UHASSELT
KNOWLEDGE IN ACTION

Maastricht University

Faculty of Medicine and Life Sciences
School for Life Sciences
Master of Biomedical Sciences

Master's thesis

Prenatal Air Pollution Exposure and Neurobehavioural Development in Early Infancy

Colien Sangiacomo

Thesis presented in fulfillment of the requirements for the degree of Master of Biomedical Sciences, specialization Environmental Health Sciences

SUPERVISOR :
dr. Charlotte COSEMANS

MENTOR :
Ms Lisa REYNDERS

2025
2026

Transnational University Limburg is a unique collaboration of two universities in two countries: the University of Hasselt and Maastricht University.

UHASSELT
KNOWLEDGE IN ACTION

www.uhasselt.be
Universiteit Hasselt
Campus Hasselt:
Martelarenlaan 42 | 3500 Hasselt
Campus Diepenbeek:
Agoralaan Gebouw D | 3590 Diepenbeek

UHASSELT
KNOWLEDGE IN ACTION

Maastricht University

Faculty of Medicine and Life Sciences
School for Life Sciences
Master of Biomedical Sciences

Master's thesis

Prenatal Air Pollution Exposure and Neurobehavioural Development in Early Infancy

Colien Sangiacomo

Thesis presented in fulfillment of the requirements for the degree of Master of Biomedical Sciences, specialization Environmental Health Sciences

SUPERVISOR :
dr. Charlotte COSEMANS

MENTOR :
Ms Lisa REYNDERS

Prenatal Air Pollution Exposure and Neurobehavioural Development in Early Infancy*

Colien Sangiacomo[1], Lisa Reynders[1], Charlotte Cosemans[1], and Michelle Plusquin[1]

[1] Environmental and Molecular Epidemiology research group, Centre for Environmental Sciences, Universiteit Hasselt, Campus Diepenbeek, Agoralaan Gebouw D - 3590 Diepenbeek

*Running title: *Associations between Air Pollution and Development*

To whom correspondence should be addressed: Michelle Plusquin, Tel: +32 (11) 26 82 89; Email: michelle.plusquin@uhasselt.be

Keywords: Ages and Stages Questionnaire, Bayley Scales of Infant and Toddler Development, particulate matter, nitrogen dioxide, black carbon

ABSTRACT

Prenatal air pollution exposure may interfere with foetal brain development, but evidence on neurobehavioural development remains limited. Additionally, the role of gestational age as an effect modifier remains underexplored. This study investigated the association between prenatal exposure to particulate matter with a diameter below 10 µm (PM_{10}) and 2.5 µm ($PM_{2.5}$), NO_2, and black carbon and neurobehavioural development in 2- to 24-month-old children from the ENVIR*ON*AGE birth cohort. Neurobehavioural development was assessed using the Ages and Stages Questionnaire (ASQ) and the Dutch version of the Bayley Scales of Infant and Toddler Development, Fourth Edition (Bayley-4-NL). ASQ associations were analysed using generalised additive mixed models with penalised thin plate regression splines and double penalisation. Gestational age was evaluated as a potential effect modifier. First-trimester exposure to $PM_{2.5}$ (β = -3.31, 95% CI: [-6.18; -0.45], p = 0.02) and PM_{10} (β = -1.99, 95% CI: [-4.00; 0.01], p = 0.03) was negatively associated with gross motor development. After adjustment for postnatal exposure, the association with $PM_{2.5}$ remained. Gestational age appeared to modify associations between prenatal air pollution exposure and fine motor and problem-solving skills. Age-specific analyses suggested that the strongest negative estimates were observed most often at 12 months. Bayley-4-NL analysis showed some positive associations that were not consistent with the ASQ findings. These results suggest that prenatal particulate matter exposure, particularly $PM_{2.5}$ during the first trimester, may impact early neurobehavioural development in infants. Larger studies are needed to confirm these findings and clarify underlying mechanisms.

INTRODUCTION

Air pollution is a global health crisis and the largest environmental threat to human health worldwide (1). 99% of people breathe air that exceeds the guideline limits of the World Health Organisation (WHO), while current European Union (EU) regulations still allow concentrations far above what is considered safe. As a result, 7.9 million deaths were attributed to air pollution in 2023 (2, 3).

Ambient air pollution consists of a complex mixture of particulate and gaseous pollutants and originates mainly from vehicle exhaust and industrial emissions (1, 4). Particulate matter and NO_2 are among the key air pollutants to be managed to prevent adverse health outcomes (1). Black carbon (BC) is a subfraction of particulate matter and is increasingly being recommended as an indicator of combustion-related air pollution exposure, although insufficient evidence exists to formulate guideline levels (3, 5). These different types of pollutants can give rise to overlapping yet distinct toxicological effects (6).

These diverse health effects are caused by the ability of air pollutants to induce oxidative stress and inflammation upon entering the body, and, for particulate matter, to penetrate deep into the lungs, evade local immune defences, and cross biological barriers (7-9). Particles are then taken up by the circulatory system and translocated throughout the body to major organs, where they accumulate and cause their toxic effects. Consequently, these particles have been found to accumulate in the human brain, as

well as on the foetal side of the human placenta, and even in the foetal brain (4, 7, 10, 11).

Prenatal exposure to these pollutants is of particular concern, given that various adverse birth outcomes have been consistently linked to ambient air pollution exposure in previous research, including small for gestational age, low birthweight, and preterm birth (12, 13). In addition, this type of exposure is thought to cause long-term health effects, which is in accordance with the Developmental Origins of Health and Disease hypothesis. This hypothesis states that environmental factors early in life shape the health of our adult life (14).

The developing brain, for instance, is especially susceptible to environmental disruption due to its plasticity, with neurodevelopment beginning in utero in the third gestational week and continuing rapidly throughout infancy (15). Neurobehavioural development comprises several interrelated domains, including cognitive, language, motor, and social-emotional development (16). These domains are some of the primary domains of healthy child development (17). As brain regions mature at different rates, environmental input across development is thought to be timing-dependent (18). In addition, because multiple biological mechanisms are involved in these maturation processes, these domains may differ in their susceptibility to air pollution exposure (19).

Accordingly, a recent systematic review reported consistent negative associations between exposure to particulate matter with an aerodynamic diameter under 2.5 μm ($PM_{2.5}$) and cognitive function, with prenatal and childhood exposure associated with declines in both verbal and nonverbal cognitive abilities in children that were on average 9 years of age (20).

Furthermore, epidemiological data from the ENVIRonmental influence ON AGEing (ENVIR*ON*AGE) birth cohort have shown that prenatal exposure interferes with early neurobehavioural development. A 5 μg/m³ increase in $PM_{2.5}$ concentration during the first trimester was associated with greater difficulties in irritability and transitions between sleep, wakefulness, and crying states in 1- to 2-month-old infants. An increase of the same magnitude in the second trimester was linked with abnormal prosocial behaviour in 4- to 6-year-old children (21). Similarly, a Chinese birth cohort found both $PM_{2.5}$ and NO_2 exposure to be associated with psychomotor developmental delay in 12-month-old infants, using the Chinese version of the Bayley Scales of Infant and Toddler Development (BSID). This association was observed for NO_2 in the first and third trimesters, as well as throughout the entire pregnancy. For $PM_{2.5}$, the association was only present in the second trimester (22). In contrast to the previously mentioned systematic review, no associations were observed with mental development, which entailed cognitive functioning, and personal, social, and language development. Consequently, findings regarding cognitive outcomes remain inconsistent (15, 22).

Although previous studies have reported associations between prenatal air pollution exposure and neurobehavioural development in children, the existing literature predominantly focuses on primary school children (23-25). Additionally, many studies investigated specific neurodevelopmental disorders, such as autism spectrum disorder, cerebral palsy, and tic disorders, rather than broader behavioural outcomes (21, 26-29).

Moreover, while gestational age is commonly included as a covariate in these studies, its role as a potential effect modifier has not been frequently explored (21, 24, 30). This is particularly relevant as infants born earlier are more vulnerable to environmental exposures, as prematurity is associated with underdeveloped organ systems and reduced capacity to cope with environmental insults. It is also linked to long-lasting cognitive and neurobehavioural impairments (31, 32). Given that preterm birth reflects disrupted foetal development, gestational age may modify how air pollution affects neurodevelopmental outcomes (31).

To address these knowledge gaps, this study aims to investigate the link between prenatal exposure to ambient air pollution and neurobehavioural development in infants aged 2 to 24 months in the ENVIR*ON*AGE birth cohort. In addition, this study aims to explore whether gestational age modifies these associations. Neurobehavioural development is assessed using the Dutch version of the Bayley Scales of Infant and Toddler Development, Fourth Edition (Bayley-4-NL) and the Ages and Stages Questionnaire® (ASQ), covering cognitive, language, motor, problem-solving, personal-social, and social-emotional domains. Exposure is defined as ambient concentrations of particulate matter with an aerodynamic diameter under 10 μm (PM_{10}), $PM_{2.5}$, NO_2, and BC.

Clarifying how prenatal exposure to air pollution is associated with differential neurobehavioural outcomes will advance scientific understanding of the effects of environmental pollution on early-life health and associated risks. Ultimately, these results may contribute to evidence-based policymaking and strategies to protect maternal and child health, with particular attention to vulnerable populations, such as early-term infants.

EXPERIMENTAL PROCEDURES

Study population and data collection – Data were collected through the ENVIR*ON*AGE birth cohort, an ongoing mother-child cohort based in Belgium. From February 2010 onwards, recruitment of mother-newborn pairs is carried out upon admission at the East-Limburg Hospital (Genk, Belgium) at the time of delivery. The cohort mostly comprises participants from Limburg, including urban, suburban, and rural areas. Mothers without planned caesarean section and able to complete extensive questionnaires in Dutch are included in the cohort after signing an informed consent form. Ethical approval was granted by the ethical committee of Hasselt University and the East-Limburg Hospital. Study protocols have been conducted in accordance with the ethical principles in the Helsinki Declaration. Detailed information on the recruitment of mother-child pairs has been reported elsewhere (33).

After delivery, lifestyle and socio-demographic data were collected through questionnaires and medical records. Detailed questionnaires were administered to obtain information on smoking status during gestation ("yes" or "no"), parity (primiparous, secundiparous, multiparous), ethnicity of the newborn (European in case of at least two European grandparents, otherwise non-European), and residential addresses. Household education was determined by the highest level of education of either the mother or the father (low, middle, high for "no diploma or primary school", "secondary school", or "college or university", respectively) as a proxy for socio-economic status. From medical records, the newborn's sex ("boy" or "girl"), date of delivery, maternal age, gestational age, and pre-pregnancy BMI (kg/m^2) were acquired. Maternal pre-pregnancy BMI was captured between the seventh and ninth week of gestation at the first antenatal visit. If missing from the medical record, pre-pregnancy BMI was derived from self-reported pre-pregnancy height and weight at delivery. To determine gestational age, the date of conception was estimated using the ultrasound imaging and the mother's last menstrual period. The season of delivery was categorised into meteorological seasons as "spring" (March 1st - May 31st), "summer" (June 1st - August 31st), "autumn" (September 1st - November 30th), or "winter" (December 1st - February 28th or 29th).

Neurobehavioural assessment – At 2, 6, 12, and 24 months of age, the ASQ was applied to assess early neurobehavioural development in the participating infants. The ASQ is a parent-administered questionnaire tailored to the infant's age, which is designed to assess communication, gross motor, fine motor, problem-solving, and personal-social skills through observation. This questionnaire is validated and widely used as a developmental screening tool across diverse populations for children aged 1 to 66 months (34). The ASQ, Third Edition (ASQ-3) consists of 30 items, grouped by developmental area, each scored on three levels ("yes", "sometimes", "not yet"). For each domain of the ASQ-3, the total ranges from 0 to 60, with higher scores indicating better developmental performance. For the ASQ: Social-Emotional-2 (ASQ:SE-2), social-emotional development scores range from 0 to 240, 345, 405, and 465, for the 2-, 6-, 12-, and 24-month questionnaires, respectively. In contrast to the ASQ-3, lower ASQ:SE-2 scores indicate better social-emotional development (35). For each of the six domains, a cutoff was predetermined and used to identify children requiring monitoring or showing signs of developmental delay (36).

In addition, during a house visit, neurobehavioural development was assessed at 6 months of age using the Bayley-4-NL. The Bayley-4-NL is a standardised and widely used measure that assesses cognition, language, and motor skills in 264 items to evaluate the risk of developmental delays and disorders in children aged 16 days to 42 months. The test was conducted by trained professionals, using structured and observation tasks based on established age-specific norms. Composite scores are determined based on age-specific normative data for the cognitive, language, and motor scales, yielding standardised scores with a mean of 100 (37, 38).

Air pollution exposure assessment – This study utilised a spatial-temporal interpolation method (detrended kriging) to estimate ambient air pollution levels around the maternal residence during the pre- and postnatal periods. The mother's residential addresses obtained via questionnaire were geocoded using QGIS v3.44.8. Briefly, ambient $PM_{2.5}$, PM_{10}, NO_2, and BC were determined using measurement data from fixed monitoring stations in the area combined with the CORINE land-cover dataset. RIO model performance has been evaluated using leave-one-out cross-validation based on Belgian monitoring stations (39, 40). Daily residential exposure was calculated in a 4 km x 4 km grid and converted to means for each trimester to explore critical exposure windows, as well as for the entire pregnancy period. Trimester-specific exposure windows were defined as 90-day intervals corresponding approximately to gestational weeks 1-13, 14-26, and 27-39. Whole-pregnancy exposure was calculated from conception until delivery. For postnatal exposure, monthly estimates were averaged into whole-period means from the first day of life up to each follow-up age category, as defined above. In the event of multiple addresses during the postnatal period, the average was calculated, assuming equal amounts of time spent at all addresses.

Statistical analysis – Statistical analyses were performed using R software v4.4.0. Continuous variables included maternal age at delivery, pre-pregnancy BMI, gestational age, age at follow-up with the Bayley-4-NL, ASQ domain scores, and Bayley-4-NL index scores, and were depicted as mean ± standard deviation (SD) for descriptive analysis. Categorical variables were household education, parity, smoking during pregnancy, season of delivery, the newborn's sex, ethnicity, age at follow-up with the ASQ, and developmental classification, and were expressed as quantities with corresponding frequencies (%).

The median, Q1, Q3, minimum, and maximum air pollution levels were calculated for each pollutant and exposure window separately and are contained in boxplots. Upon visual inspection of the residual and QQ plots, trimester means were compared on a significance level of 0.05 using repeated-measures ANOVA with Greenhouse-Geisser correction. Subsequent post hoc analyses were performed using paired t-tests, of which p-values were adjusted using the Benjamini-Hochberg False Discovery Rate (FDR) procedure.

Due to the non-normality of several outcome measures, Spearman's rank correlation coefficients were calculated to explore associations between each pollutant exposure window and the mean ASQ domain score across available follow-up time points.

Associations between prenatal air pollution exposure and neurobehavioural outcome domains, as measured with the ASQ, were investigated using generalised additive mixed models (GAMMs) assuming a Gaussian distribution. A child-specific random intercept was included to account for within-subject correlation across repeated outcome assessments. As visual inspection of residuals versus fitted plots and preliminary GAMMs indicated potential non-linearity in several associations, pollutants were modelled using penalised thin plate regression splines with shrinkage and double penalisation, allowing unsupported smooth terms to be shrunk towards zero, thereby reducing the risk of overfitting. Smooth terms for the exposure variables were fitted with a restricted basis dimension ($k = 4$), whereafter basis dimension adequacy was assessed. Subsequently, smooth terms with estimated degrees of freedom (edf) above 1 were visually inspected to evaluate non-linearity. Sensitivity analyses were performed using the same GAMM approach, additionally adjusting for whole-period postnatal exposure to the corresponding pollutant, to evaluate whether associations with prenatal exposure were independent of postnatal exposure. Thereafter, an interaction term between gestational age and prenatal air pollution was added to assess whether the association between exposure and outcome differed by gestational age using the same modelling approach mentioned above.

As a complementary exploratory analysis, age-specific GAMMs were fitted to examine whether the association between air pollution exposure windows and ASQ domain scores differed across follow-up ages. These models were run for each pollutant-domain combination, wherein age-specific smooths were fitted using an interaction between exposure and age. Age-specific average slopes were extracted to summarise the estimated direction and magnitude of associations at each follow-up age.

Associations between prenatal air pollution exposure and index scores for cognition, language, and motor skills obtained with the

Bayley-4-NL were explored using linear models.

Model assumptions were evaluated by visual inspection of residual and QQ plots. Covariates were selected *a priori* based on literature and Directed Acyclic Graphs (Supplementary Fig. S1). ASQ models were adjusted for categorical age at follow-up, sex, ethnicity of the newborn, season of delivery, gestational age, household education, parity, pre-pregnancy BMI, maternal age, and smoking during pregnancy. Bayley-4-NL models included the same covariates, except that age at follow-up was included as a continuous variable because these outcomes were assessed at a single follow-up around 6 months. Trimester-specific models were mutually adjusted for each other to account for the correlation between exposure windows. P-values from all models, except the age-specific models, were corrected using the FDR procedure.

RESULTS

Population characteristics – In this study, a total of 193 participants were included. One participant was excluded due to a known neurodevelopmental disorder. A flow chart of the recruitment and selection process is provided in Supplementary Fig. S2. Mode imputation was used for nine participants with missing covariate data (household education, ethnicity, and smoking during pregnancy). General characteristics of the study population are described in Table 1. Mothers were on average 31.2 ± 3.8 years old at delivery and had a pre-pregnancy BMI of 25.4 ± 5.3 kg/m². The most common household education level was high (82%). Most mothers were primiparous (67%). Autumn was the season with the most deliveries (30%). Few mothers smoked during pregnancy (3.1%). Infants had an average gestational age of 275 ± 9 days, and sex was nearly evenly distributed, with a slight predominance of girls (50%). Vastly more children were of European descent (96%). Follow-up ages corresponded closely to the intended 2-, 6-, 12-, and 24-month assessment windows. Population characteristics for the subfraction of participants followed up with the Bayley-4-NL are presented in Supplementary Table S1.

Mean ± SD of ASQ-3 and ASQ:SE-2 scores for each domain at each assessment were calculated and presented in Table 2. The proportion of children scoring below the ASQ-3 cutoff values or above the ASQ:SE-2 cutoff values at each follow-up are shown in Supplementary Table S2 as n (%). The highest proportion of scores indicating the need for monitoring or possible delay was observed at the 2-month follow-up for all domains, except for gross motor, where the highest proportion was observed at 12 months. Thereafter, proportions were generally lower, without a clear temporal pattern across domains.

Table 1 – Population characteristics of participants included in the assessment of neurobehavioural development using the ASQ (n = 193).

Characteristic	Mean ± SD or n (%)
Maternal	
Age at delivery (years)	31.2 ± 3.8
Pre-pregnancy BMI	25.4 ± 5.3
Household education	
Low	3 (1.6%)
Middle	32 (17%)
High	158 (82%)
Parity	
Primiparous	130 (67%)
Secundiparous	46 (24%)
Multiparous	17 (8.8%)
Smoking during pregnancy	
No	187 (97%)
Yes	6 (3.1%)
Season of delivery	
Winter	51 (26%)
Spring	40 (21%)
Summer	44 (23%)
Autumn	58 (30%)
Infant	
Gestational age (days)	275 ± 9
Sex	
Male	96 (50%)
Female	97 (50%)
Ethnicity	
Non-European	7 (3.6%)
European	186 (96%)
Age at ASQ (days)	
2 months	57 ± 10
6 months	181 ± 13
12 months	363 ± 16
24 months	732 ± 22

ASQ: Ages and Stages Questionnaire, SD: standard deviation, BMI: body mass index (kg/m²)

Air pollution exposure – Residential air pollution exposure distributions are shown by trimester and for the whole pregnancy period for each pollutant in Figure 1. Boxplots display the median, interquartile range, minimum, and

maximum exposure values, while black dots indicate the mean exposure. Descriptive statistics for these exposure distributions are contained in Supplementary Table S3.
Significant differences were found between the means of trimester 1 and 3 (adjusted $p < 0.001$), trimester 1 and 2 (adjusted $p = 0.04$), and trimester 2 and 3 (adjusted $p < 0.01$) for residential PM_{10}. For residential $PM_{2.5}$, significant differences were present between trimester 1 and 3 (adjusted $p = 0.03$).

Exposure-outcome associations – Whole-pregnancy exposure estimates were mostly moderately to strongly positively correlated across pollutants, as displayed in Figure 2. In addition, whole-pregnancy estimates were correlated with trimester-specific estimates, particularly within the same pollutant. Cross-pollutant correlations between trimester-specific exposure windows were slightly less consistent. Overall, neurobehavioural outcomes tended to be weakly to moderately negatively correlated with prenatal air pollution exposure estimates. Negative correlations were most apparent for gross motor, fine motor, and problem-solving scores. In contrast, correlations with communication and social-emotional scores were weaker or less consistent, and personal-social scores showed negative correlations only for some pollutants.

Associations between each exposure window and domain were estimated with GAMMs and are depicted with unadjusted p-values in forest plots (Fig. 3A). Detailed model estimates, 95% confidence intervals (CI), p-values before and after correction with the FDR procedure are provided in Supplementary Table S4.

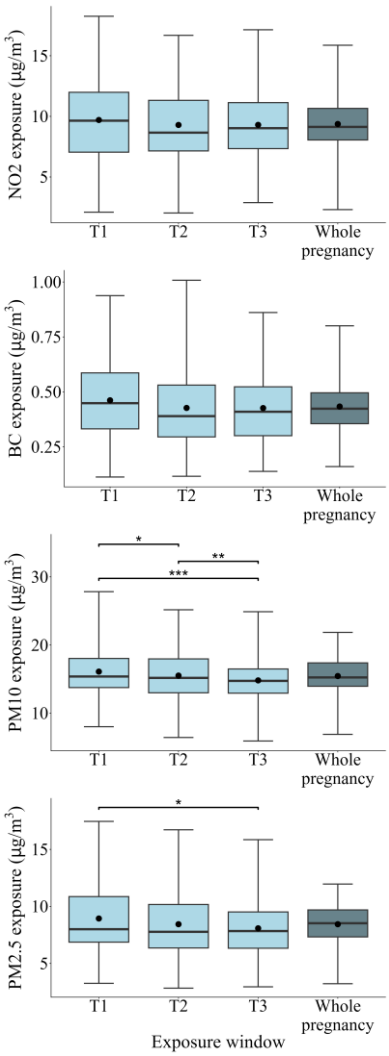


Figure 1 – Air pollution exposure per time window. Exposure to NO_2, BC, PM_{10}, and $PM_{2.5}$ (µg/m³) was estimated using a spatiotemporal interpolation method (detrended kriging) for each trimester and the whole pregnancy. The median, interquartile range, minimum, and maximum exposure are depicted, with the mean indicated as a dot. Significant differences between trimesters were found using the paired t-test. n = 193. **p<0.05; **p<0.01; ***p<0.001. T1-3: trimester 1-3, BC: black carbon, PM_{10}: particulate matter <10 µm, $PM_{2.5}$: particulate matter <2.5 µm.*

Table 2 – **ASQ total scores for each neurobehavioural domain.** Communication, gross motor, fine motor, problem-solving, and personal-social skills were evaluated with the ASQ, Third Edition, in which higher scores indicate better performance. Social-emotional skills were assessed using the ASQ: Social-Emotional, where lower scores indicate better development. Infants were assessed at 2, 6, 12, and 24 months of age. Scores are presented as mean ± standard deviation.

Age	Com	n	GM	n	FM	n	ProbSolv	n	PersSoc	n	SocEmo	n
2	41 ± 13.5	109	51.7 ± 8.2	109	43 ± 9.3	108	42.3 ± 12.1	106	43.1 ± 8.6	106	26.7 ± 19.2	105
6	48.1 ± 8.8	89	37.8 ± 11.9	88	48.9 ± 10.8	88	50.3 ± 9.4	88	41.9 ± 13.3	88	20.9 ± 13.4	85
12	48.5 ± 10.5	51	37.4 ± 19	51	52.1 ± 6.9	51	48 ± 10.4	49	44.2 ± 8.9	49	24 ± 11.1	49
24	54.4 ± 6.8	54	53.2 ± 7.7	54	50.2 ± 8	53	46.3 ± 9.6	53	50.5 ± 7.4	53	31.3 ± 18.1	52

ASQ: Ages and Stages Questionnaire, Com: communication, GM: gross motor, FM: fine motor, ProbSolv: problem-solving, PersSoc: personal-social, SocEmo: social-emotional.

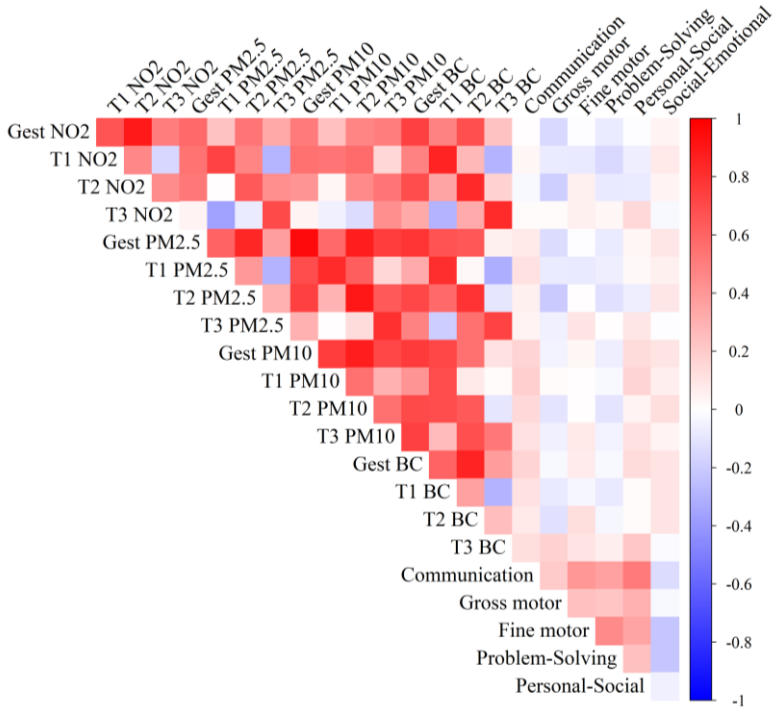


Figure 2 – Correlation of air pollution exposures and ASQ neurobehavioural total scores. Spearman's rank correlation coefficients were calculated to explore associations between exposure windows for each pollutant and the neurobehavioural outcome domains, as measured with ASQ. ASQ domain scores represent the participant-specific mean total score across available assessment ages. n = 193.
ASQ: Ages and Stages Questionnaire, T1-3: trimester 1-3, Gest: gestational, BC: black carbon, PM_{10}: particulate matter <10 µm, $PM_{2.5}$: particulate matter <2.5 µm.

Overall, the automated shrinkage mixed pipeline supported structural linearity for prenatal air pollution across the four evaluation timepoints (edf = 1.00). Across models, the edf values of the pollutant smooths were generally close to 1, indicating approximately linear exposure-response functions. Therefore, average marginal effects were presented as beta estimates per 5 µg/m³ increase for NO_2, $PM_{2.5}$, and PM_{10}, and per 0.1 µg/m³ increase for BC.

Gross motor scores were negatively associated with exposure to PM_{10} (β = -1.99, 95% CI: [-4.00; 0.01], p = 0.03) as well as to $PM_{2.5}$ (β = -3.31, 95% CI: [-6.18; -0.45], p = 0.02) in the first trimester. However, these associations did not remain statistically significant after correction with the FDR procedure. Although several other larger effect estimates were observed for $PM_{2.5}$ and PM_{10} in relation to gross motor, problem-solving, and social-emotional scores, these associations were not statistically significant. For several exposure-outcome combinations, particularly for communication, personal-social scores, and some third-trimester exposure windows, estimates were shrunk towards zero, suggesting little evidence for an association.

The same modelling approach was applied including gestational age as an interaction term to assess whether this covariate modified exposure-outcome associations. Estimates were visualised in forest plots with unadjusted p-values (Fig. 3B). Detailed model estimates, CI, and FDR-corrected p-values are provided in Supplementary Table S5. In these interaction models, first-trimester exposure x gestational age interaction terms were negatively associated with problem-solving scores for NO_2 (β = -0.35, 95% CI: [-0.67; -0.02], p = 0.04), $PM_{2.5}$ (β = -0.37, 95% CI: [-0.68; -0.06], p = 0.02), PM_{10} (β = -0.31, 95% CI: [-0.56; -0.06], p = 0.02) and BC (β = -0.11, 95% CI: [-0.22; 0.00], p = 0.05). For fine motor scores, significant associations with PM_{10} were observed in opposite directions for trimester 1 (β = -0.25, 95% CI: [-0.48; -0.03], p = 0.03) and trimester 2 (β = 0.21, 95% CI: [0.02; 0.40], p = 0.03). These significant associations also did not remain after FDR correction. In contrast to the main GAMM models, where several pollutant smooths were shrunk towards zero, the linear exposure x gestational age interaction terms generally yielded nonzero estimates across exposure windows and developmental domains.

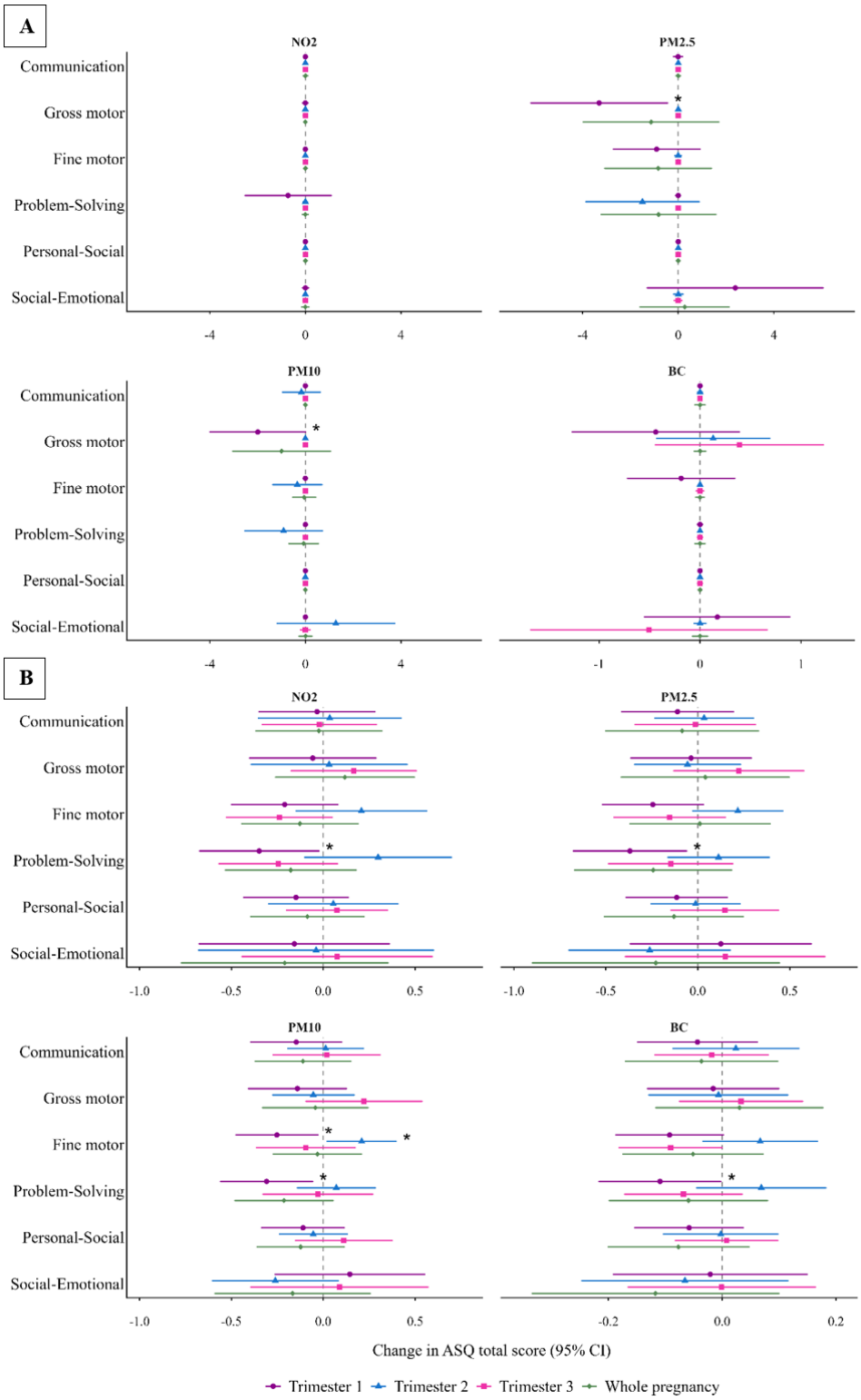


Figure 3 – The association between prenatal air pollution exposure and ASQ total scores. Estimates are given as a change in ASQ total scores for a 5 µg/m³ increase in $PM_{2.5}$, PM_{10}, and NO_2 concentration, and a 0.1 µg/m³ increase in BC. Generalised additive mixed models using penalised thin plate regression splines and double penalisation were used and adjusted for categorical age at follow-up, sex, ethnicity of the newborn, season of delivery, gestational age, household education, parity, pre-pregnancy BMI, maternal age, and smoking during pregnancy. Trimester-specific models were mutually adjusted for each other. Panel A shows the main models. B shows corresponding models including gestational age as an interaction term with prenatal air pollution exposure. n = 193. **p<0.05, ASQ: Ages and Stages Questionnaire, CI: confidence interval, BC: black carbon, PM_{10}: particulate matter <10 µm, $PM_{2.5}$: particulate matter <2.5 µm.*

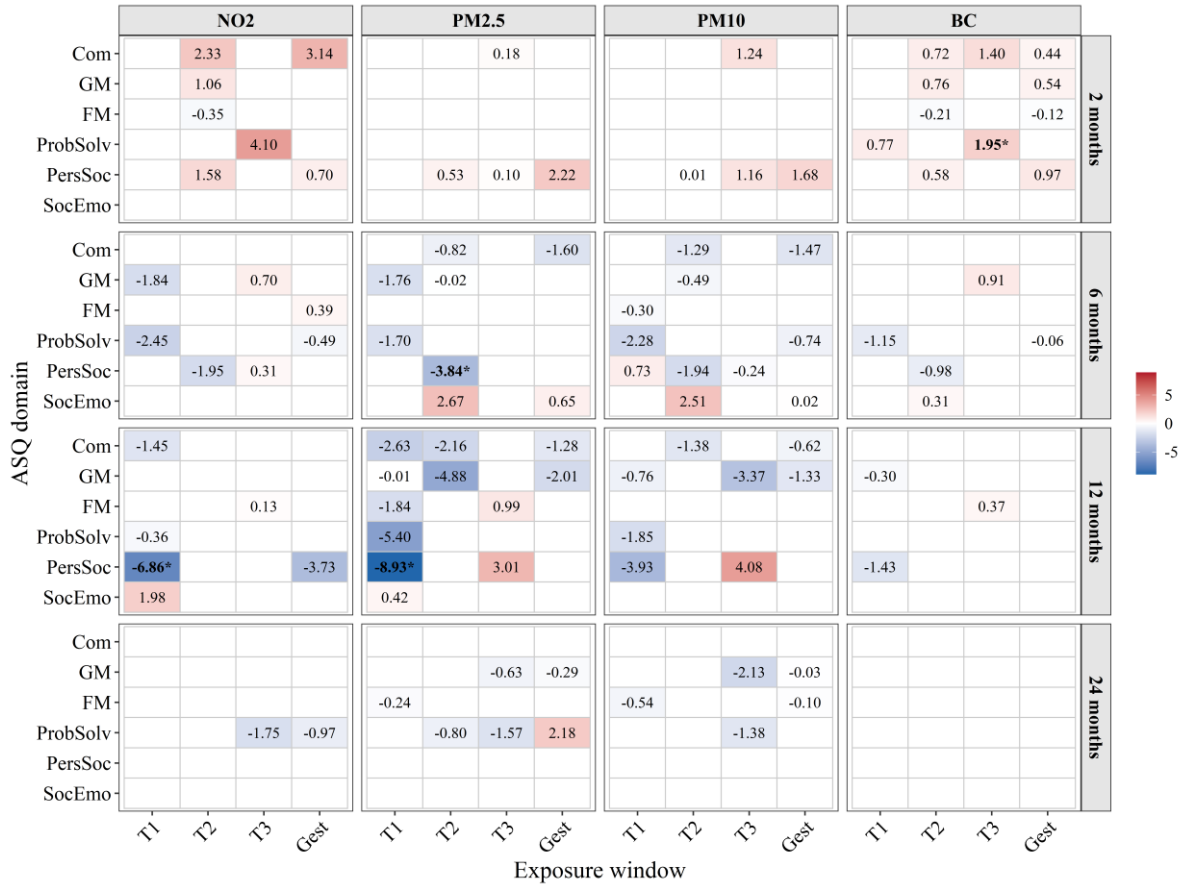


Figure 4 – **Age-specific associations between air pollution exposure windows and ASQ domains.** To explore how associations differed across follow-up ages, generalised additive mixed models with double penalisation and thin plate regression splines, and age-specific smooths using an interaction between exposure and age were fitted for the different prenatal air pollution exposure windows. Models were adjusted for categorical age at follow-up, sex, ethnicity of the newborn, season of delivery, gestational age, household education, parity, pre-pregnancy BMI, maternal age, and smoking during pregnancy. Estimates were provided as a change in score per 5 µg/m³ increment in air pollution concentration for NO_2, $PM_{2.5}$, and PM_{10}, and 0.1 µg/m³ for BC. Blank cells indicate beta estimates with absolute values <0.01. n = 193. **p<0.05, ASQ: Ages and Stages Questionnaire, BC: black carbon, PM_{10}: particulate matter <10 µm, $PM_{2.5}$: particulate matter <2.5 µm, Com: communication, GM: gross motor, FM: fine motor, ProbSolv: problem-solving, PersSoc: personal-social, SocEmo: social-emotional, T1-3: trimester 1-3, Gest: gestational.*

Furthermore, exploratory age-specific models were fitted to examine whether the estimated associations between whole-pregnancy air pollution exposure and ASQ scores appeared stronger at specific follow-up ages (Fig. 4). The strongest negative estimates were observed most often at 12 months, although no consistent pattern was observed across pollutants, exposure windows, or ASQ domains. A limited number of age-specific negative associations reached statistical significance. These included second-trimester $PM_{2.5}$ exposure with personal-social scores at 6 months (β = -3.84, 95% CI: [-7.39; -0.30], p = 0.03), and first-trimester NO_2 (β = -6.86, 95% CI: [-11.99; -1.74], p = 0.01) and $PM_{2.5}$ (β = -8.93, 95% CI: [-17.02; -0.84], p = 0.03) exposure with personal-social scores at 12 months. In addition, one positive association was significant between third-trimester BC exposure and problem solving at 2 months (β = 1.95, 95% CI: [0.23; 3.66], p = 0.03). Several other estimates were close to zero. Nonzero age-specific beta estimates with corresponding CI and p-values are presented in Supplementary Table S6.

In contrast to the negative patterns in the ASQ analyses, Bayley-4-NL language scores were positively associated with $PM_{2.5}$ (β = 4.49, 95% CI: [0.62; 8.35], p = 0.03) and PM_{10} (β = 5.26, 95% CI: [2.01; 8.51], p < 0.01) in the linear models, although proving not to be robust after FDR correction (Table 3). Detailed model estimates, CI, p-values, and FDR-corrected p-values are provided in Supplementary Table S7.

Table 3 – Associations between prenatal air pollution exposure and Bayley Scales of Infant and Toddler Development index scores (n = 39). Neurobehavioural development was evaluated in three domains, cognition, language, and motor skills, in 6-month-old infants. Linear models were adjusted for age at follow-up, sex, ethnicity of the newborn, season of delivery, gestational age, household education, parity, pre-pregnancy BMI, maternal age, and smoking during pregnancy. Trimester-specific models were mutually adjusted for each other. Estimates were provided as a change in score per 5 μg/m³ increment in air pollution concentration for NO_2, $PM_{2.5}$, and PM_{10}, and 0.1 μg/m³ for BC.

		NO_2		$PM_{2.5}$		PM_{10}		BC	
Domain	Window	β [95% CI]	p	β [95% CI]	p	β [95% CI]	p	β [95% CI]	p
Cog	T1	-4.39 [-12.82; 4.04]	0.29	-3.15 [-9.44; 3.14]	0.31	-3.24 [-8.98; 2.49]	0.25	-0.69 [-3.56; 2.17]	0.62
	T2	3.74 [-10.70; 18.18]	0.60	2.69 [-8.49; 13.86]	0.62	1.67 [-6.34; 9.68]	0.67	0.75 [-3.40; 4.91]	0.71
	T3	-0.86 [-14.40; 12.68]	0.90	0.26 [-11.71; 12.23]	0.96	1.32 [-6.40; 9.04]	0.73	0.90 [-4.00; 5.80]	0.71
	Gest	-1.72 [-10.83; 7.39]	0.70	-0.65 [-10.60; 9.30]	0.89	-0.63 [-7.49; 6.23]	0.85	0.83 [-3.43; 5.09]	0.69
Lan	T1	3.00 [-2.49; 8.49]	0.27	4.49 [0.62; 8.35]	**0.02**	5.26 [2.01; 8.51]	**0.00**	1.18 [-0.67; 3.02]	0.20
	T2	0.24 [-9.16; 9.64]	0.96	-3.69 [-10.56; 3.18]	0.28	-4.23 [-8.77; 0.31]	0.07	-0.44 [-3.12; 2.24]	0.74
	T3	0.51 [-8.31; 9.32]	0.91	2.38 [-4.98; 9.74]	0.51	1.13 [-3.24; 5.51]	0.60	-0.58 [-3.74; 2.58]	0.71
	Gest	3.71 [-2.20; 9.62]	0.21	3.35 [-3.15; 9.85]	0.30	2.50 [-1.97; 6.96]	0.26	0.20 [-2.65; 3.05]	0.89
Mot	T1	-6.07 [-14.95; 2.81]	0.17	-2.19 [-9.12; 4.74]	0.52	-0.83 [-7.22; 5.55]	0.79	-1.31 [-4.39; 1.77]	0.39
	T2	10.92 [-4.29; 26.13]	0.15	2.12 [-10.19; 14.44]	0.73	-1.15 [-10.07; 7.76]	0.79	2.47 [-2.00; 6.93]	0.27
	T3	-4.60 [-18.86; 9.66]	0.51	0.40 [-12.79; 13.59]	0.95	1.53 [-7.06; 10.12]	0.72	-1.42 [-6.68; 3.85]	0.58
	Gest	0.39 [-9.53; 10.32]	0.94	-0.41 [-11.22; 10.40]	0.94	-0.95 [-8.39; 6.50]	0.80	0.39 [-4.24; 5.03]	0.86

p<0.05 are highlighted in bold, CI: confidence interval, T1-3: trimester 1-3, Gest: gestational, BC: black carbon, PM_{10}: particulate matter <10 μm, $PM_{2.5}$: particulate matter <2.5 μm, Cog: cognition, Lan: language, Mot: motor.

Sensitivity analyses – A sensitivity analysis additionally adjusting for postnatal air pollution exposure showed partial consistency with the main GAMM results. In the whole-pregnancy models, an additional significant association was observed between $PM_{2.5}$ exposure and lower problem-solving scores (β = -3.68, 95% CI: [-7.68; 0.33], p = 0.04) before correction of the p-values. In the trimester-specific models, the association between first-trimester $PM_{2.5}$ exposure and gross motor scores (β = -3.62, 95% CI: [-6.72; -0.53], p = 0.01) remained consistent with the main analysis. However, the postnatal-adjusted trimester models also showed some deviation from the main findings, with additional significant associations observed between second-trimester PM_{10} exposure and communication scores (β = -1.86, 95% CI: [-3.73; 0.01], 0.03), and between problem-solving scores and both second-trimester $PM_{2.5}$ (β = -2.63, 95% CI: [-5.44; 0.19], p = 0.04) and PM_{10} exposure (β = -2.07, 95% CI: [-4.10; -0.04], p = 0.03). These associations did not remain statistically significant after FDR correction (Supplementary Table S8).

DISCUSSION

This study found evidence of negative associations between prenatal exposure to particulate matter and neurobehavioural development in early childhood, particularly for gross motor development. In the main analysis, first-trimester exposure to $PM_{2.5}$ and PM_{10} was negatively associated with gross motor scores. Sensitivity analyses adjusting for postnatal exposure suggested that these associations were only partly independent of postnatal air pollution exposure. The association with first-trimester PM_{10} was no longer significant, whereas the associations with first-trimester $PM_{2.5}$ remained. Moreover, gestational age appeared to modify associations between prenatal air pollution exposure and fine motor and problem-solving skills. For fine motor skills, the interaction effect size was negative for first-trimester PM_{10}, and positive for second-trimester PM_{10}. For problem-solving, the interaction effect sizes were negative for all pollutants. This suggests that gestational age may influence susceptibility to prenatal air pollution exposure. Finally, exploratory age-specific analyses suggested that the estimated associations may differ across follow-up ages, with the strongest negative estimates observed at 12 months, especially between first-trimester NO_2 and $PM_{2.5}$, and personal-social skills.

These associations were observed at mean air pollution levels of 15.45 μg/m³, 8.44 μg/m³, 9.37 μg/m³, and 0.43 μg/m³ for PM_{10}, $PM_{2.5}$, NO_2, and BC, respectively. These levels are far

below the EU air quality standards, which are at 40 µg/m³ for PM_{10} and NO_2, and 20 µg/m³ for $PM_{2.5}$ annually (41). Specific air quality standards for BC do not yet exist, as the WHO states that insufficient quantitative evidence is currently available to derive air quality guideline levels for this type of pollutant (3). Consequently, the observation of associations at low exposure levels supports the need for stricter air quality standards to safeguard public health.

Early childhood represents a critical period for brain development, with developmental processes during this period forming an important foundation for later cognitive, motor, adaptive, and behavioural functioning (42). In this study, these aspects were assessed using the ASQ, which evaluates six developmental domains. For each domain, except for social-emotional skills, higher scores indicate better performance (35). The findings of this study suggest slower gross motor development in association with prenatal air pollution exposure during the first trimester. In addition, gestational age appeared to modify the associations between prenatal air pollution exposure and fine motor and problem-solving skills, particularly for exposures during the first and second trimester.

A biological explanation for the associations observed in this study is plausible. Previous research has demonstrated the presence of black carbon particles at the foetal side of the placenta and in the foetal brain from the first trimester onwards (10, 11). Since the formation of neural circuits and the proliferation of neuroblasts begin as early as the first trimester, and neural circuits form the basis of both simple functions and more complex neurobehavioural functioning, environmental insults during this period may interfere with neurodevelopment (43, 44). Furthermore, cerebellar neurogenesis starts around the eighth week postconception, which may explain why motor-related domains, including gross and fine motor skills, could be affected during the first trimester (45). Therefore, the timing of exposure may be important in determining which parts of neurodevelopment are most affected.

Air pollution may affect neurodevelopment mainly through systemic inflammation (46). Systemic inflammation can lead to microglial activation, oxidative stress, and neuroinflammation, subsequently resulting in neurotoxicity (46). This neurotoxicity could then interfere with neurodevelopment in infants. Additionally, systemic inflammation may increase the permeability of the blood-brain barrier, allowing the smallest subfraction of $PM_{2.5}$ to enter the brain and cause more toxicity (46).

Gestational age may further influence these associations by reflecting differences in foetal maturity and developmental vulnerability at birth (47). In the long term, preterm infants are inherently at increased risk of neurodevelopmental impairment, including impairments in cognition and motor skills (31, 48). In this study, gestational age appeared to modify several associations between prenatal air pollution exposure and neurobehavioural outcomes, particularly for problem-solving, which reflects aspects of cognitive development, and fine motor skills. This may indicate that the role of gestational age varies across developmental domains.

Previous studies using the ASQ to assess neurobehavioural development have also reported associations with prenatal air pollution exposure. Overall, the previous studies suggest that prenatal $PM_{2.5}$ exposure may be associated with lower ASQ scores across the developmental domains that are most commonly assessed, namely gross motor, fine motor, communication, problem-solving, and personal-social skills. However, studies differ in whether the strongest associations are found for gross motor, fine motor, communication, problem-solving, or personal-social domains (49-52). In addition, uncertainty remains regarding sensitive exposure windows. Previous studies provide conflicting evidence regarding the most sensitive exposure window for motor development, with reported associations varying across the first, second, third, and all trimesters (49-51). While sensitive prenatal exposure windows have been examined in several studies, fewer studies have investigated whether associations with ASQ scores differ according to the child's age at assessment. One other birth cohort study reported that whole-pregnancy $PM_{2.5}$ exposure was associated with lower ASQ scores at 2, 6, and 24 months for communication, gross motor, and personal-social scores, while no significant associations were observed at 12 months. This contrasts with the exploratory age-specific findings of the present study, in which the strongest negative estimates were observed most often at 12 months. The findings of the present study are therefore partly consistent with previous research, particularly regarding the involvement of motor development.

Evidence from studies on prenatal smoke exposure also supports the relevance of prenatal exposure to airborne pollutants. A study investigating active and passive smoking during pregnancy in relation to ASQ scores found that the percentage of infants showing signs of developmental delay was significantly higher among smoke-exposed children than among non-exposed children for most psychomotor aspects (24). Correspondingly, a study in mice found negative effects of second-hand smoking during pregnancy on offspring neurodevelopment, specifically in hyperactivity, working memory, and emotional processing. The study concluded that these effects were primarily attributable to exposure to smoke itself rather than nicotine alone, suggesting that the harmful effects cannot be explained solely by nicotine exposure (53).

Findings from studies using other neurobehavioural assessment tools also support a possible association between prenatal air pollution exposure and early motor or behavioural development, although the evidence remains heterogeneous. Studies assessing neurobehavioural development in neonates shortly after delivery reported associations between prenatal air pollution markers and motor difficulties, including hypotonia, active tone, and passive tone (54, 55). Another study in infants aged 1 to 2 months, using the Neonatal Behavioural Assessment Scale, found first-trimester $PM_{2.5}$ exposure to be associated with lower range-of-state scores, reflecting aspects such as irritability and lability of state changes (21). In older children, evidence is less consistent. Some studies reported associations between prenatal particulate matter or NO_2 exposure and behavioural problems, including peer problems, abnormal behaviour and delinquent behaviours, while other studies reported fewer overall problems in association with prenatal $PM_{2.5}$ exposure (21, 56, 57).

Long-term implications of the findings of this study remain uncertain. However, previous research suggests that early developmental differences identified by the ASQ may be relevant for later developmental functioning (58-60). Longitudinal studies using this instrument have found significant correlations between early developmental assessment and later cognitive performance (58). One study found that differences in both motor skills and communication skills in infancy were predictive of cognitive abilities at school age, particularly working memory and processing speed (59). Additionally, systematic reviews suggest that all ASQ domains may be significant predictors of later cognitive difficulties (58, 60).

The BSID is considered the gold standard for assessing developmental functioning in young children (61). However, in this study, the Bayley-4-NL sample size was too small to consider these findings conclusive. In contrast to the ASQ analyses, the Bayley-4-NL analyses showed some significant estimates in a positive direction for language scores. Given the smaller Bayley-4-NL sample size and the use of simpler linear models to limit model complexity, these findings may reflect limited statistical power and instability.

This research has several strengths. Firstly, a validated spatial-temporal interpolation method, which has been used in previous studies, was used to obtain ambient air pollution estimates (62). Second, two independent methods were used to assess neurobehavioural development: the ASQ and the Bayley-4-NL. The ASQ is an accurate screening tool that has shown high sensitivity and specificity for detecting developmental delay, while the BSID is viewed as the gold standard for screening developmental functioning in young children (42, 61, 63). Third, the inclusion of several air pollution indicators provided a broader assessment of prenatal exposure than studies focusing on a single pollutant. Next, the use of repeated neurobehavioural assessments across early childhood is a strength, as it allowed developmental outcomes to be followed up across the first two years of life. Finally, the use of GAMMs allowed potential non-linear exposure-response relationships to be explored, avoiding the assumption that associations between prenatal air pollution and neurobehavioural outcomes were strictly linear.

This study also has some limitations. First of all, because high-resolution air pollution estimates were not available, exposure estimates were calculated for 4 km x 4 km grids. Therefore, local exposure contrasts, such as near busy roads, as well as meteorological influences, may not have been fully captured. Furthermore, the sample size at later time points of the ASQ was limited due to loss to follow-up. Consequently, although multiple pollutants were included in this study, pollutants were modelled separately due to limited power for more complex models. Third, the sensitivity analyses indicated that some associations were attenuated or no longer

statistically significant after adjustment for postnatal exposure, suggesting that prenatal and postnatal exposure effects could not be fully separated. Also, the smaller Bayley-4-NL sample size limited the interpretation of the Bayley-4-NL results, particularly because simpler linear models had to be used to limit model complexity. Lastly, although all models were adjusted for a variety of covariates, residual confounding is possible.

The present study contributes to the existing literature by examining multiple prenatal exposure windows, several air pollution indicators, and repeated neurobehavioural assessments within the first two years of life. In addition, the inclusion of gestational age as an effect modifier provided additional insight into whether susceptibility to prenatal air pollution exposure differed according to foetal maturity and developmental vulnerability at birth. The results add to the evidence that prenatal air pollution exposure may influence early neurobehavioural development and that susceptibility may differ according to both exposure timing and child-related vulnerability.

From a public health perspective, these findings suggest that prenatal air pollution exposure is relevant for early child development even at concentrations below current regulatory standards. This is important because pregnant women and young children cannot control their environmental exposures themselves. Therefore, reducing air pollution exposure during pregnancy should be a societal and policy priority.

Future research should build on these findings by using larger birth cohorts with sufficient follow-up across multiple developmental stages. This would make it possible to investigate whether early differences in ASQ scores persist, disappear, or develop into more pronounced behavioural difficulties later in childhood. In addition, specific exposure thresholds that are protective of neurodevelopment still need to be identified, as the present findings suggest that associations may occur even at exposure levels below current EU air quality standards. Finally, mechanistic research is needed to clarify how prenatal exposure to particulate matter and combustion-related pollutants may interfere with foetal brain development.

CONCLUSION

In conclusion, this study found evidence suggesting that prenatal exposure to particulate matter, particularly $PM_{2.5}$ during the first trimester, may be negatively associated with gross motor development in early childhood. In addition, gestational age appeared to modify associations between prenatal air pollution exposure and fine motor and problem-solving skills. These findings were observed at air pollution levels below current EU air quality standards, highlighting the relevance of low-level prenatal exposure. Future research in larger study populations is needed to confirm these findings, identify exposure thresholds that are protective of neurodevelopment, and clarify the mechanisms linking prenatal air pollution exposure to early neurobehavioural development.

REFERENCES

1. Atkinson R, Bardach A, Chen J, Ciapponi A, Guan W, Hoek G, et al. WHO global air quality guidelines [Internet]. [cited 2026 Apr 16]. Available from: https://iris.who.int/server/api/core/bitstreams/551b515e-2a32-4e1a-a58c-cdaecd395b19/content2021 [
2. Health Effects Institute. 2025. State of Global Air 2025: A Report on Air Pollution and Its Role in the World's Leading Causes of Death. Boston, MA: Health Effects Institute.
3. Ambient (outdoor) air pollution [Internet]. [cited 2026 Apr 16]. Available from: https://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-quality-and-health2024 [
4. Cory-Slechta DA, Merrill A, Sobolewski M. Air Pollution-Related Neurotoxicity Across the Life Span. Annu Rev Pharmacol Toxicol. 2023;63:143-63.
5. Janssen NA, Hoek G, Simic-Lawson M, Fischer P, van Bree L, ten Brink H, et al. Black carbon as an additional indicator of the adverse health effects of airborne particles compared with PM10 and PM2.5. Environ Health Perspect. 2011;119(12):1691-9.
6. Maji S, Ahmed S, Kaur-Sidhu M, Mor S, Ravindra K. Health Risks of Major Air Pollutants, their Drivers and Mitigation Strategies: A Review. Air, Soil and Water Research. 2023;16:11786221231154659.
7. Kwon HS, Ryu MH, Carlsten C. Ultrafine particles: unique physicochemical properties relevant to health and disease. Exp Mol Med. 2020;52(3):318-28.
8. Strak M, Janssen NA, Godri KJ, Gosens I, Mudway IS, Cassee FR, et al. Respiratory health effects of airborne particulate matter: the role of particle size, composition, and oxidative potential-the RAPTES project. Environ Health Perspect. 2012;120(8):1183-9.
9. Shang L, Yang L, Yang W, Huang L, Qi C, Yang Z, et al. Effects of prenatal exposure to NO(2) on children's neurodevelopment: a systematic review and meta-analysis. Environ Sci Pollut Res Int. 2020;27(20):24786-98.
10. Bove H, Bongaerts E, Slenders E, Bijnens EM, Saenen ND, Gyselaers W, et al. Ambient black carbon particles reach the fetal side of human placenta. Nat Commun. 2019;10(1):3866.
11. Bongaerts E, Lecante LL, Bove H, Roeffaers MBJ, Ameloot M, Fowler PA, et al. Maternal exposure to ambient black carbon particles and their presence in maternal and fetal circulation and organs: an analysis of two independent population-based observational studies. Lancet Planet Health. 2022;6(10):e804-e11.
12. Grabowski B, Feduniw S, Orzel A, Drab M, Modzelewski J, Pruc M, et al. Does Exposure to Ambient Air Pollution Affect Gestational Age and Newborn Weight?-A Systematic Review. Healthcare (Basel). 2024;12(12).
13. Bekkar B, Pacheco S, Basu R, DeNicola N. Association of Air Pollution and Heat Exposure With Preterm Birth, Low Birth Weight, and Stillbirth in the US: A Systematic Review. JAMA Netw Open. 2020;3(6):e208243.
14. Godfrey KM, Barker DJ. Fetal programming and adult health. Public Health Nutr. 2001;4(2B):611-24.
15. DeMaster D, Bick J, Johnson U, Montroy JJ, Landry S, Duncan AF. Nurturing the preterm infant brain: leveraging neuroplasticity to improve neurobehavioral outcomes. Pediatr Res. 2019;85(2):166-75.
16. Thompson RA. Early Brain Development and Public Health. Dela J Public Health. 2024;10(4):6-11.
17. Schneider N, Greenstreet E, Deoni SCL. Connecting inside out: Development of the social brain in infants and toddlers with a focus on myelination as a marker of brain maturation. Child Dev. 2022;93(2):359-71.
18. Cross D, Fani N, Powers A, Bradley B. Neurobiological Development in the Context of Childhood Trauma. Clin Psychol (New York). 2017;24(2):111-24.
19. Rauh VA, Margolis AE. Research Review: Environmental exposures, neurodevelopment, and child mental health - new paradigms for the study of brain and behavioral effects. J Child Psychol Psychiatry. 2016;57(7):775-93.
20. Alter NC, Whitman EM, Bellinger DC, Landrigan PJ. Quantifying the association between PM(2.5) air pollution and IQ loss in children: a systematic review and meta-analysis. Environ Health. 2024;23(1):101.

21. Cosemans C, Madhloum N, Sleurs H, Alfano R, Verheyen L, Wang C, et al. Prenatal particulate matter exposure is linked with neurobehavioural development in early life. Environ Res. 2024;252(Pt 1):118879.
22. Chen Y, Kuang T, Zhang T, Cai S, Colombo J, Harper A, et al. Associations of air pollution exposures in preconception and pregnancy with birth outcomes and infant neurocognitive development: analysis of the Complex Lipids in Mothers and Babies (CLIMB) prospective cohort in Chongqing, China. BMJ Open. 2024;14(7):e082475.
23. Rivas I, Basagana X, Cirach M, Lopez-Vicente M, Suades-Gonzalez E, Garcia-Esteban R, et al. Association between Early Life Exposure to Air Pollution and Working Memory and Attention. Environ Health Perspect. 2019;127(5):57002.
24. Chiu YM, Wilson A, Hsu HL, Jamal H, Mathews N, Kloog I, et al. Prenatal ambient air pollutant mixture exposure and neurodevelopment in urban children in the Northeastern United States. Environ Res. 2023;233:116394.
25. McGuinn LA, Bellinger DC, Colicino E, Coull BA, Just AC, Kloog I, et al. Prenatal PM(2.5) exposure and behavioral development in children from Mexico City. Neurotoxicology. 2020;81:109-15.
26. Chang YT, Jung CR, Chang YC, Chuang BR, Chen ML, Hwang BF. Prenatal and postnatal exposure to PM(2) (.5) and the risk of tic disorders. Paediatr Perinat Epidemiol. 2023;37(3):191-200.
27. Zhuo H, Ritz B, Su JG, Nianogo RA, Warren J, Liew Z. Ambient air pollution during pregnancy and offspring cerebral palsy. Environ Int. 2026;210:110201.
28. Wang L, Li W, Yao Y, Jiang X, Ma D, Liu Y, et al. Maternal exposure to indoor and outdoor air pollution during pregnancy increases offspring risk of autism spectrum disorder. Environ Res. 2026;288(Pt 2):123274.
29. O'Sharkey K, Mitra S, Chow T, Paik SA, Thompson L, Su J, et al. Prenatal exposure to criteria air pollution and traffic-related air toxics and risk of autism spectrum disorder: A population-based cohort study of California births (1990-2018). Environ Int. 2025;201:109562.
30. Sun X, Liu C, Ji H, Li W, Miao M, Yuan W, et al. Prenatal exposure to ambient PM(2.5) and its chemical constituents and child intelligence quotient at 6 years of age. Ecotoxicol Environ Saf. 2023;255:114813.
31. Kvaratskhelia N, Rurua N, Vadachkoria SG. Biomedical and Psychosocial Determinants of Early Neurodevelopment After Preterm Birth. Glob Pediatr Health. 2023;10:2333794X231160366.
32. Hirschel J, Carlhan-Ledermann A, Ferraz C, Brand LA, Filippa M, Gentaz E, et al. Maternal Voice and Tactile Stimulation Modulate Oxytocin in Mothers of Hospitalized Preterm Infants: A Randomized Crossover Trial. Children (Basel). 2023;10(9).
33. Janssen BG, Madhloum N, Gyselaers W, Bijnens E, Clemente DB, Cox B, et al. Cohort Profile: The ENVIRonmental influence ON early AGEing (ENVIRONAGE): a birth cohort study. Int J Epidemiol. 2017;46(5):1386-7m.
34. Ages & Stages Questionnaires (ASQ-3) [Internet]. Brookes Publishing Co.; [cited 2026 Apr 17]. Available from:
https://agesandstages.com/products-pricing/asq3/. [
35. Batts-Hatfield MA. Training module: interpreting results and next steps: PowerPoint slides with notes [Internet]. Baltimore: Paul H. Brookes Publishing Co.; 2018 [cited 2026 May 21]. Available from: https://agesandstages.com/wp-
content/uploads/2018/02/interpretingresults_slidepresentation_020818.pdf.
36. Bricker D, Squires J, Mounts L, Potter L, Nickel R, Twombly E, et al. Ages & Stages Questionnaires® A Parent-Completed, Child-Monitoring System Second Edition. 1999.
37. Balasundaram P, Avulakunta ID. Bayley Scales Of Infant and Toddler Development. StatPearls. Treasure Island (FL)2026.
38. Physiopedia. Bayley Scales of Infant and Toddler Development [Internet]. 2025 [cited 2026 Oct 17]. Available
from: https://www.physio-pedia.com/Bayley_Scales_of_Infant_and_Toddler_Development. [
39. Belgian Interregional Environment Agency. RIO-IFDM [Internet]. Brussels: IRCEL-CELINE; [cited 2026 May 29]. Available from: https://www.irceline.be/nl/documentatie/modellen/rio-ifdm.
40. Janssen S, Dumont G, Fierens F, Mensink C. Spatial interpolation of air pollution measurements using CORINE land cover data. Atmospheric Environment. 2008;42(20):4884-903.

41. European Commission. EU air quality standards [Internet]. Brussels: European Commission; [cited 2026 May 29]. Available from: https://environment.ec.europa.eu/topics/air/air-quality/eu-air-quality-standards_en.
42. Singh A, Yeh CJ, Boone Blanchard S. Ages and Stages Questionnaire: a global screening scale. Bol Med Hosp Infant Mex. 2017;74(1):5-12.
43. Thomason ME. Development of Brain Networks In Utero: Relevance for Common Neural Disorders. Biol Psychiatry. 2020;88(1):40-50.
44. Tau GZ, Peterson BS. Normal development of brain circuits. Neuropsychopharmacology. 2010;35(1):147-68.
45. Leibovitz Z, Lerman-Sagie T, Haddad L. Fetal Brain Development: Regulating Processes and Related Malformations. Life (Basel). 2022;12(6).
46. Costa LG, Cole TB, Dao K, Chang YC, Coburn J, Garrick JM. Effects of air pollution on the nervous system and its possible role in neurodevelopmental and neurodegenerative disorders. Pharmacol Ther. 2020;210:107523.
47. Hwarng GYH, Ereno IL, Ho SKY, Allen JC, Moorakonda RB, Yeo CL. Accuracy of parent-reported ages and stages questionnaire in assessing the motor and language skills of preterm infants. J Neonatal Perinatal Med. 2021;14(2):193-202.
48. Hee Chung E, Chou J, Brown KA. Neurodevelopmental outcomes of preterm infants: a recent literature review. Transl Pediatr. 2020;9(Suppl 1):S3-S8.
49. Lei X, Zhang Y, Wang Z, Lu Z, Pan C, Zhang S, et al. Effects of prenatal exposure to PM(2.5) and its composition on cognitive and motor functions in children at 12 months of age: The Shanghai Birth Cohort Study. Environ Int. 2022;170:107597.
50. Ha S, Yeung E, Bell E, Insaf T, Ghassabian A, Bell G, et al. Prenatal and early life exposures to ambient air pollution and development. Environ Res. 2019;174:170-5.
51. Wang P, Zhao Y, Li J, Zhou Y, Luo R, Meng X, et al. Prenatal exposure to ambient fine particulate matter and early childhood neurodevelopment: A population-based birth cohort study. Sci Total Environ. 2021;785:147334.
52. Ahmed SM, Mishra GD, Moss KM, Yang IA, Lycett K, Knibbs LD. Maternal and Childhood Ambient Air Pollution Exposure and Mental Health Symptoms and Psychomotor Development in Children: An Australian Population-Based Longitudinal Study. Environ Int. 2022;158:107003.
53. Hall BJ, Cauley M, Burke DA, Kiany A, Slotkin TA, Levin ED. Cognitive and Behavioral Impairments Evoked by Low-Level Exposure to Tobacco Smoke Components: Comparison with Nicotine Alone. Toxicol Sci. 2016;151(2):236-44.
54. Zhang X, Spear E, Gennings C, Curtin PC, Just AC, Bragg JB, et al. The association of prenatal exposure to intensive traffic with early preterm infant neurobehavioral development as reflected by the NICU Network Neurobehavioral Scale (NNNS). Environ Res. 2020;183:109204.
55. Chen B, Huang S, He J, He Q, Chen S, Liu X, et al. Sex-specific influence of prenatal air pollutant exposure on neonatal neurobehavioral development and the sensitive window. Chemosphere. 2020;254:126824.
56. Harris MH, Gold DR, Rifas-Shiman SL, Melly SJ, Zanobetti A, Coull BA, et al. Prenatal and childhood traffic-related air pollution exposure and childhood executive function and behavior. Neurotoxicol Teratol. 2016;57:60-70.
57. Yorifuji T, Kashima S, Diez MH, Kado Y, Sanada S, Doi H. Prenatal exposure to outdoor air pollution and child behavioral problems at school age in Japan. Environ Int. 2017;99:192-8.
58. Schonhaut L, Maturana A, Cepeda O, Seron P. Predictive Validity of Developmental Screening Questionnaires for Identifying Children With Later Cognitive or Educational Difficulties: A Systematic Review. Front Pediatr. 2021;9:698549.
59. Piek JP, Dawson L, Smith LM, Gasson N. The role of early fine and gross motor development on later motor and cognitive ability. Hum Mov Sci. 2008;27(5):668-81.
60. Cairney DG, Kazmi A, Delahunty L, Marryat L, Wood R. The predictive value of universal preschool developmental assessment in identifying children with later educational difficulties: A systematic review. PLoS One. 2021;16(3):e0247299.
61. Kerstjens JM, Nijhuis A, Hulzebos CV, van Imhoff DE, van Wassenaer-Leemhuis AG, van Haastert IC, et al. The Ages and Stages Questionnaire and Neurodevelopmental Impairment in Two-Year-Old Preterm-Born Children. PLoS One. 2015;10(7):e0133087.

62. De Prins S, Koppen G, Jacobs G, Dons E, Van de Mieroop E, Nelen V, et al. Influence of ambient air pollution on global DNA methylation in healthy adults: a seasonal follow-up. Environ Int. 2013;59:418-24.
63. Del Rosario C, Slevin M, Molloy EJ, Quigley J, Nixon E. How to use the Bayley Scales of Infant and Toddler Development. Arch Dis Child Educ Pract Ed. 2021;106(2):108-12.

This text was supported by GenAI.

Acknowledgements – First, I would like to thank my promoter, Dr. Charlotte Cosemans, and Prof. Dr. Michelle Plusquin for the opportunity to work on this project. I would also like to thank my supervisor, Ms. Lisa Reynders, for her guidance, feedback, and advice during this internship. I am grateful to all members of ENVIR*ON*AGE for their willingness to help and for welcoming me into their research group. Lastly, many thanks to Ms. Lore Verheyen for her guidance on air pollution exposure assessment, and to Dr. Brigitte Reimann for her statistical advice.

Author contributions – MP and CC conceived and designed the research. LR provided guidance during the internship and writing process. CS performed data analysis and wrote the paper. All authors carefully edited the manuscript.

Supplementary Table S1: Population characteristics for the subsection of participants assessed using the Bayley-4-NL (n = 39). Higher index scores in cognition, motor, and language skills indicate better performance.

Characteristic	Mean ± SD or n (%)
Maternal	
Age at delivery (years)	30.9 ± 3.4
Pre-pregnancy BMI	23.5 ± 4.6
Household education	
Low	0 (0%)
Middle	5 (13%)
High	34 (87%)
Parity	
Primiparous	32 (82%)
Secundiparous	5 (13%)
Multiparous	2 (5.1%)
Smoking during pregnancy	0 (0%)
Season of delivery	
Autumn	14 (36%)
Spring	3 (7.7%)
Summer	13 (33%)
Winter	9 (23%)
Infant	
Gestational age (days)	277 ± 7
Sex	
Male	20 (51%)
Female	19 (49%)
Ethnicity	
European	39 (100%)
Non-European	0 (0%)
Bayley-4-NL	
Age at follow-up (days)	188.1 ± 5.2
Cognitive index	108 ± 7
Language index	102.5 ± 5.8
Motor index	107 ± 9

BMI: body mass index (kg/m²), Bayley-4-NL: Dutch version of the Bayley Scales of Infant and Toddler Development, Fourth edition.

Supplementary Table S2: Proportion of infants classified as delayed or requiring monitoring per neurobehavioural domain measured with the Ages and Stages Questionnaire (n = 193). For communication, gross motor, fine motor, problem-solving, and personal-social skills, higher scores indicate better performance. For social-emotional development, lower scores indicate better performance. Infants were followed up at 2, 6, 12, and 24 months of age. Proportions are presented as n (%). The adjacent "n" columns indicate the total number of children assessed for that domain at each age.

Age	Com	n	GM	n	FM	n	ProbSolv	n	PersSoc	n	SocEmo	n
2	41 (37.6%)	109	29 (26.6%)	109	31 (28.7%)	108	38 (35.8%)	106	50 (47.2%)	106	54 (51.4%)	105
6	9 (10.1%)	89	25 (28.4%)	88	16 (18.2%)	88	8 (9.1%)	88	29 (33%)	88	21 (24.7%)	85
12	6 (11.8%)	51	19 (37.3%)	51	5 (9.8%)	51	5 (10.2%)	49	5 (10.2%)	49	7 (14.3%)	49
24	1 (1.9%)	54	10 (18.5%)	54	12 (22.6%)	53	8 (15.1%)	53	7 (13.2%)	53	9 (17.3%)	52

Com: communication, GM: gross motor, FM: fine motor, ProbSolv: problem-solving, PersSoc: personal-social, SocEmo: social-emotional.

Supplementary Table S3: Characteristics of prenatal air pollution exposure windows (n = 193). Exposure to NO_2, BC, PM_{10}, and $PM_{2.5}$ (μg/m³) was estimated using a spatiotemporal interpolation method (detrended kriging) for each trimester and the whole pregnancy. The median, mean, quartile 1 (Q1), quartile 3 (Q3), interquartile range (IQR), minimum, and maximum exposure are displayed.

Pollutant	Exposure window	Mean	Median	IQR (Q1-Q3)	Minimum	Maximum
NO_2	Trimester 1	9.70	9.64	4.94 (7.05-11.99)	2.10	18.26
	Trimester 2	9.29	8.66	4.17 (7.15-11.32)	2.03	16.69
	Trimester 3	9.30	9.03	3.79 (7.34-11.13)	2.89	17.14
	Whole pregnancy	9.37	9.13	2.60 (8.05-10.66)	2.31	15.87
BC	Trimester 1	0.46	0.45	0.25 (0.33-0.59)	0.11	0.94
	Trimester 2	0.43	0.39	0.24 (0.30-0.53)	0.12	1.01
	Trimester 3	0.43	0.41	0.22 (0.30-0.52)	0.14	0.86
	Whole pregnancy	0.43	0.42	0.14 (0.36-0.50)	0.16	0.80
PM_{10}	Trimester 1	16.10	15.38	4.27 (13.76-18.03)	8.02	27.83
	Trimester 2	15.52	15.18	4.97 (12.99-17.97)	6.44	25.17
	Trimester 3	14.81	14.74	3.55 (12.94-16.49)	5.92	24.89
	Whole pregnancy	15.45	15.25	3.43 (13.95-17.38)	6.89	21.86
$PM_{2.5}$	Trimester 1	8.94	8.00	3.99 (6.87-10.86)	3.26	17.45
	Trimester 2	8.44	7.77	3.81 (6.36-10.17)	2.83	16.72
	Trimester 3	8.08	7.84	3.18 (6.34-9.52)	2.95	15.85
	Whole pregnancy	8.44	8.53	2.37 (7.33-9.69)	3.23	11.96

BC: black carbon, PM_{10}: particulate matter <10 μm, $PM_{2.5}$: particulate matter <2.5 μm.

Supplementary Table S4: The association between prenatal air pollution exposure and ASQ total scores (n = 193). Estimates are given as a change in ASQ total score for a 5 µg/m³ increase in $PM_{2.5}$, PM_{10}, and NO_2 concentration, and a 0.1 µg/m³ increase in BC. Generalised additive mixed models using penalised thin plate regression splines and double penalisation were used and adjusted for categorical age at follow-up, sex, ethnicity of the newborn, season of delivery, gestational age, household education, parity, pre-pregnancy BMI, maternal age, and smoking during pregnancy. Trimester-specific models were mutually adjusted for each other. Adjusted p-values were corrected using the Benjamini-Hochberg False Discovery Rate procedure.

	Pollutant	β [95% CI]	P-value	Adjusted p-value
Communication				
Trimester 1	NO_2	0.00 [-0.03; 0.03]	0.94	1.00
	$PM_{2.5}$	-0.01 [-0.20; 0.18]	0.34	1.00
	PM_{10}	0.00 [-0.06; 0.06]	0.41	1.00
	BC	0.00 [-0.02; 0.02]	0.80	1.00
Trimester 2	NO_2	0.00 [-0.06; 0.06]	0.69	1.00
	$PM_{2.5}$	0.00 [-0.04; 0.04]	0.46	1.00
	PM_{10}	-0.17 [-0.96; 0.63]	0.28	1.00
	BC	0.00 [-0.03; 0.03]	0.79	1.00
Trimester 3	NO_2	0.00 [-0.03; 0.03]	0.76	1.00
	$PM_{2.5}$	0.00 [-0.05; 0.05]	0.95	1.00
	PM_{10}	0.00 [-0.08; 0.08]	0.86	1.00
	BC	0.00 [-0.01; 0.01]	0.71	1.00
Whole pregnancy	NO_2	0.00 [-0.10; 0.10]	0.68	0.96
	$PM_{2.5}$	0.00 [-0.10; 0.10]	0.58	0.96
	PM_{10}	0.00 [-0.06; 0.06]	0.55	0.96
	BC	0.00 [-0.05; 0.05]	0.68	0.96
Gross motor				
Trimester 1	NO_2	0.00 [-0.12; 0.12]	0.35	0.9981
	$PM_{2.5}$	-3.31 [-6.18; -0.45]	**0.02**	1.00
	PM_{10}	-1.99 [-4.00; 0.01]	**0.03**	1.00
	BC	-0.44 [-1.27; 0.39]	0.14	1.00
Trimester 2	NO_2	0.00 [-0.05; 0.05]	0.66	1.00
	$PM_{2.5}$	0.00 [-0.07; 0.07]	1.00	1.00
	PM_{10}	0.00 [-0.07; 0.06]	0.89	1.00
	BC	0.13 [-0.43; 0.69]	0.25	1.00
Trimester 3	NO_2	0.00 [-0.09; 0.09]	0.46	1.00
	$PM_{2.5}$	0.00 [-0.07; 0.07]	0.70	1.00
	PM_{10}	0.00 [-0.05; 0.05]	0.97	1.00
	BC	0.39 [-0.44; 1.22]	0.17	1.00
Whole pregnancy	NO_2	0.00 [-0.06; 0.06]	0.83	1.00
	$PM_{2.5}$	-1.14 [-3.97; 1.69]	0.20	1.00
	PM_{10}	-1.00 [-3.05; 1.05]	0.17	1.00
	BC	0.00 [-0.06; 0.06]	0.61	1.00
Fine motor				
Trimester 1	NO_2	0.00 [-0.07; 0.07]	0.43	1.00
	$PM_{2.5}$	-0.91 [-2.72; 0.91]	0.16	1.00
	PM_{10}	0.00 [-0.10; 0.09]	0.42	1.00
	BC	-0.19 [-0.72; 0.35]	0.23	1.00
Trimester 2	NO_2	0.00 [-0.02; 0.02]	0.92	1.00
	$PM_{2.5}$	0.00 [-0.13; 0.13]	0.36	1.00
	PM_{10}	-0.34 [-1.38; 0.70]	0.24	1.00
	BC	0.00 [-0.01; 0.01]	0.97	1.00
Trimester 3	NO_2	0.00 [-0.05; 0.05]	0.50	1.00
	$PM_{2.5}$	0.00 [-0.07; 0.07]	0.96	1.00
	PM_{10}	0.00 [-0.02; 0.02]	0.94	1.00
	BC	0.00 [-0.04; 0.04]	0.47	1.00

Whole pregnancy	NO_2	0.00 [-0.07; 0.07]	0.98	1.00
	$PM_{2.5}$	-0.84 [-3.08; 1.40]	0.22	0.96
	PM_{10}	-0.05 [-0.52; 0.43]	0.32	0.96
	BC	0.00 [-0.04; 0.04]	0.69	0.96
Problem-Solving				
Trimester 1	NO_2	-0.72 [-2.54; 1.09]	0.21	1.00
	$PM_{2.5}$	0.00 [-0.11; 0.11]	0.41	1.00
	PM_{10}	0.00 [-0.03; 0.03]	0.69	1.00
	BC	0.00 [-0.02; 0.02]	0.43	1.00
Trimester 2	NO_2	0.00 [-0.09; 0.09]	0.54	1.00
	$PM_{2.5}$	-1.50 [-3.87; 0.87]	0.11	1.00
	PM_{10}	-0.91 [-2.53; 0.71]	0.14	1.00
	BC	0.00 [-0.01; 0.01]	0.67	1.00
Trimester 3	NO_2	0.00 [-0.06; 0.06]	0.99	1.00
	$PM_{2.5}$	0.00 [-0.04; 0.04]	0.89	1.00
	PM_{10}	0.00 [-0.07; 0.07]	0.86	1.00
	BC	0.00 [-0.02; 0.02]	0.64	1.00
Whole pregnancy	NO_2	0.00 [-0.13; 0.12]	0.42	0.96
	$PM_{2.5}$	-0.82 [-3.21; 1.57]	0.23	0.96
	PM_{10}	-0.07 [-0.70; 0.55]	0.31	0.96
	BC	0.00 [-0.05; 0.05]	0.90	0.98
Personal-Social				
Trimester 1	NO_2	0.00 [-0.03; 0.03]	0.54	1.00
	$PM_{2.5}$	0.00 [-0.03; 0.03]	0.79	1.00
	PM_{10}	0.00 [-0.03; 0.03]	0.57	1.00
	BC	0.00 [-0.01; 0.01]	0.94	1.00
Trimester 2	NO_2	0.00 [-0.03; 0.03]	0.86	1.00
	$PM_{2.5}$	0.00 [-0.04; 0.04]	0.60	1.00
	PM_{10}	0.00 [-0.02; 0.02]	0.90	1.00
	BC	0.00 [-0.01; 0.01]	0.99	1.00
Trimester 3	NO_2	0.00 [-0.08; 0.08]	0.38	1.00
	$PM_{2.5}$	0.00 [-0.05; 0.05]	0.51	1.00
	PM_{10}	0.00 [-0.03; 0.03]	0.64	1.00
	BC	0.00 [-0.02; 0.02]	0.42	1.00
Whole pregnancy	NO_2	0.00 [-0.04; 0.04]	0.84	0.98
	$PM_{2.5}$	0.00 [-0.05; 0.05]	0.72	0.96
	PM_{10}	0.00 [-0.03; 0.03]	0.61	0.96
	BC	0.00 [-0.02; 0.02]	0.58	0.96
Social-Emotional				
Trimester 1	NO_2	0.00 [-0.14; 0.14]	0.47	1.00
	$PM_{2.5}$	2.39 [-1.30; 6.07]	0.10	1.00
	PM_{10}	0.00 [-0.04; 0.04]	0.40	1.00
	BC	0.17 [-0.55; 0.89]	0.27	1.00
Trimester 2	NO_2	0.00 [-0.04; 0.04]	0.90	1.00
	$PM_{2.5}$	0.00 [-0.20; 0.21]	0.42	1.00
	PM_{10}	1.27 [-1.18; 3.73]	0.15	1.00
	BC	0.00 [-0.06; 0.06]	0.69	1.00
Trimester 3	NO_2	0.00 [-0.09; 0.08]	0.64	1.00
	$PM_{2.5}$	0.00 [-0.16; 0.16]	0.57	1.00
	PM_{10}	0.00 [-0.20; 0.20]	0.50	1.00
	BC	-0.51 [-1.68; 0.66]	0.19	1.00
Whole pregnancy	NO_2	0.00 [-0.15; 0.15]	0.94	0.98
	$PM_{2.5}$	0.27 [-1.59; 2.13]	0.30	0.96
	PM_{10}	0.01 [-0.27; 0.29]	0.37	0.96
	BC	0.00 [-0.08; 0.08]	0.93	0.98

p<0.05 are highlighted in bold, ASQ: Ages and Stages Questionnaire, CI: confidence interval, BC: black carbon, PM_{10}: particulate matter <10 µm, $PM_{2.5}$: particulate matter <2.5 µm.

Supplementary Table S5: The association between the interaction of gestational age with prenatal air pollution exposure and ASQ total scores (n = 193). Estimates are given as a change in ASQ total score for a 5 µg/m³ increase in $PM_{2.5}$, PM_{10}, and NO_2 concentration, and a 0.1 µg/m³ increase in BC. Generalised additive mixed models using penalised thin plate regression splines and double penalisation were used and adjusted for categorical age at follow-up, sex, ethnicity of the newborn, season of delivery, gestational age, household education, parity, pre-pregnancy BMI, maternal age, and smoking during pregnancy. Trimester-specific models were mutually adjusted for each other. Adjusted p-values were corrected using the Benjamini-Hochberg False Discovery Rate procedure.

	Pollutant	β [95% CI]	P-value	Adjusted p-value
Communication				
Trimester 1	NO_2	-0.03 [-0.35; 0.28]	0.83	0.96
	$PM_{2.5}$	-0.11 [-0.41; 0.19]	0.48	0.90
	PM_{10}	-0.15 [-0.39; 0.10]	0.24	0.76
	BC	-0.04 [-0.15; 0.06]	0.42	0.88
Trimester 2	NO_2	0.04 [-0.35; 0.42]	0.86	0.96
	$PM_{2.5}$	0.03 [-0.23; 0.30]	0.80	0.96
	PM_{10}	0.01 [-0.19; 0.22]	0.90	0.96
	BC	0.02 [-0.09; 0.13]	0.67	0.96
Trimester 3	NO_2	-0.02 [-0.33; 0.29]	0.89	0.96
	$PM_{2.5}$	-0.01 [-0.34; 0.31]	0.93	0.96
	PM_{10}	0.02 [-0.27; 0.31]	0.90	0.96
	BC	-0.02 [-0.12; 0.08]	0.72	0.96
Whole pregnancy	NO_2	-0.02 [-0.37; 0.32]	0.89	0.93
	$PM_{2.5}$	-0.09 [-0.50; 0.33]	0.69	0.87
	PM_{10}	-0.11 [-0.37; 0.15]	0.41	0.84
	BC	-0.04 [-0.17; 0.10]	0.59	0.84
Gross motor				
Trimester 1	NO_2	-0.06 [-0.40; 0.29]	0.75	0.96
	$PM_{2.5}$	-0.04 [-0.36; 0.29]	0.83	0.96
	PM_{10}	-0.14 [-0.41; 0.13]	0.30	0.82
	BC	-0.02 [-0.13; 0.10]	0.79	0.96
Trimester 2	NO_2	0.03 [-0.39; 0.46]	0.88	0.96
	$PM_{2.5}$	-0.06 [-0.34; 0.23]	0.71	0.96
	PM_{10}	-0.05 [-0.28; 0.17]	0.63	0.96
	BC	-0.01 [-0.13; 0.12]	0.92	0.96
Trimester 3	NO_2	0.17 [-0.18; 0.51]	0.34	0.82
	$PM_{2.5}$	0.22 [-0.13; 0.58]	0.22	0.76
	PM_{10}	0.22 [-0.10; 0.54]	0.17	0.76
	BC	0.03 [-0.08; 0.14]	0.55	0.94
Whole pregnancy	NO_2	0.12 [-0.26; 0.49]	0.54	0.84
	$PM_{2.5}$	0.04 [-0.42; 0.50]	0.86	0.93
	PM_{10}	-0.04 [-0.33; 0.24]	0.77	0.91
	BC	0.03 [-0.12; 0.18]	0.68	0.87
Fine motor				
Trimester 1	NO_2	-0.21 [-0.50; 0.08]	0.16	0.75
	$PM_{2.5}$	-0.24 [-0.52; 0.03]	0.08	0.59
	PM_{10}	-0.25 [-0.48; -0.03]	**0.03**	0.50
	BC	-0.09 [-0.19; 0.00]	0.06	0.50
Trimester 2	NO_2	0.21 [-0.15; 0.56]	0.25	0.76
	$PM_{2.5}$	0.22 [-0.03; 0.46]	0.08	0.59
	PM_{10}	0.21 [0.02; 0.40]	**0.03**	0.50
	BC	0.07 [-0.03; 0.17]	0.19	0.76
Trimester 3	NO_2	-0.24 [-0.53; 0.05]	0.10	0.69
	$PM_{2.5}$	-0.15 [-0.46; 0.15]	0.32	0.82
	PM_{10}	-0.10 [-0.36; 0.17]	0.49	0.90

	BC	-0.09 [-0.18; 0.00]	0.05	0.50
Whole pregnancy	NO_2	-0.13 [-0.44; 0.19]	0.43	0.84
	$PM_{2.5}$	0.01 [-0.37; 0.39]	0.95	0.95
	PM_{10}	-0.03 [-0.27; 0.21]	0.80	0.91
	BC	-0.05 [-0.17; 0.07]	0.42	0.84
Problem-Solving				
Trimester 1	NO_2	-0.35 [-0.67; -0.02]	**0.04**	0.50
	$PM_{2.5}$	-0.37 [-0.68; -0.06]	**0.02**	0.50
	PM_{10}	-0.31 [-0.56; -0.06]	**0.02**	0.50
	BC	-0.11 [-0.22; 0.00]	**0.05**	0.50
Trimester 2	NO_2	0.30 [-0.10; 0.70]	0.14	0.74
	$PM_{2.5}$	0.11 [-0.16; 0.39]	0.43	0.88
	PM_{10}	0.07 [-0.14; 0.28]	0.51	0.92
	BC	0.07 [-0.04; 0.18]	0.24	0.76
Trimester 3	NO_2	-0.24 [-0.57; 0.08]	0.14	0.74
	$PM_{2.5}$	-0.15 [-0.49; 0.19]	0.40	0.88
	PM_{10}	-0.03 [-0.33; 0.27]	0.85	0.96
	BC	-0.07 [-0.17; 0.04]	0.20	0.76
Whole pregnancy	NO_2	-0.18 [-0.53; 0.18]	0.33	0.84
	$PM_{2.5}$	-0.24 [-0.67; 0.19]	0.27	0.84
	PM_{10}	-0.21 [-0.48; 0.05]	0.12	0.84
	BC	-0.06 [-0.20; 0.08]	0.41	0.84
Personal-Social				
Trimester 1	NO_2	-0.15 [-0.43; 0.14]	0.31	0.82
	$PM_{2.5}$	-0.11 [-0.39; 0.16]	0.41	0.88
	PM_{10}	-0.11 [-0.33; 0.11]	0.34	0.82
	BC	-0.06 [-0.15; 0.04]	0.23	0.76
Trimester 2	NO_2	0.05 [-0.30; 0.41]	0.76	0.96
	$PM_{2.5}$	-0.01 [-0.25; 0.23]	0.93	0.96
	PM_{10}	-0.05 [-0.24; 0.13]	0.56	0.94
	BC	0.00 [-0.10; 0.10]	0.96	0.98
Trimester 3	NO_2	0.07 [-0.20; 0.35]	0.60	0.95
	$PM_{2.5}$	0.15 [-0.14; 0.44]	0.32	0.82
	PM_{10}	0.11 [-0.15; 0.37]	0.41	0.88
	BC	0.01 [-0.08; 0.10]	0.86	0.96
Whole pregnancy	NO_2	-0.09 [-0.39; 0.22]	0.58	0.84
	$PM_{2.5}$	-0.13 [-0.51; 0.25]	0.50	0.84
	PM_{10}	-0.12 [-0.36; 0.11]	0.31	0.84
	BC	-0.08 [-0.20; 0.05]	0.22	0.84
Social-Emotional				
Trimester 1	NO_2	-0.16 [-0.68; 0.36]	0.55	0.94
	$PM_{2.5}$	0.13 [-0.37; 0.62]	0.62	0.96
	PM_{10}	0.14 [-0.26; 0.55]	0.49	0.90
	BC	-0.02 [-0.19; 0.15]	0.81	0.96
Trimester 2	NO_2	-0.04 [-0.68; 0.60]	0.91	0.96
	$PM_{2.5}$	-0.26 [-0.70; 0.18]	0.25	0.76
	PM_{10}	-0.26 [-0.60; 0.08]	0.14	0.74
	BC	-0.07 [-0.25; 0.12]	0.48	0.90
Trimester 3	NO_2	0.08 [-0.44; 0.59]	0.78	0.96
	$PM_{2.5}$	0.15 [-0.39; 0.69]	0.59	0.95
	PM_{10}	0.09 [-0.39; 0.57]	0.72	0.96
	BC	0.00 [-0.17; 0.16]	0.99	0.99
Whole pregnancy	NO_2	-0.21 [-0.77; 0.35]	0.47	0.84
	$PM_{2.5}$	-0.23 [-0.90; 0.45]	0.51	0.84
	PM_{10}	-0.17 [-0.59; 0.26]	0.44	0.84
	BC	-0.12 [-0.33; 0.10]	0.29	0.84

$p<0.05$ are highlighted in bold, ASQ: Ages and Stages Questionnaire, CI: confidence interval, BC: black carbon, PM_{10}: particulate matter <10 µm, $PM_{2.5}$: particulate matter <2.5 µm.

Supplementary Table S6: Age-specific associations between air pollution exposure windows and ASQ domains (n = 193). To explore how associations differed across follow-up ages, generalised additive mixed models with double penalisation and thin plate regression splines, and age-specific smooths using an interaction between exposure and age were fitted for all prenatal air pollution exposure windows. Models were adjusted for categorical age at follow-up, sex, ethnicity of the newborn, season of delivery, gestational age, household education, parity, pre-pregnancy BMI, maternal age, and smoking during pregnancy. Estimates were provided as a change in score per 5 $\mu g/m^3$ increment in air pollution concentration for NO_2, $PM_{2.5}$, and PM_{10}, and a 0.1 $\mu g/m^3$ increment for BC. Estimates with absolute values <0.01 were omitted for readability.

Domain	Window	Pollutant	Age	β (95% CI)	P-value
Communication	Trimester 1	$PM_{2.5}$	12	-2.63 [-8.83; 3.57]	0.41
		NO_2	12	-1.45 [-4.83; 1.93]	0.40
	Trimester 2	$PM_{2.5}$	12	-2.16 [-8.34; 4.02]	0.49
		$PM_{2.5}$	6	-0.82 [-3.12; 1.48]	0.48
		PM_{10}	12	-1.38 [-5.13; 2.37]	0.47
		PM_{10}	6	-1.29 [-3.63; 1.05]	0.28
		NO_2	2	2.33 [-0.78; 5.44]	0.14
		BC	2	0.72 [-0.35; 1.79]	0.19
	Trimester 3	$PM_{2.5}$	2	0.18 [-1.02; 1.38]	0.77
		PM_{10}	2	1.24 [-1.19; 3.67]	0.32
		BC	2	1.40 [-0.21; 3.00]	0.09
	Whole pregnancy	$PM_{2.5}$	6	-1.60 [-5.95; 2.76]	0.47
		$PM_{2.5}$	12	-1.28 [-6.12; 3.56]	0.60
		PM_{10}	6	-1.47 [-4.80; 1.87]	0.39
		PM_{10}	12	-0.62 [-3.34; 2.10]	0.65
		NO_2	2	3.14 [-1.00; 7.28]	0.14
		BC	2	0.44 [-0.79; 1.67]	0.48
Fine motor	Trimester 1	$PM_{2.5}$	12	-1.84 [-6.60; 2.93]	0.45
		$PM_{2.5}$	24	-0.24 [-1.73; 1.24]	0.75
		PM_{10}	24	-0.54 [-2.39; 1.31]	0.57
		PM_{10}	6	-0.30 [-1.53; 0.93]	0.63
	Trimester 2	NO_2	2	-0.35 [-1.76; 1.07]	0.63
		BC	2	-0.21 [-0.84; 0.42]	0.51
	Trimester 3	$PM_{2.5}$	12	0.99 [-1.89; 3.87]	0.50
		NO_2	12	0.13 [-0.85; 1.10]	0.80
		BC	12	0.37 [-0.62; 1.36]	0.47
	Whole pregnancy	PM_{10}	24	-0.10 [-1.09; 0.88]	0.84
		NO_2	6	0.39 [-1.45; 2.22]	0.68
		BC	2	-0.12 [-0.76; 0.52]	0.72
Gross motor	Trimester 1	$PM_{2.5}$	6	-1.76 [-4.88; 1.37]	0.27
		$PM_{2.5}$	12	-0.01 [-0.55; 0.53]	0.96
		PM_{10}	12	-0.76 [-3.80; 2.28]	0.63
		NO_2	6	-1.84 [-4.94; 1.26]	0.24
		BC	12	-0.30 [-1.55; 0.94]	0.63
	Trimester 2	$PM_{2.5}$	12	-4.88 [-13.29; 3.53]	0.26
		$PM_{2.5}$	6	-0.02 [-0.47; 0.42]	0.92
		PM_{10}	6	-0.49 [-2.20; 1.21]	0.57
		NO_2	2	1.06 [-1.52; 3.64]	0.42
		BC	2	0.76 [-0.39; 1.90]	0.19
	Trimester 3	$PM_{2.5}$	24	-0.63 [-3.51; 2.26]	0.67
		PM_{10}	12	-3.37 [-8.37; 1.62]	0.19
		PM_{10}	24	-2.13 [-6.00; 1.75]	0.28
		NO_2	6	0.70 [-1.55; 2.95]	0.54
		BC	6	0.91 [-0.37; 2.20]	0.16
	Whole pregnancy	$PM_{2.5}$	12	-2.01 [-8.27; 4.24]	0.53
	Whole pregnancy	$PM_{2.5}$	24	-0.29 [-2.61; 2.03]	0.81

		$PM_{2.5}$	6	-0.01 [-0.40; 0.38]	0.97
		PM_{10}	12	-1.33 [-5.33; 2.67]	0.51
		PM_{10}	24	-0.03 [-0.66; 0.59]	0.92
		PM_{10}	6	-0.01 [-0.32; 0.30]	0.96
		BC	2	0.54 [-0.87; 1.96]	0.45
Personal-Social	Trimester 1	$PM_{2.5}$	12	-8.93 [-17.02; -0.84]	**0.03**
		PM_{10}	12	-3.93 [-9.08; 1.22]	0.13
		PM_{10}	6	0.73 [-1.22; 2.69]	0.46
		NO_2	12	-6.86 [-11.99; -1.74]	**0.01**
		BC	12	-1.43 [-3.57; 0.71]	0.19
	Trimester 2	$PM_{2.5}$	6	-3.84 [-7.39; -0.30]	**0.03**
		$PM_{2.5}$	2	0.53 [-1.19; 2.26]	0.54
		PM_{10}	6	-1.94 [-4.55; 0.67]	0.14
		PM_{10}	2	0.01 [-0.22; 0.24]	0.93
		NO_2	6	-1.95 [-5.05; 1.16]	0.22
		NO_2	2	1.58 [-1.18; 4.33]	0.26
		BC	6	-0.98 [-2.24; 0.28]	0.13
		BC	2	0.58 [-0.41; 1.56]	0.25
	Trimester 3	$PM_{2.5}$	2	0.10 [-0.78; 0.97]	0.83
		$PM_{2.5}$	12	3.01 [-1.54; 7.56]	0.19
		PM_{10}	6	-0.24 [-1.55; 1.07]	0.72
		PM_{10}	2	1.16 [-1.17; 3.48]	0.33
		PM_{10}	12	4.08 [-0.87; 9.04]	0.11
		NO_2	6	0.31 [-1.19; 1.82]	0.68
	Whole pregnancy	$PM_{2.5}$	2	2.22 [-1.75; 6.19]	0.27
		PM_{10}	2	1.68 [-1.20; 4.55]	0.25
		NO_2	12	-3.73 [-9.18; 1.72]	0.18
		NO_2	2	0.70 [-1.68; 3.08]	0.56
		BC	2	0.97 [-0.61; 2.54]	0.23
Problem-Solving	Trimester 1	$PM_{2.5}$	12	-5.40 [-12.90; 2.11]	0.16
		$PM_{2.5}$	6	-1.70 [-4.58; 1.18]	0.25
		PM_{10}	6	-2.28 [-5.07; 0.50]	0.11
		PM_{10}	12	-1.85 [-5.76; 2.06]	0.35
		NO_2	6	-2.45 [-5.51; 0.61]	0.12
		NO_2	12	-0.36 [-2.27; 1.54]	0.71
		BC	6	-1.15 [-2.43; 0.12]	0.08
		BC	2	0.77 [-0.41; 1.95]	0.20
	Trimester 2	$PM_{2.5}$	24	-0.80 [-3.74; 2.13]	0.59
	Trimester 3	$PM_{2.5}$	24	-1.57 [-5.77; 2.63]	0.46
		PM_{10}	24	-1.38 [-4.58; 1.82]	0.40
		NO_2	24	-1.75 [-5.54; 2.04]	0.36
		NO_2	2	4.10 [-0.12; 8.33]	0.06
		BC	2	1.95 [0.23; 3.66]	**0.03**
	Whole pregnancy	$PM_{2.5}$	24	2.18 [-8.49; 12.86]	0.69
		PM_{10}	6	-0.74 [-3.26; 1.78]	0.57
		NO_2	24	-0.97 [-4.12; 2.19]	0.55
		NO_2	6	-0.49 [-2.70; 1.71]	0.66
		BC	6	-0.06 [-0.60; 0.48]	0.83
Social-Emotional	Trimester 1	$PM_{2.5}$	12	0.42 [-2.91; 3.74]	0.81
		NO_2	12	1.98 [-3.10; 7.06]	0.44
		BC	12	0.01 [-0.24; 0.25]	0.95
	Trimester 2	$PM_{2.5}$	6	2.67 [-1.94; 7.27]	0.26
		PM_{10}	6	2.51 [-1.29; 6.32]	0.20
		BC	6	0.31 [-0.80; 1.42]	0.58
	Whole pregnancy	$PM_{2.5}$	6	0.65 [-3.03; 4.33]	0.73
		PM_{10}	6	0.02 [-0.58; 0.63]	0.94

p<0.05 are highlighted in bold, ASQ: Ages and Stages Questionnaire, BC: black carbon, PM_{10}: particulate matter <10 µm, $PM_{2.5}$: particulate matter <2.5 µm.

Supplementary Table S7: Associations between prenatal air pollution exposure and Bayley Scales of Infant and Toddler Development index scores (n = 39). Neurobehavioural development was evaluated in three domains, cognition, language, and motor skills, in 6-month-old infants using the Dutch version of the Bayley Scales of Infant and Toddler Development, Fourth Edition. Linear models were adjusted for age at follow-up, sex, ethnicity of the newborn, season of delivery, gestational age, household education, parity, pre-pregnancy BMI, maternal age, and smoking during pregnancy. Trimester-specific models were mutually adjusted for each other. Estimates were provided as a change in score per 5 µg/m³ increment in air pollution concentration for NO_2, $PM_{2.5}$, and PM_{10}, and a 0.1 µg/m³ increment for BC. Adjusted p-values were corrected using the Benjamini-Hochberg False Discovery Rate procedure.

Outcome	Window	Pollutant	β [95% CI]	p-value	Adjusted p-value
Cognition	Trimester 1	NO_2	-4.39 [-12.82; 4.04]	0.293	0.965
		$PM_{2.5}$	-3.15 [-9.44; 3.14]	0.312	0.965
		PM_{10}	-3.24 [-8.98; 2.49]	0.255	0.965
		BC	-0.69 [-3.56; 2.17]	0.623	0.965
	Trimester 2	NO_2	3.74 [-10.7; 18.18]	0.598	0.965
		$PM_{2.5}$	2.69 [-8.49; 13.86]	0.624	0.965
		PM_{10}	1.67 [-6.34; 9.68]	0.670	0.965
		BC	0.75 [-3.4; 4.91]	0.711	0.965
	Trimester 3	NO_2	-0.86 [-14.4; 12.68]	0.897	0.965
		$PM_{2.5}$	0.26 [-11.71; 12.23]	0.965	0.965
		PM_{10}	1.32 [-6.4; 9.04]	0.727	0.965
		BC	0.9 [-4.00; 5.8]	0.709	0.965
	Whole pregnancy	NO_2	-1.72 [-10.83; 7.39]	0.702	0.965
		$PM_{2.5}$	-0.65 [-10.6; 9.3]	0.894	0.965
		PM_{10}	-0.63 [-7.49; 6.23]	0.852	0.965
		BC	0.83 [-3.43; 5.08]	0.693	0.965
Language	Trimester 1	NO_2	3 [-2.49; 8.49]	0.271	0.965
		$PM_{2.5}$	4.49 [0.62; 8.35]	**0.025**	0.593
		PM_{10}	5.26 [2.01; 8.51]	**0.003**	0.132
		BC	1.18 [-0.67; 3.02]	0.201	0.965
	Trimester 2	NO_2	0.24 [-9.16; 9.64]	0.958	0.965
		$PM_{2.5}$	-3.69 [-10.56; 3.18]	0.278	0.965
		PM_{10}	-4.23 [-8.77; 0.31]	0.066	0.965
		BC	-0.44 [-3.12; 2.24]	0.737	0.965
	Trimester 3	NO_2	0.51 [-8.31; 9.32]	0.907	0.965
		$PM_{2.5}$	2.38 [-4.98; 9.74]	0.511	0.965
		PM_{10}	1.13 [-3.24; 5.51]	0.598	0.965
		BC	-0.58 [-3.74; 2.58]	0.707	0.965
	Whole pregnancy	NO_2	3.71 [-2.2; 9.62]	0.209	0.965
		$PM_{2.5}$	3.35 [-3.15; 9.85]	0.299	0.965

Outcome	Window	Pollutant	β [95% CI]	p-value	Adjusted p-value
		PM_{10}	2.5 [-1.97; 6.96]	0.261	0.965
		BC	0.2 [-2.65; 3.05]	0.887	0.965
Motor	Trimester 1	NO_2	-6.07 [-14.95; 2.81]	0.171	0.965
		$PM_{2.5}$	-2.19 [-9.12; 4.74]	0.521	0.965
		PM_{10}	-0.83 [-7.22; 5.55]	0.790	0.965
		BC	-1.31 [-4.39; 1.77]	0.389	0.965
	Trimester 2	NO_2	10.92 [-4.29; 26.13]	0.151	0.965
		$PM_{2.5}$	2.12 [-10.19; 14.44]	0.725	0.965
		PM_{10}	-1.15 [-10.07; 7.76]	0.792	0.965
		BC	2.47 [-2; 6.93]	0.266	0.965
	Trimester 3	NO_2	-4.6 [-18.86; 9.66]	0.512	0.965
		$PM_{2.5}$	0.4 [-12.79; 13.59]	0.951	0.965
		PM_{10}	1.53 [-7.06; 10.12]	0.717	0.965
		BC	-1.42 [-6.68; 3.85]	0.584	0.965
	Whole pregnancy	NO_2	0.39 [-9.53; 10.32]	0.936	0.965
		$PM_{2.5}$	-0.41 [-11.22; 10.4]	0.939	0.965
		PM_{10}	-0.95 [-8.39; 6.5]	0.795	0.965
		BC	0.39 [-4.24; 5.03]	0.863	0.965

p<0.05 are highlighted in bold, CI: confidence interval, BC: black carbon, PM_{10}: particulate matter <10 µm, $PM_{2.5}$: particulate matter <2.5 µm.

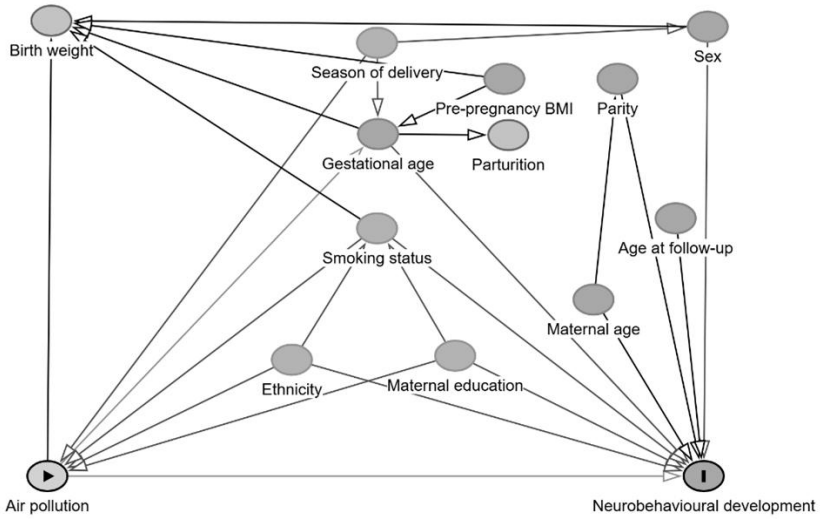
Supplementary Table S8: Sensitivity analysis for the association between prenatal air pollution exposure and ASQ total scores, adjusting for postnatal exposure (n = 193). Estimates are given as a change in ASQ total score for a 5 µg/m³ increase in $PM_{2.5}$, PM_{10}, and NO_2 concentration, and a 0.1 µg/m³ increase in BC. Generalised additive mixed models using penalised thin plate regression splines and double penalisation were used and adjusted for postnatal air pollution exposure from the first day of life until the age at follow-up, categorical age at follow-up, sex, ethnicity of the newborn, season of delivery, gestational age, household education, parity, pre-pregnancy BMI, maternal age, and smoking during pregnancy. Trimester-specific models were mutually adjusted for each other. Adjusted p-values were corrected using the Benjamini-Hochberg False Discovery Rate procedure.

	Pollutant	β [95% CI]	P-value	Adjusted p-value
Communication				
Trimester 1	NO_2	0.00 [-0.03; 0.03]	0.80	0.96
	$PM_{2.5}$	-1.18 [-3.30; 0.95]	0.14	0.83
	PM_{10}	0.00 [-0.02; 0.02]	0.52	0.92
	BC	0.00 [-0.01; 0.01]	0.59	0.93
Trimester 2	NO_2	0.00 [-0.06; 0.06]	0.89	0.96
	$PM_{2.5}$	-0.94 [-2.96; 1.09]	0.17	0.83
	PM_{10}	-1.86 [-3.73; 0.01]	**0.03**	0.66
	BC	0.00 [-0.02; 0.02]	0.87	0.96
Trimester 3	NO_2	0.00 [-0.06; 0.06]	0.92	0.96
	$PM_{2.5}$	0.00 [-0.06; 0.06]	0.94	0.96
	PM_{10}	0.00 [-0.06; 0.06]	0.54	0.93
	BC	0.00 [-0.02; 0.02]	0.57	0.93
Whole pregnancy	NO_2	0.00 [-0.06; 0.06]	0.92	0.97
	$PM_{2.5}$	-2.02 [-5.31; 1.28]	0.12	0.50
	PM_{10}	-1.24 [-3.34; 0.85]	0.13	0.50

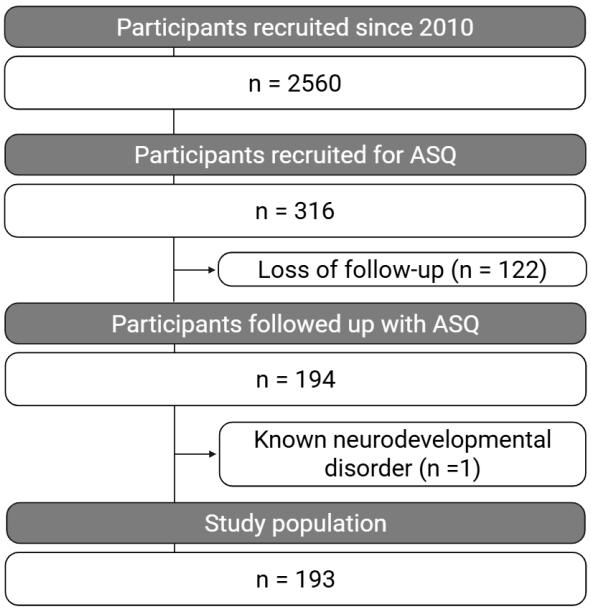
	BC	0.00 [-0.03; 0.03]	0.97	0.97
Gross motor				
Trimester 1	NO_2	0.00 [-0.08; 0.08]	0.44	0.92
	$PM_{2.5}$	-3.62 [-6.72; -0.53]	**0.01**	0.66
	PM_{10}	-1.66 [-3.72; 0.40]	0.06	0.78
	BC	-0.27 [-1.00; 0.47]	0.22	0.91
Trimester 2	NO_2	0.00 [-0.11; 0.11]	0.65	0.93
	$PM_{2.5}$	0.00 [-0.09; 0.09]	0.49	0.92
	PM_{10}	0.00 [-0.06; 0.06]	0.50	0.92
	BC	0.00 [-0.05; 0.05]	0.72	0.95
Trimester 3	NO_2	0.22 [-1.02; 1.46]	0.27	0.91
	$PM_{2.5}$	0.00 [-0.07; 0.07]	0.86	0.96
	PM_{10}	0.00 [-0.06; 0.06]	0.88	0.96
	BC	0.58 [-0.43; 1.60]	0.13	0.83
Whole pregnancy	NO_2	0.00 [-0.11; 0.11]	0.63	0.97
	$PM_{2.5}$	-2.43 [-6.40; 1.53]	0.12	0.50
	PM_{10}	-0.91 [-3.07; 1.25]	0.19	0.57
	BC	0.00 [-0.07; 0.07]	0.58	0.97
Fine motor				
Trimester 1	NO_2	0.00 [-0.08; 0.08]	0.50	0.92
	$PM_{2.5}$	-1.42 [-3.56; 0.72]	0.10	0.82
	PM_{10}	0.00 [-0.06; 0.06]	0.36	0.92
	BC	-0.13 [-0.59; 0.34]	0.26	0.91
Trimester 2	NO_2	0.00 [-0.03; 0.03]	0.91	0.96
	$PM_{2.5}$	-0.04 [-0.54; 0.45]	0.31	0.92
	PM_{10}	-0.52 [-1.80; 0.76]	0.20	0.91
	BC	0.00 [-0.01; 0.01]	0.83	0.96
Trimester 3	NO_2	0.00 [-0.03; 0.03]	0.84	0.96
	$PM_{2.5}$	0.00 [-0.13; 0.13]	0.48	0.92
	PM_{10}	0.00 [-0.06; 0.06]	0.60	0.93
	BC	0.00 [-0.02; 0.02]	0.94	0.96
Whole pregnancy	NO_2	0.00 [-0.05; 0.05]	0.95	0.97
	$PM_{2.5}$	-2.34 [-5.66; 0.97]	0.09	0.50
	PM_{10}	-0.57 [-2.13; 0.99]	0.22	0.57
	BC	0.00 [-0.04; 0.04]	0.57	0.97
Problem-Solving				
Trimester 1	NO_2	-1.12 [-3.28; 1.04]	0.16	0.83
	$PM_{2.5}$	-0.41 [-1.90; 1.08]	0.25	0.91
	PM_{10}	0.00 [-0.02; 0.02]	0.73	0.95
	BC	-0.08 [-0.49; 0.33]	0.28	0.91
Trimester 2	NO_2	0.00 [-0.05; 0.05]	0.57	0.93
	$PM_{2.5}$	-2.63 [-5.44; 0.19]	**0.04**	0.66
	PM_{10}	-2.07 [-4.10; -0.04]	**0.03**	0.66
	BC	0.00 [-0.02; 0.02]	0.49	0.92
Trimester 3	NO_2	0.00 [-0.05; 0.05]	0.87	0.96
	$PM_{2.5}$	0.00 [-0.03; 0.03]	0.81	0.96
	PM_{10}	0.00 [-0.04; 0.04]	0.66	0.93
	BC	0.00 [-0.02; 0.02]	0.75	0.95
Whole pregnancy	NO_2	-0.19 [-1.30; 0.92]	0.29	0.64
	$PM_{2.5}$	-3.68 [-7.68; 0.33]	**0.04**	0.50
	PM_{10}	-1.84 [-4.28; 0.59]	0.07	0.50
	BC	0.00 [-0.02; 0.02]	0.59	0.97
Personal-Social				
Trimester 1	NO_2	0.00 [-0.05; 0.04]	0.42	0.92
	$PM_{2.5}$	0.00 [-0.03; 0.03]	0.94	0.96
	PM_{10}	0.00 [-0.02; 0.02]	0.74	0.95
	BC	0.00 [-0.01; 0.01]	0.71	0.95
Trimester 2	NO_2	0.00 [-0.04; 0.04]	0.66	0.93

	$PM_{2.5}$	0.00 [-0.06; 0.06]	0.38	0.92
	PM_{10}	0.00 [-0.03; 0.03]	0.53	0.92
	BC	0.00 [-0.01; 0.01]	0.66	0.93
Trimester 3	NO_2	0.00 [-0.05; 0.05]	0.42	0.92
	$PM_{2.5}$	0.00 [-0.05; 0.05]	0.48	0.92
	PM_{10}	0.00 [-0.03; 0.03]	0.71	0.95
	BC	0.00 [-0.02; 0.02]	0.42	0.92
Whole pregnancy	NO_2	0.00 [-0.03; 0.03]	0.90	0.97
	$PM_{2.5}$	0.00 [-0.05; 0.05]	0.97	0.97
	PM_{10}	0.00 [-0.03; 0.03]	0.90	0.97
	BC	0.00 [-0.01; 0.01]	0.92	0.97
Social-Emotional				
Trimester 1	NO_2	1.61 [-1.74; 4.96]	0.16	0.83
	$PM_{2.5}$	3.48 [-0.61; 7.57]	**0.05**	0.70
	PM_{10}	0.16 [-0.88; 1.19]	0.28	0.91
	BC	0.96 [-0.43; 2.34]	0.09	0.79
Trimester 2	NO_2	0.00 [-0.14; 0.14]	0.66	0.93
	$PM_{2.5}$	0.00 [-0.12; 0.12]	0.47	0.92
	PM_{10}	2.08 [-0.84; 5.00]	0.08	0.79
	BC	0.00 [-0.05; 0.05]	0.98	0.98
Trimester 3	NO_2	0.00 [-0.14; 0.14]	0.46	0.92
	$PM_{2.5}$	-0.01 [-0.32; 0.30]	0.35	0.92
	PM_{10}	-0.12 [-1.16; 0.91]	0.29	0.91
	BC	-0.58 [-1.83; 0.66]	0.17	0.83
Whole pregnancy	NO_2	0.00 [-0.06; 0.06]	0.78	0.97
	$PM_{2.5}$	1.22 [-2.58; 5.03]	0.24	0.57
	PM_{10}	0.91 [-1.67; 3.48]	0.23	0.57
	BC	0.00 [-0.07; 0.07]	0.86	0.97

p<0.05 are highlighted in bold, ASQ: Ages and Stages Questionnaire, CI: confidence interval, BC: black carbon, PM_{10}: particulate matter <10 µm, $PM_{2.5}$: particulate matter <2.5 µm.



Supplementary Figure S1: Directed Acyclic Graph. Covariates were selected *a priori* based on the literature and Directed Acyclic Graphs. All models were adjusted for age at follow-up, sex, ethnicity of the newborn, season of delivery, gestational age, household education, parity, pre-pregnancy BMI, maternal age, and smoking during pregnancy.



Supplementary Figure S2: Flow chart of the study population selection (n = 193).