3; 5.7)	0.8 (-32.1; 33.6)	-24.1 (-60.8; 12.7)
MEAN	-3.0 (-15.4; 9.4)	-0.7 (-12.4; 11.0)	-14.5 (-45.2; 16.2)	16.2 (–15.3; 47.7)	7.9 (-11.2; 26.9)	10.1 (-7.7; 28.0)	-23 (-79.8; 33.8)	-8.8 (-68.3; 50.7)
PNC100	-1.0 (-7.9; 5.9)	3.9 (-2.8; 10.7)	-4.9 (-21.6; 11.8)	-4.5 (-18.4; 9.5)	0.9 (-16.3; 18.0)	9.9 (–2.8; 22.7)	-13.2 (-49.9; 23.4)	-7.6 (-51.8; 36.6)
LAG	-4.3 (-10.8; 2.1)	-6.1 (-12.5; 0.3)	5.4 (-9.1; 19.9)	-1.2 (-14.9; 12.4)	1.6 (-7.4; 10.7)	4.4 (-3.9; 12.7)	–7.3 (–34.3; 19.7)	25.3 (-7.8; 58.3)
LAG2	-1.2 (-8.3; 5.9)	4.5 (-1.4; 10.3)	-12.9 (-29.3; 3.6)	13.6 (-2.2; 29.3)	1.0 (-13.0; 15.1)	-3.1 (-14.5; 8.4)	5.7 (-27.8; 39.2)	-31.0 (-72.7; 10.7)
MEAN	-5.6 (-19.5; 8.3)	1.7 (-9.7; 13.0)	-20.4 (-54.4; 13.6)	18.6 (–15.9; 53.0)	4.8 (-17.3; 27.1)	14.7 (-3.2; 32.6)	-20.7 (-77.7; 36.2)	-14.6 (-75.3; 46.1)
PNC50- 100	-2.1 (-12.0; 8.0)	3.7 (-4.7; 12.0)	-3.6 (-26.7; 19.5)	1.4 (–15.7; 18.5)	0.7 (-9.7; 11.0)	3.6 (–9.5; 16.7)	11.8 (–24.3; 47.9)	2.7 (-36.8; 42.0)
LAG	-9.8 (-17.8; -2.0)	-1.5 (-10.0; 7.1)	1.4 (-17.2; 20.0)	-0.9 (-14.5; 12.7)	-13.5 (-25.9; -1.2)	1.6 (-7.1; 10.2)	-11.7 (-55.7; 32.3)	-16.2 (-47.3; 15.0)
LAG2	-3.5 (-10.5; 3.6)	4.0 (-3.4; 11.4)	-18.3 (-35.0; -1.7)	5.8 (-13.6; 25.1)	-4.7 (-17.3; 8.1)	-2.2 (-16.4; 12.1)	-0.3 (-44.2; 43.5)	-22.1 (-65.5; 21.4)
MEAN	-13.6 (-30.4; 3.3)	3.2 (-8.2; 14.5)	-26.6 (-59.7; 6.5)	3.9 (–28.6; 36.3)	-20.3 (-39.3; -1.3)	4.6 (–19.5; 28.5)	9.3 (-55.4; 74.2)	-46.2 (-101.1; 8.6)
BC	-4.2 (-15.9; 7.5)	-0.1 (-9.7; 9.4)	12.2 (–20.9; 45.3)	-8.0 (-31.0; 15.0)	0.1 (-18.4; 18.6)	1.5 (–15.3; 18.2)	8.8 (-34.9; 52.5)	-13.1 (-49.7; 23.4)
LAG	-12.6 (-23.9; -1.2)	3.3 (-9.1; 15.8)	4.1 (-21.1; 29.3)	9.9 (–10.4; 30.2)	-26.1 (-48.1; -4.3)	-2.0 (-10.4; 6.5)	-43.5 (-77.7; -9.2)	-24.7 (-52.8; 3.3)
LAG2	-0.9 (-10.5; 8.9)	5.3 (-4.0; 14.4)	-18.7 (-42.9; 5.4)	18.0 (–7.9; 43.9)	-11.1 (-27.5; 5.3)	-1.2 (-15.3; 12.8)	-8.7 (-51.5; 34.2)	-7.2 (-51.4; 37.1)
MEAN	-10.9 (-24.1; 2.3)	3.9 (-10.9; 18.7)	-5.1 (-47.6; 37.3)	18.2 (–18.9; 55.3)	-43.7 (-86.4; -0.9)	-1.3 (-31.5; 28.8)	–54.3 (–134.3; 25.8)	-43.9 (-119.6; 31.9)
PNCMOD	-1.1 (-5.0; 2.7)	3.1 (-1.9; 8.1)	-2.2 (-12.8; 8.4)	-0.2 (-9.9; 9.5)	-7.1 (-18.1; 4.0)	2.2 (-7.9; 12.4)	-21.0 (-37.7; -4.2)	-5.1 (-26.5; 16.4)
LAG	-1.3 (-5.7; 3.2)	-1.0 (-5.8; 4.0)	9.6 (-0.7; 20.0)	-0.8 (-12.6; 10.9)	10.2 (1.2; 19.3)	7.2 (–3.2; 17.7)	13.9 (–12.2; 40.0)	31.7 (15.0; 48.4)
LAG2	0.6 (-3.5; 4.8)	3.1 (-1.0; 7.3)	0.2 (-10.5; 11.0)	12.4 (2.0; 22.9)	1.7 (-2.5; 5.9)	1.3 (-4.7; 7.2)	11.3 (-5.0; 27.7)	-5.4 (-23.1; 12.2)
MEAN	-1.6 (-9.8; 6.8)	7.2 (-1.3; 15.8)	9.0 (-8.4; 26.4)	24.2 (1.9; 46.4)	6.2 (-9.6; 21.9)	17.1 (7.0; 27.2)	4.0 (-20.0; 27.9)	33.6 (0.4; 66.7)

<u>Abbreviations</u>: PNC = particle number concentration; BC = black carbon; MOD = <u>modelled</u>; LAG = previous day average; LAG2 = previous two days average; MEAN = three day average of same day, previous and two days ago. Bold p < 0.05.

(Table A.13) were generally similar but with wider confidence intervals compared to the associations found in the pooled panel (Table A.14). In this model, all pollutants were consistently significantly associated with an increase in wheeze and SOB at rest. PNC20 and PNC100 were furthermore associated with an increase in bronchodilator use, PNC50-100 with LRS and BC with phlegm. Moreover, compared to the pooled model, PNC20 was no longer associated with changes in phlegm and BC had a consistent negative association with SOB during exercise.

3.5.2. Two pollutant models

In general for both panels, school and asthma, the effect estimates for PNC20 with the different symptoms were similar to the single pollutant estimates, though with typically wider confidence intervals, and as a result fewer statistically significant associations (Tables A.15 and A.16). The positive association between PNC20 and cough, and negative associations between PNC20 and SOB in rest, remained constant, even after adjusting for the various air pollutants.

4. Discussion

The current study successfully differentiated aviation-related UFP from UFP emitted by motorized traffic by monitoring various size fractions of PNC and BC and by dispersion modelling of aviation particle emissions. Overall, we conclude that exposure to both traffic-related UFP and UFP primarily from aviation were independently associated with an increase in respiratory symptoms in 7–11 yr. old children living near the airport. No consistent associations were observed between aviation-related UFP and spirometry. Traffic-related air pollutants were associated with a decrease in morning FEV1 and PEF in all panels and models, except for the non-asthma strata (school panel).

4.1. Comparison traffic and aircraft emissions

Austin et al. (2021) monitored time-resolved UFP and BC concentrations near an international airport for multipollutant Principal Component Analysis (Austin, 2021). They found that total PNC of UFP could not effectively discriminate between various sources. However, a combination of BC and individual size distributions of PNC jointly

Adjusted associations between 24-hour average exposure to air pollution and daily symptoms in school and asthma panel separately. Effect estimates (OR) and 95 % CI expressed per 3,598pt/cm³ for PNC20, 6,460pt/cm³ for PNC100, 994pt/cm³ for PNC50-100, 0.7 µg/m³ for BC and 7,554pt/cm³ for PNCMOD.

Exposure	School panel (n = 161)			Asthma panel (N = 19)				
	Cough	Bronchodilator	Wheeze	LRS	Cough	Bronchodilator	Wheeze	LRS
PNC20	1.01 (0.95;1.06)	1.03 (0.88;1.21)	1.20 (1.06;1.36)	1.03 (0.96;1.11)	1.11 (1.00;1.22)	0.99 (0.83;1.18)	0.85 (0.62;1.15)	0.94 (0.85;1.03)
LAG	1.00 (0.96;1.04)	1.19 (1.07;1.33)	1.18 (1.01;1.38)	1.06 (0.99;1.15)	1.05 (1.00;1.11)	0.96 (0.80;1.16)	1.12 (0.99;1.27)	1.00 (0.93;1.07)
LAG2	1.02 (0.97;1.07)	1.13 (1.00;1.29)	1.22 (1.02;1.46)	1.00 (0.92;1.10)	1.02 (0.93;1.12)	1.01 (0.85;1.19)	1.02 (0.86;1.21)	0.96 (0.89;1.05)
MEAN	1.02 (0.92;1.14)	1.32 (1.03;1.69)	1.47 (1.08;2.00)	1.05 (0.89;1.23)	1.22 (1.03;1.44)	0.90 (0.66;1.21)	0.94 (0.67;1.32)	0.87 (0.74;1.02)
PNC100	1.01 (0.95;1.07)	1.04 (0.87;1.25)	1.20 (1.00;1.44)	1.03 (0.95;1.11)	1.11 (0.99;1.24)	0.92 (0.74;1.15)	0.82 (0.58;1.16)	0.91 (0.82;1.02)
LAG	0.99 (0.95;1.03)	1.25 (1.08;1.45)	1.26 (1.05;1.50)	1.09 (1.01;1.18)	1.05 (0.98;1.12)	0.93 (0.76;1.17)	1.15 (0.99;1.33)	0.99 (0.91;1.08)
LAG2	1.02 (0.97;1.08)	1.12 (0.97;1.30)	1.26 (1.03;1.55)	0.97 (0.89;1.08)	1.02 (0.93;1.11)	1.02 (0.86;1.20)	1.07 (0.88;1.29)	0.98 (0.89;1.08)
MEAN	1.01 (0.90;1.14)	1.39 (1.03;1.88)	1.65 (1.14;2.40)	1.04 (0.88;1.25)	1.20 (1.01;1.42)	0.83 (0.60;1.16)	0.95 (0.65;1.41)	0.84 (0.70;1.02)
PNC50-	1.01 (0.93;1.09)	1.17 (0.99;1.39)	1.04 (0.81;1.34)	0.98 (0.90;1.07)	1.00 (0.88;1.12)	0.71 (0.58;0.87)	0.90 (0.69;1.18)	0.90 (0.77;1.06)
100								
LAG	0.96 (0.89;1.03)	1.20 (0.99;1.45)	1.36 (1.17;1.58)	1.12 (1.02;1.22)	0.99 (0.86;1.13)	1.03 (0.84;1.26)	1.07 (0.87;1.32)	1.02 (0.89;1.17)
LAG2	1.01 (0.95;1.08)	1.08 (0.90;1.30)	1.27 (1.12;1.44)	0.94 (0.86;1.03)	0.98 (0.89;1.08)	1.17 (1.01;1.35)	1.19 (0.95;1.50)	1.05 (0.94;1.17)
MEAN	0.98 (0.84;1.13)	1.32 (0.94;1.84)	1.75 (1.23;2.52)	1.00 (0.85;1.19)	0.96 (0.78;1.17)	0.85 (0.61;1.19)	1.14 (0.85;1.52)	0.95 (0.79;1.15)
BC	0.96 (0.87;1.05)	1.18 (0.92;1.51)	1.20 (0.87;1.66)	1.04 (0.90;1.20)	1.01 (0.89;1.15)	0.77 (0.59;1.01)	0.90 (0.75;1.07)	0.88 (0.79;0.99)
LAG	1.02 (0.94;1.11)	1.08 (0.88;1.33)	1.22 (1.08;1.40)	1.15 (1.03;1.30)	1.03 (0.91;1.16)	1.04 (0.85;1.27)	1.06 (0.88;1.28)	0.99 (0.88;1.13)
LAG2	0.98 (0.90;1.06)	1.12 (0.82;1.54)	1.28 (1.10;1.49)	1.01 (0.91;1.14)	0.98 (0.88;1.09)	1.12 (0.92;1.38)	1.15 (0.86;1.53)	1.04 (0.92;1.18)
MEAN	0.98 (0.87;1.10)	1.12 (0.76;1.67)	1.46 (1.11;1.93)	1.12 (0.92;1.37)	0.99 (0.79;1.22)	0.91 (0.63;1.32)	1.04 (0.70;1.52)	0.89 (0.74;1.07)
PNCMOD	0.99 (0.95;1.01)	1.01 (0.87;1.17)	1.15 (1.01;1.33)	1.02 (0.97;1.07)	1.07 (1.02;1.14)	0.77 (0.67;0.90)	0.89 (0.73;1.07)	0.95 (0.86;1.03)
LAG	1.01 (0.98;1.04)	1.19 (1.07;1.31)	1.15 (1.04;1.25)	1.05 (1.00;1.11)	1.02 (0.97;1.07)	1.02 (0.88;1.19)	0.89 (0.80;1.01)	0.91 (0.85;0.97)
LAG2	1.01 (0.98;1.04)	1.17 (0.97;1.40)	1.11 (0.99;1.25)	0.99 (0.95;1.04)	1.01 (0.96;1.07)	1.12 (1.01;1.25)	0.95 (0.85;1.06)	0.96 (0.90;1.02)
MEAN	1.01 (0.94;1.08)	1.27 (1.04;1.55)	1.35 (1.07;1.70)	1.08 (0.97;1.20)	1.18 (1.02;1.36)	0.89 (0.69;1.14)	0.78 (0.63;0.98)	0.81 (0.69;0.95)

Abbreviations: LRS = lower respiratory symptoms; PNC = particle number concentration; MOD = modelled; LAG = previous day average; LAG2 = previous two days average; MEAN = three day average of same day, previous and two days ago. Bold p < 0.05.

explained 61 % of the total variability in the mobile monitoring data. They concluded that aviation-related exposure resulted in elevated PNC levels in smaller size fractions, whereas motorized traffic-related exhaust resulted in higher PNC levels in larger size fractions, accompanied by increased BC levels. This was similarly concluded by multiple prior studies (Lammers, 2020; Hudda, 2014; Hudda, 2018; Austin, 2021; Habre, 2018; He, 2018; Samad, 2022; Wing, 2020). The low correlation observed between PNC20 and PNC50-100 (Pearson r: 0.16-0.21) as well as between PNC20 and BC (Pearson r: -0.05-0.2) in the current study further supported the possibility to separate effect estimates associated with these sources. Additionally, Hudda et al. (2018; 2020) found between 1.7-4.2 fold higher PNC levels inside residential homes, associated with downwind aviation-related exposures (Hudda, 2018; Hudda, 2020). Which coincides with the smaller UFP fraction (PNC20) released from airplanes. Consequently, the use of PNC20 as a proxy for aviationrelated exhaust was justified, while BC and PNC50-100 were more closely associated with traffic-related exhaust.

The difference in particle size can be attributed to the variation in exhaust compositions between aviation and traffic emissions. Standard jet fuels (kerosine) used in aviation contain a relatively high sulfur content, ranging from 550-750 ppm (Barrett, 2012). In contrast, diesel exhaust, a primary contributor to traffic emissions, has seen a significant lowering of the sulfur content since 2006, due to more stringent regulations to lower diesel sulfur content to 15 ppm (Martel et al., 2023). Additionally, traffic exhaust exhibits a relatively higher carbon content compared to aviation-related exhaust, resulting in the formation of predominantly larger-sized particles (Stacey, 2019).

The modelled aviation calculations were included to address potential limitations of the school measurements, including the contribution of other sources to PNC20 measurements and the 24-hr measurements at a fixed site, not being the residential homes. The correlations between the measured PNC20 and modelled PNC at both the schools and homes were respectively 0.8 and 0.7, further supporting the use of the measurements of PNC20, as a proxy for 24-hour average exposure. The consistency of associations with respiratory symptoms of measured PNC20 and modelled aviation-specific PNC supports the interpretation that the associations are related to aviation emissions.

4.2. Supervised and daily spirometry

Inconsistent associations were observed between both aviation- and traffic-related air pollutants and the various spirometry measurements within the school panel. PNC20 had a negative association with both FEV1 and FVC, but positive with PEF within the supervised school model. Whereas the traffic-pollutants were positively associated with FEV1, FVC, MMEF, but negatively with PEF. For the majority of these associations, the observed relationships substantially attenuated after adjusting for the first measurement day. The hourly model did not show any consistent associations. With the daily spirometry measurements, PNC20 was associated with a decrease in evening FEV1 within the school panel. PNC100 showed no clear associations. PNC50-100 and BC were overall consistently negatively associated with morning FEV1.

A limited number of studies have thus far focused on aviation exposure and respiratory function. A cross-over study done by Habre et al. (2018) found no associations between short-term aviation related UFP exposure and FEV1 or eNO in mild to moderate asthmatic adults (Habre, 2018). Lammers et al. (2020) observed a minor but statistically significant decrease in FVC, but no significant associations with FEV1 or FeNO in healthy young adults (Lammers, 2020). Discrepancies amongst studies could be attributed to variations in study design, sample population, exposure duration, distance from airport, other local sources and aviation-related exposure levels observed. The current study observed 24-hr average PNC20 concentrations of 4,000pt/cm³, with maximum values around 18,000pt/cm³. These concentrations were at the lower limit compared to other studies reporting on PNC levels in urban areas nearby airports, which are commonly between $10,000 - 30,000 \text{ pt/cm}^3$, with maximum PNC levels fluctuating between 40,000 - 110,000pt/ cm³. Moreover, the last study looked at healthy adults, not children, with or without asthma.

4.3. Associations with daily symptoms

Relatively consistent findings across the various models were observed with regards to the associations of air pollutants and respiratory symptoms. PNC20 was associated with an increase in bronchodilator use and wheeze in the main school model, the asthmatic strata in the school panel, the pooled panel and the two-pollutant model. Additionally, PNC20 was associated with an increase in phlegm in the school and pooled panel. Interestingly, in the asthma panel, both aviation and generic UFP were associated with an increase in cough, which was also noticeable in the two-pollutant model and the pooled panel. The similar associations with modelled PNC from aviation, further supports the interpretation that the associations with measured PNC20 predominantly reflects aviation emissions.

A cross-sectional study done by Lin et al. (2008) investigated whether residents living near three airports had higher hospital admission rates for respiratory diseases compared to those living farther away from the airports. Using exposure indicator dominant wind-flow patterns (>75 %ile), they found a slight increase in relative risk of 1.75 95 %CI 1.60–1.93) among children aged 0–9 years old (Lin, 2008).Other studies focusing on occupational-related aviation exposure, especially amongst female flight attendants, observed associations with symptoms such as cough, phlegm and runny nose (Tunnicliffe, 1999; Yang, 2003). In general, studies observe that ambient UFP can exacerbate, but not necessarily increase, the onset of asthmatic symptoms (Guarnieri and Balmes, 2014; Goldizen et al., 2016; Vallabani, 2023; Zammit, 2020; Knol, 2009).

Based on the pooled model, there was no evidence that UFP from aviation was associated with a stronger health response compared with UFP from motorized traffic. The effect estimates for the various symptoms, expressed per interquartile range, were quite comparable (Table A.13), which was also observed in previous studies (Austin, 2021; Bendtsen, 2021).

The finding of a positive association with symptoms not supported by an association with objectively measured spirometry, is unlikely explained by reporting bias. At residential level it is not easy for the children or their parents to recognize when concentrations related to Schiphol Airport emissions are increased. Wind direction alone is insufficient. Furthermore the different findings for cough versus more asthmatic symptoms argue against reporting bias. The associations for UFP mainly related to traffic are even less likely to be related to reporting bias, as daily traffic exposure was difficult to predict for the volunteers. Furthermore, assessing health effects of traffic-related pollution was not the goal of the research and thus not communicated to the volunteers.

4.4. Strengths and limitations

The main strength of the study was our monitoring of particle size distributions using the SMPS combined with BC measurements, allowing us to separate UFP from predominantly aviation and other combustion sources. In addition, we used a dispersion model to calculate concentrations related to aviation particle emissions at the schools and residential addresses. Associations between measured PNC20 at school and modelled PNC from aviation at residence showed similar associations with health, supporting the conclusion that aviation-related UFP emissions were associated with health. Given the strong correlation between total PNC and both PNC100 and PNC20, a CPC monitor could have also been used for the exposure measurements in this study area in close proximity to the airport, focusing on areas not adjacent to major highways. Furthermore, PNC20 was employed as a more specific indicator for aviation-related exposure, allowing us to more accurately distinguish between health effects associated with aviation and those stemming from combustion sources. A second strength was the long observation period of almost a year, with different groups of children participating in the study period. A relatively large study population was included, resulting in a large number of observations and subsequently small confidence intervals for effect estimates. Consequently, the lack of consistent significant associations for the supervised spirometry was unlikely due to a lack of statistical power.

was the increased control over the measurements and additional information they provided about an inflammatory marker. However, the measurements were only performed weekly, resulting in a smaller number of observations compared to symptom reporting and daily spirometry tests. A disadvantage of the daily measurements was that the tests were unsupervised, which may have introduced variability in the measurements.

The measurements at the schools do not fully represent personal exposure of the children and we did not take into account infiltration rates of the various pollutants. However, in the design of the study, we attempted to increase the representativity of the school fixed sites for exposure of the children to outdoor generated UFP. First, the study was conducted in small communities, limiting other major sources. Badhoevedorp and Aalsmeer had respectively 13,000 and 33,000 inhabitants during the study period. Second, a priori we included various criteria for the inclusion of the schools, such as predominantly children living in the close neighborhood and schools not located near major roads as described.

A previous study in Amsterdam investigated the temporal correlation of PNC measured by condensation particle counters measured at a central site for 1.5 years with concentration at 50 residential sites across the city (outdoors and indoors) (Puustinen, 2007; Hoek, 2008). For 24hour average concentrations, the median temporal correlation between central site and outdoor sites was 0.76 for PNC. The correlation is a very important metric for temporal studies. The correlation of central site outdoor with indoor concentration was 0.42 (Hoek, 2008). The correlation was 0.59 for night-time hours only (0.74 for measured residential outdoor), avoiding indoor sources of UFP. We suspect that in the smaller communities we now studied these correlations will be higher because of fewer sources and because the spatial distribution of aviation exposure is smoother compared to road-traffic from specific roads.

Despite a large recruitment effort, we were able to include only 19 asthmatic children in the asthma panel. The small sample size may have limited the statistical power to detect associations in this group. Differences in associations between the panels could be further attributed to the heterogeneity of the sample populations and the differences in observation periods. Additionally, for the measured exposures, because of a larger distance between the school site and residences, the site may have represented 24-hr average exposure less well. This does not apply to modelled exposures. Nonetheless, due to the design of the study, we were able to combine data from multiple observation periods. This substantially increased the value of the panel study, as panel studies with relatively short observation period are known to be vulnerable to measurement or confounder bias (Roemer et al., 1993; van der Zee, 2000). Hence, the combined estimates from all schools were primarily considered and we attached less value to the significant associations observed in just one panel.

5. Conclusion

The study contributed to the limited knowledge on aviation-related acute health effects on respiratory function within children living in the vicinity of a major airport. Overall, we conclude that exposure to PNC primarily from aviation, PNC in general and PNC primarily from traffic were associated with an increase in respiratory symptoms in 7–11 yr. old children living in the Schiphol area. No consistent associations between supervised spirometry and the various air pollutants was observed across the different panels and models. BC and UFP between 50–100 nm were associated with increased respiratory symptoms and lower spirometry in the daily diary study. Associations between UFP from aviation and respiratory health were independent of the associations between BC and respiratory health, consistent with the low correlation between these pollutants.

An advantage of the supervised spirometry tests in the school panel,

CRediT authorship contribution statement

Esther S. Lenssen: Writing – review & editing, Writing – original draft, Visualization. Nicole A.H. Janssen: Writing – review & editing, Writing – original draft, Methodology, Funding acquisition, Conceptualization. Marieke Oldenwening: Writing – review & editing, Investigation. Kees Meliefste: Investigation. Dave de Jonge: Investigation. Regina J.M. Kamstra: Writing – review & editing. Daniëlle van Dinther: Investigation. Saskia van der Zee: Writing – review & editing. Rinske H. Keuken: Writing – review & editing. Gerard Hoek: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

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Appendix A. Supplementary data

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