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Single and combined effects of prenatal exposure to air pollutants on children's cognitive performance

Sharanpreet Kaur [a,b], Josefa Canals-Sans [a,b,c,d,*], Carmen Hernández-Martínez [a,b,c], Mònica Guxens [e,f,g,h,i]

[a] Nutrition and Mental Health Research Group (NUTRISAM), Universitat Rovira i Virgili (URV), Spain
[b] Universitat Rovira i Virgili (URV), Research Center for Behavior Assessment (CRAMC), Department of Psychology, Tarragona, Spain
[c] Institut d'Investigació Sanitària Pere Virgili (IISPV), Reus, Spain
[d] IU-RESCAT: University Research Institute on Sustainable, Climate Change and Energy Transition, Universitat Rovira I Virgili, Tarragona, Spain
[e] Instituto de Salud Global de Barcelona (ISGlobal), Barcelona, Spain
[f] Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain
[g] Universitat Pompeu Fabra, Barcelona, Spain
[h] Spanish Consortium for Research on Epidemiology and Public Health (CIBERESP), Instituto de Salud Carlos III, Madrid, Spain
[i] Department of Child and Adolescent Psychiatry/Psychology, Erasmus MC, University Medical Centre, Rotterdam, the Netherlands

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ABSTRACT

Background: Prenatal air pollution exposure has been increasingly recognised for its impact on children's cognitive development and overall health. This study explored the association between prenatal exposure to air pollutants and cognitive performance in two age groups of children, also assessing combined pollutants and identifying sensitive prenatal exposure windows.

Methods: A total of 781 children were included: 295 preschool-aged (4-5 years) and 486 school-aged (10-11 years), recruited from the EPINED epidemiological project in Tarragona, Spain. Cognitive performance was assessed using the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-IV) and Wechsler Intelligence Scale for Children (WISC-IV). Associations were examined using linear distributed lag models, and combined effects of pollutants were evaluated using weighted quantile sum regression, adjusting for socio-familial, individual, and environmental factors.

Results: In preschool-aged children, $PM_{2.5}$, $PM_{2.5abs}$, PM_{coarse}, PM_{10}, NO_x, and NO_2 were associated with lower fluid reasoning [$\beta = -0.97$-(-2.29)], working memory [$\beta = -0.82$-(-3.79)] and full-scale IQ [$\beta = -0.63$-(-2.08)]. In school-aged children, most pollutants were associated with reduced verbal comprehension [$\beta = -0.87$-(-3.84)] and full-scale IQ [$\beta = -0.85$-(-1.99)] and subtle effects were observed for perceptual reasoning and working memory. Across both age groups, these associations were greater during the third trimester. Whereas the combined pollutant effects indicated the second trimester as a critical window for verbal comprehension in school-aged children, suggesting pollutant contribution varies across gestation.

Conclusions: Prenatal exposure to air pollutants, particularly in late pregnancy, is associated with lower full-scale IQ and other aspects of cognitive performance, highlighting critical windows of vulnerability for foetal brain development.

1. Introduction

Air pollution remains one of the most pervasive and insidious environmental threats to children's health (WHO, 2025). Globally, prenatal exposure to air pollutants is increasingly recognised as a significant risk factor for altered child neurodevelopment and cognitive functioning (Amnuaylojaroen et al., 2024; Kaur et al., 2023). The prenatal period marks an exceptional window of vulnerability, since the developing brain undergoes rapid and highly orchestrated processes such as neurogenesis, neuronal migration, synaptic formation, axonal and dendritic

* Corresponding author. Universitat Rovira i Virgili, Department of Psychology, Faculty of Educational Sciences and Psychology, Carretera de Valls, s/n, 43007 – Tarragona, Spain.
E-mail address: josefa.canals@urv.cat (J. Canals-Sans).

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branching, and myelination (Broséus et al., 2024; Zhao et al., 2021; Wang et al., 2022). Disruption of these processes by environmental perturbations may lead to persistent deficits in the neurodevelopment of children (Shang et al., 2020; Chiu et al., 2023).

Emerging epidemiological evidence associates maternal exposure to fine particulate matter ($PM_{2.5}$: particulate matter $\leq$2.5 μm, PM_{10}: particulate matter $\leq$10 μm), nitrogen oxides (NO_x, NO_2: nitrogen dioxide) and other traffic-related air pollutants during pregnancy with lower cognitive scores, slower psychomotor development, and changes in white-matter structure in children (Guxens et al., 2018; Guilbert et al., 2023; Tokuda et al., 2023; Perera et al., 2024). For example, higher prenatal levels of $PM_{2.5}$ and PM_{10} have been associated with poorer composite cognitive and motor scores at two years of age, especially when exposure occurs in mid and late pregnancy (Morgan et al., 2023). Additionally, studies have shown that in utero exposure to NO_2 and $PM_{2.5}$ was associated with impaired cognitive performance and behaviour difficulties in children aged 4-6 years (Ni et al., 2022). In particular, $PM_{2.5}$ has been associated with lower Intelligence Quotient (IQ), reduced working memory and processing speed (Holm et al., 2023), as well as poorer performance in the conflict attentional network (Rivas et al., 2019). Furthermore, it has been reported that higher prenatal NO_2 was associated with impaired attentional performance in children at age 4-5 years (Sentís et al., 2017). However, previous findings were heterogeneous: a large European meta-analysis of six birth cohorts did not find consistent associations between prenatal PMs ($PM_{2.5}$, PM_{10}, PM_{coarse} (particulate matter 2.5-10 μm), and $PM_{2.5abs}$ (particulate matter absorbance, a proxy for black carbon) exposures and cognitive development across all domains, though it did find associations between NO_2 exposure and psychomotor development (Guxens et al., 2014). Similarly, Tokuda et al. (2023) reported no significant association between prenatal $PM_{2.5}$ exposure and cognitive performance, measured by Wechsler Intelligence Scale for Children subscales, such as verbal comprehension, perceptual reasoning, processing speed, working memory and total IQ, in children aged 5 to 6 years. Kusters et al. (2022) also found no association between prenatal pollutant exposure and working memory, processing speed and full-scale IQ. However, they report a significant association between PM_{coarse} and fewer attention problems.

Notably, much of the existing literature relies on single-pollutant models, which cannot capture real-world exposure patterns where multiple pollutants co-occur and are often highly correlated. From a biological perspective, simultaneous exposure to multiple pollutants may result in additive or synergistic effects through shared and interacting mechanisms, such as oxidative stress, neuroinflammation, and interference with critical neurodevelopmental processes. Moreover, different pollutants may affect distinct pathways of brain development, potentially leading to a compounded impact on cognitive function (Allen et al., 2017; Guxens et al., 2022; Lagunas-Rangel et al., 2025). Such approaches may contribute to inconsistent findings and obscure the combined and interactive effects of pollutant mixtures. To our knowledge, one previous study has investigated the combined effect of pollutants and cognitive outcomes in early school-aged children, suggesting its adverse effect on children's memory and attention (Chiu et al., 2023). Therefore, there is a need to investigate further the combined effect of the pollutants on children's cognitive performances.

Importantly, the timing of exposure within gestation has been reported to determine the magnitude and nature of the effect. Studies applying modelling of critical windows suggest that late prenatal exposure to $PM_{2.5}$ is particularly harmful to cognitive outcomes (Hsu et al., 2024). On the other hand, exposure to $PM_{2.5}$ and NO_2 during the first and second trimesters of pregnancy was associated with a lower Mental Development Index (MDI) at 1-3 years of age in children (Perera et al., 2024). Other authors highlight that $PM_{2.5}$ exposure during the first trimester of pregnancy leads to externalising problems and negatively affects working memory only during second trimester exposure in children (Tokuda et al., 2023). Additional studies demonstrate that the second trimester of pregnancy may be a sensitive window for exposure to $PM_{2.5}$, leading to poor neurobehavioural performance in newborns (Chen et al., 2020). Furthermore, exposure to $PM_{2.5}$ and PM_{10} in mid to late pregnancy was associated with motor, cognitive and communication language problems later in children (Guilbert et al., 2023; Morgan et al., 2023).

Despite the growing body of research, important knowledge gaps remain regarding the neurodevelopmental consequences of prenatal exposure to air pollutants. Most previous studies have focused on infants and preschool-aged children; therefore, the present work aims to extend this research by examining whether these effects persist into later developmental stages, considering also school-aged children. Based on the prior evidence, we hypothesise that higher prenatal exposure to key air pollutants, including fine particulate matter ($PM_{2.5}$, PM_{10}, PM_{coarse}, $PM_{2.5abs}$), nitrogen oxides (NO_x and NO_2) and ozone (O_3) is associated with poorer cognitive performance in preschool-aged and school-aged children, as assessed through standardised age-appropriate intelligence tests subscales (verbal comprehension, perceptual reasoning, processing speed, working memory, full scale IQ and vocabulary acquisition). In addition to the primary hypothesis-driven analysis, we conduct a series of exploratory analyses to a) investigate potential sensitive windows of exposure during pregnancy, and b) evaluate the combined effects of multiple co-occurring pollutants while accounting for socio-familial, individual and environmental factors.

2. Methods

2.1. Study design and participants

Participants were recruited from EPINED (Neurodevelopmental Disorders Epidemiological Project), a two-phase epidemiological study conducted between 2014 and 2019 in Tarragona province, Catalonia, Spain, that investigated the prevalence of autism and ADHD in the school population (Canals Sans et al., 2021; Morales Hidalgo et al., 2021). The study was approved by the Sant Joan University Hospital ethics committee (13-10-31/10proj5), and parents provided informed consent after being fully informed about the study procedures. In the first phase (screening), a population-based sample of schoolchildren was recruited through collaboration with local schools across Tarragona province. Schools were invited to participate, and all eligible children within participating schools were screened using questionnaires assessing symptoms of autism and/or ADHD. In total, 6894 children were screened, of whom 3727 parents agreed to participate in further assessment. In the second phase (clinical diagnosis), a total of 781 children who screened positive for symptoms of autism and/or ADHD, along with a subsample of screen-negative children, were invited to undergo comprehensive individual assessments conducted by trained psychologists and psychiatrists according to DSM-5 criteria.

For the present analysis, as detailed in the flowchart in Fig. 1, we included children from the second phase with available maternal pregnancy and cognitive data, comprising 295 preschool-aged children (4-5 years) and 486 school-aged children (10-11 years). Of these, 232 were diagnosed with neurodevelopmental disorders (ADHD and/or autism), while 549 had no diagnosis. The sample size was determined by the available participants in the second phase of the EPINED study with complete exposure and outcome data.

2.2. Cognitive performance assessment

The assessment of cognitive functioning in children was conducted with the Wechsler Preschool and Primary Scale of Intelligence, 4th Ed. (WPPSI-IV) for children aged 2-6 years and the Wechsler Intelligence Scale for Children, 4th Ed. (WISC-IV) for those aged 6-16 years (Wechsler, 2005, 2014). Both tests evaluate intellectual quotient (IQ) and cognitive abilities across several core domains that are conceptually equivalent. The verbal reasoning, language comprehension, and

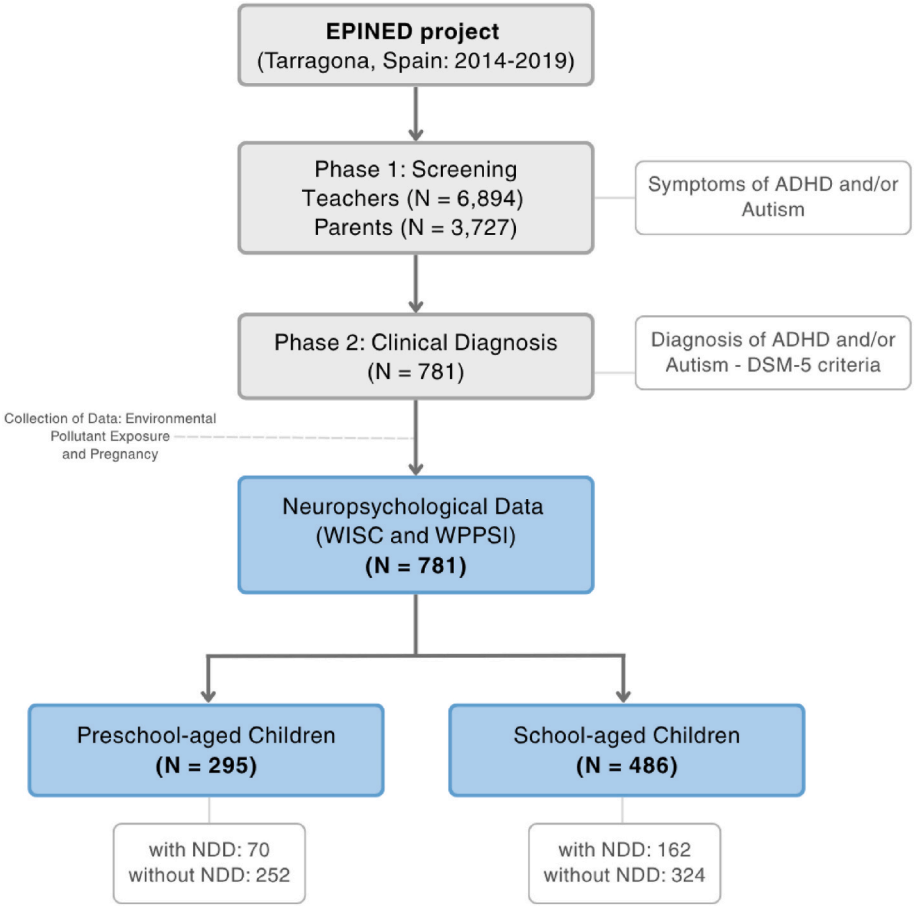


Fig. 1. Flow chart of design and participants included in the study.

acquired knowledge were assessed through the Verbal Comprehension Index (VCI). In the WPPSI-IV, the VCI is based on two subsets: Similarities and Information, whereas in the WISC-IV, it comprises three subtests: Similarities, Vocabulary and Comprehension. Nonverbal reasoning abilities were assessed through the Fluid Reasoning Index (FRI) of the WPPSI-IV, which comprises the Matrix and Picture Concepts subtests. Both Indices evaluate children's capacity to analyse and integrate visual information, detect patterns, and solve novel visuospatial problems, whereas in WISC-IV, it is named the Perceptual Reasoning Index (PRI), which includes three subtests: Block Design, Picture Concepts, and Matrix Reasoning. In the WPPSI-IV, the Working Memory Index (WMI) is assessed using visual working-memory subtests, such as Picture Memory and Zoo Locations. In contrast, in the WISC-IV, the WMI is assessed using auditory working-memory subtests, including Digit span and Letter-number sequencing. Finally, the Processing Speed Index (PSI) in WPPSI-IV is assessed through the Bug Search, or Cancellation subsets, and in WISC-IV is assessed by comparable subsets such as Coding and Symbol Search. In the WISC-IV, the Full-Scale IQ (FSIQ) is composed of the 10 core subtests that constitute the four primary index scores. In the WPPSI-IV, the FSIQ is composed of the VCI scores plus the Block Design, Matrix, Picture Memory and Bug Search subtests. Additionally, we also used the WPPSI-IV Vocabulary Acquisition Index (VAI), a secondary index derived from the Receptive Vocabulary and Picture Naming subtests, to assess early language and vocabulary skills. Cognitive indices were analysed separately to capture domain-specific aspects of cognitive functioning, which may be differentially sensitive to environmental exposures, and to account for age-specific differences in subtest composition between the WPPSI-IV and WISC-IV.

2.3. Estimation of air pollution exposure

Parental reports of residential history since the child's birth were used to estimate prenatal air pollutant exposure at each address, employing a back-extrapolation method that applied background monitoring data to calculate weekly concentrations for the entire pregnancy. Traffic-related exposure at birth addresses was assessed using a Land Use Regression (LUR) model that provides annual average pollutant concentrations at high spatial resolution, assigned to individual residential addresses based on geographic predictors such as traffic and land use. To obtain exposures over the study period, these annual estimates were temporally extrapolated to daily values using the ratio method based on routine background monitoring stations, resulting in daily mean concentrations for six pollutants: $PM_{2.5}$ (aerodynamic $\leq$2.5 μm), PM_{10} (aerodynamics $\leq$10 μm), PM_{coarse} (PM mass between PM_{10}-$PM_{2.5}$), $PM_{2.5absorbance}$ (a black carbon marker - was computed by deducting $PM_{2.5}$ from PM_{10}), NO_2, and NO_x. Particulate matter and nitrogen oxides were monitored at 20-40 sites for two weeks per site across warm, cold, and intermediate seasons (Eeftens et al., 2012). For pollutants with limited monitoring data (PM_{10}, $PM_{2.5}$, $PM_{2.5abs}$, PM_{coarse}, and NO_x), daily NO_2 ratios were used as proxies. The Ozone (O_3) concentrations were estimated from the ELAPSE project using 2010 AirBase v8 data (EEA, 2015), calculated as daily 8-h maximum averages for warm (April-September) and cold seasons (October-March) (de Hoogh et al., 2018). The LUR models were calibrated using measurements from the reference year (2009 for ESCAPE and 2010 for ELAPSE). In Catalonia, the LUR model achieved R^2 values ranging between 62% and 76% for $PM_{2.5}$, PM_{coarse}, PM_{10}, $PM_{2.5abs}$, NO_x, NO_2, and O_3 (Eeftens et al., 2012; de Hoogh et al., 2018).

To obtain daily exposures over the full study period, pollutant

concentrations were extrapolated using the ratio method based on routine background monitoring stations located within 100 km of the study areas. Daily pollutant concentrations at selected stations were averaged, and the ratio between each day's average and the reference-year annual mean was calculated and applied to estimate exposures. Spanish monitoring stations were used for NO_2, and Catalan stations for O_3 due to gaps in the Spanish dataset.

2.4. Covariables

We included several covariates as potential confounders in the statistical models, as they may influence neuropsychological performance. Covariate selection was informed by a directed acyclic graph (DAG) developed a priori (Supplementary SFig. 1). Covariates were collected across different phases of the study. During the first screening phase, child's *sex* was recorded as male or female (Bölte et al., 2023); family *socioeconomic status (SES)* (Lu et al., 2025) was calculated based on maternal and paternal education and family income, and classified as low, medium, or high according to the Catalan occupational classification (CCO-2011) and parents reported residential address information used for air pollution exposure assessment. Additional covariates were collected during the second phase from parents via questionnaires or interviews, such as maternal pregnancy factors, including *alcohol or tobacco* use during pregnancy (yes/no) (Jacobson et al., 2021; Puga et al., 2024), *gestational weight gain* (kg, continuous) (Y. Zhang et al., 2025), and whether the child was *small for gestational age* (yes/no) (Ceran et al., 2022; Reichman et al., 2023). The presence of *neurodevelopmental disorders*, such as autism and/or ADHD, was estimated according to the primary aims of the project (yes/no) (Canals Sans et al., 2021; Morales Hidalgo et al., 2021). Prenatal environmental factors included the *Normalised Difference Vegetation Index (NDVI)* (continuous), which reflects the surrounding greenness within a 300-m buffer of each residence (Weier and Herring, 2000). Satellite images from 2009 to 2015 were obtained from the USGS website and processed to remove low-quality data, including water, snow, and saturated pixels. The *Deprivation Index*, a continuous measure of socioeconomic disadvantage in Spanish census tracts based on regional socioeconomic indicators, was included in the analysis (Duque et al., 2021; Xia and Vieira, 2025). Categorical variables were used where clinically meaningful groupings were appropriate, while continuous variables were retained in their original scale to preserve information and statistical power.

2.5. Statistical analysis

Weekly prenatal exposure data for multiple air pollutants were merged with child cognitive outcomes assessed using the WPPSI-IV/WISC-IV subscales. All covariates were treated as categorical where appropriate. Pollutant exposures were standardised with their respective conventional units: 20 $\mu g/m^3$ for NO_x, 10 $\mu g/m^3$ for NO_2, O_3, and PM_{10}, 5 $\mu g/m^3$ for $PM_{2.5}$ and PM_{coarse} and 10^{-5} m^{-1} for $PM_{2.5absorbance}$ (Beelen et al., 2013; Eeftens et al., 2012). Analyses were conducted using complete-case data for all exposure and outcome variables; outcome variables had low rates of missingness (preschool-aged: 3.7-4.4% across WPPSI-IV subscales; school-aged: 0.8-1.0% across WISC-IV subscales). These missing outcome data were primarily related to neurodevelopmental disorders (language disorders and intellectual disability), which precluded reliable administration of specific cognitive subscales. For covariates, pregnancy weight gain (~10% data missingness) was imputed using the sample mean to retain sample size. Multicollinearity among covariates was assessed using variance inflation factors (VIFs: 1.00-1.50), indicating no evidence of collinearity. To identify potential sensitive windows of prenatal exposure, we implemented linear *distributed lag models (DLMs)* for gestational weeks 1-38, regressing each cognitive outcome on a pollutant-specific cross-basis function while adjusting for covariates. Weekly exposure data were modelled in the DLMs, and trimester-specific effects were subsequently derived by aggregating the estimated weekly lag-response coefficients over predefined gestational periods. Exposure-response relationships were modelled linearly, whereas lag-response relationships were modelled using third-degree (cubic) polynomials to capture smooth, nonlinear temporal effects across gestation. Weekly effect estimates with 95% confidence intervals were extracted, and trimester-average effects, trimester 1 (T1): weeks 1-13; trimester 2 (T2): weeks 14-26; trimester 3 (T3): weeks 27-38, were computed using standard error propagation. Due to the high correlation among pollutants and the complexity of distributed lag structures, DLMs were implemented as single-pollutant models. Additionally, postnatal exposure was excluded due to high correlation with prenatal exposure (Spearman $\rho > 0.9$), precluding reliable estimation and interpretation of independent effects. To evaluate the combined effects of pollutants, Weighted Quantile Sum (WQS) regression was applied to trimester-averaged exposures, estimating pollutant weights from 500 bootstrap resamples (with a 60% training/40% validation split) (Carrico et al., 2015). Models were fit for each cognitive outcome in the full sample using the same covariate set as in the DLMs. All analyses were conducted in R (version 4.5.1) using the dlnm and gWQS packages (Gasparrini, 2011; Gennings et al., 2025).

3. Results

3.1. Characteristics of participants and pollutants

Table 1 summarises the socio-demographic, pre- and perinatal, and cognitive characteristics of the study sample. Males constituted the majority in both age groups, accounting for 60.7% of preschool-aged children and 63.4% of school-aged children. The prevalence of autism and/or ADHD was higher among school-aged children (33.3%) compared to preschool-aged children (23.7%). Parental socioeconomic status was comparable across groups, with most families classified as medium SES. Neuropsychological assessments indicated that mean cognitive scores fell within the average range for both age groups, with preschool-aged and school-aged children demonstrating IQs in the normal/average range.

Most pollutants exhibited strong positive correlations, particularly between $PM_{2.5abs}$ and NO_x/NO_2 ($r = 0.94$), suggesting common emission sources or atmospheric behaviour. Moderate to strong correlations were observed among PM_{coarse}, $PM_{2.5abs}$, and $PM_{2.5}$ ($r = 0.77$-0.83). In contrast, O_3 shows consistently negative correlations, most notably with $PM_{2.5}$ ($r = -0.40$), reflecting its distinct photochemical formation mechanisms (Table 2).

3.2. Trimester-specific effects of prenatal pollutant exposure

Table 3 presents associations between prenatal air pollution exposure and WPPSI-IV cognitive performance in preschool-aged children. Overall, $PM_{2.5}$, PM_{10}, PM_{coarse}, $PM_{2.5abs}$, NO_x, and NO_2 were the most consistently associated with WMI and FRI. In particular, $PM_{2.5}$ showed consistent negative associations across multiple domains, including VCI, FRI, WMI, and FSIQ. Stronger associations were observed for $PM_{2.5abs}$, NO_x, and NO_2, with the largest effects generally seen for WMI and FRI. In contrast, no associations were observed for PSI. Trimester-specific analyses indicated that associations were generally strongest in the third trimester. The largest magnitude associations were observed for NO_x, NO_2, and $PM_{2.5abs}$, particularly for FRI and WMI, with comparatively smaller effects for FSIQ. PM_{10} and PM_{coarse} showed similar but weaker patterns, mainly in late pregnancy for FRI and WMI. Furthermore, PM_{coarse} and $PM_{2.5}$ were more strongly associated with VCI during the third trimester. In contrast, O_3 exposure was positively associated with several cognitive domains, with the most consistent but weaker associations observed for VCI, FRI, WMI and FSIQ, particularly in the third trimester.

Table 4 presents associations between prenatal air pollution exposure and WISC-IV cognitive performance in school-aged children.

Table 1
Socio-demographic, pre- and perinatal, and cognitive characteristics of the study participants.

		Preschool-aged (N = 295)	*School-aged* (N = 486)
Children			
Age (years)		4.64 ± 0.65 (4-6; 4-5)	10.61 ± 0.61 (10-11; 10-11)
Sex	Male	179 (60.7)	308 (63.4)
	Female	116 (39.9)	178 (36.6)
ADHD and/or Autism		70 (23.7)	162 (33.3)
Cognitive Performance			
WPPSI-IV (n)			
	VCI (282)	94.83 ± 17.37 (45-138; 85-106)	-
	FRI (284)	102.65 ± 15.84 (49-140; 94-114)	-
	WMI (284)	97.91 ± 14.63 (52-141; 87-97)	-
	PSI (282)	94.92 ± 14.04 (54-132; 85-103)	-
	FSIQ (282)	96.96 ± 15.97 (48-130; 89-110)	-
	VAI (283)	93.97 ± 17.24 (46-147; 82-106)	-
WISC-IV (n)			
	VCI (481)	-	103.53 ± 13.46 (53-136; 95-113)
	PRI (482)	-	104.84 ± 15.12 (53-148; 93-114)
	WMI (481)	-	95.46 ± 15.00 (50-147; 85-105)
	PSI (482)	-	100.01 ± 13.72 (62-138; 93-110)
	FSIQ (481)	-	101.21 ± 14.65 (49-144; 91-110)
Parents/Family			
SES	Low	56 (19.0)	91 (18.7)
	Medium	184 (62.4)	304 (62.6)
	High	55 (18.6)	91 (18.7)
Pregnancy			
Weeks of pregnancy		38.72 ± 2.82 (27-42; 38-40)	38.99 ± 2.48 (26-42; 38-40)
Weight gain (in kgs)		13.88 ± 7.37 (-17-48; 10-18)	14.25 ± 6.61 (-10-44; 10-18)
Alcohol/tobacco (yes)		55 (18.6)	94 (19.3)
SGA (yes)		54 (18.3)	79 (16.3)

n (%); M ± SD (range; IQR). Abbreviations: SES: Socio-economic status; SGA: Small for gestational age; WPPSI: Wechsler Preschool and Primary Scale of Intelligence; VCI: Verbal Comprehension Index; FRI: Fluid Reasoning Index; PRI: Perceptual Reasoning Index; WMI: Working Memory Index; PSI: Processing Speed Index; FSIQ: Full Scale IQ. VAI: Vocabulary Acquisition Index.

Overall, $PM_{2.5}$, PM_{10}, PM_{coarse}, $PM_{2.5abs}$, NO_x, and NO_2 were the most consistent associations observed for VCI and FSIQ. $PM_{2.5}$ showed consistent negative associations with VCI, PSI, and FSIQ, while PM_{10} was additionally associated with PRI. In contrast, PM_{coarse}, PM_{abs}, NO_x, and NO_2 exhibited stronger associations with VCI, PRI, and FSIQ, and weaker associations with WMI. Trimester-specific analyses indicated that associations were generally strongest in the third trimester. The largest magnitude associations were observed for NO_x, NO_2, $PM_{2.5abs}$, and PM_{coarse}, particularly for VCI, with similar but smaller effects for FSIQ. Patterns for PRI and WMI were less consistent across pollutants and trimesters. Furthermore, no clear associations were observed between O_3 exposure and cognitive performance across domains in school-aged children.

3.3. Combined effects of prenatal pollutant mixtures

The WQS analysis revealed trimester-specific contributions of prenatal air pollutant mixtures to WPPSI-IV cognitive performance (Fig. 2; S Table 1). The overall trimester-specific mixture estimates were not statistically significant across cognitive domains. In the first trimester, $PM_{2.5}$ contributed most strongly to working memory (WMI; 74%) and showed notable contributions to VCI (37%) and FSIQ (53%). PM_{10} also contributed to VCI (29%) and PSI (54%), while O_3 showed moderate contributions across domains, including fluid reasoning FRI (44%) and FSIQ (27%). In the second trimester, contributions were more distributed across pollutants. $PM_{2.5}$ remained an important contributor to FRI (47%) and WMI (24%), while PM_{10} contributed to WMI (33%) and FRI (33%). NO_2 showed a dominant contribution to FSIQ (61%), and O_3 contributed moderately across several domains, including VCI (28%) and WMI (36%). In the third trimester, O_3 emerged as the dominant contributor across multiple cognitive domains, particularly for VAI (88%), FSIQ (74%), FRI (65%), VCI (60%), and PSI (49%). NO_x also showed increased contributions in late pregnancy, particularly for WMI (38%) and PSI (41%). Contributions from $PM_{2.5}$ and PM_{10} were generally smaller in this trimester, and $PM_{2.5abs}$ showed negligible contributions across all outcomes.

For WISC-IV outcomes (Fig. 3; STable 2), WQS analysis showed trimester-specific patterns in the relative contributions of prenatal air pollutant mixtures. Most trimester-specific combined pollutant estimates were not statistically significant, except for VCI in the second trimester, which showed a significant association (−3.17, 95% CI: −5.91, −0.42). In the first trimester, $PM_{2.5}$ contributed most strongly across several domains, particularly for PRI (84%), WMI (38%), and FSIQ (45%), while O_3 also contributed notably to VCI (37%) and FSIQ (34%). PM_{10} and PM_{coarse} showed more moderate contributions across domains. In the second trimester, $PM_{2.5}$ remained a major contributor, particularly for VCI (63%), PRI (65%), and FSIQ (54%). PM_{10} contributed substantially to WMI (63%) and FSIQ (34%), while NO_x showed a notable contribution to PSI (43%). Contributions from O_3 were generally smaller in this trimester. In the third trimester, contributions were more distributed across pollutants. PM_{10} contributed most to VCI (53%), while O_3 showed the largest contributions to PRI (41%) and PSI (27%). PM_{coarse} contributed notably to FSIQ (39%) and PSI (27%), and NO_x showed moderate contributions to WMI (26%). Contributions from $PM_{2.5}$ were comparatively smaller in this trimester.

Table 2
Correlation and descriptive statistics of prenatal pollutant exposures.

Pollutants	Spearman correlation[a]							Descriptive statistics				
	$PM_{2.5}$	*PM_{10}*	*$PM_{2.5abs}$*	*PM_{coarse}*	*NO_2*	*NO_x*	*O_3*	*Mean*	*SD*	*25*th	*50*th	*75*th
$PM_{2.5}$	1.00							14.94	1.93	13.84	15.12	16.15
PM_{10}	0.38	1.00						32.77	5.64	29.46	33.03	35.64
$PM_{2.5abs}$	0.77	0.41	1.00					1.86	0.49	1.54	1.83	2.15
PM_{coarse}	0.78	0.39	0.83	1.00				18.69	4.44	15.56	18.46	21.34
NO_2	0.60	0.36	0.94	0.75	1.00			31.58	13.65	22.89	30.97	39.74
NO_x	0.59	0.36	0.94	0.75	1.00	1.00		52.70	23.76	37.39	51.55	66.91
O_3	−0.40	−0.22	−0.30	−0.32	−0.21	−0.21	1.00	70.06	9.40	64.52	68.59	76.45

Abbreviations: IQR: Interquartile range; SD: standard deviation; $PM_{2.5}$: Particulate matter with aerodynamic diameter ≤2.5 μm; PM_{10}: Particulate matter with aerodynamic diameter ≤10 μm; PM_{coarse}: Particulate matter 2.5–10 μm; $PM_{2.5abs}$: Absorbance of PM < 2.5 μm; NO_2: Nitrogen dioxide; NO_x: Nitrogen oxides; O_3: Ozone.
[a] Spearman correlation between pollutants, p-values <0.001.

Table 3
Cognitive performance by prenatal air pollution exposure from WPPSI-IV in preschool-aged children.

Pollutants	Trimesters	VCI	*p*	FRI	*p*	WMI	*p*	PSI	*p*	FSIQ	*p*	VAI	*p*
		β *(CI 95%)*		β *(CI 95%)*		β *(CI 95%)*		β *(CI 95%)*		β *(CI 95%)*		β *(CI 95%)*	
$PM_{2.5}$	Overall	**−0.97 (-1.50, -0.44)**	**<0.001**	**−0.95 (-1.45, -0.44)**	**<0.001**	**−1.16 (-1.60, -0.71)**	**<0.001**	−0.16 (−0.59, 0.26)	0.454	**−0.92 (-1.39, -0.45)**	**<0.001**	−0.47 (−0.98, 0.03)	0.067
	1	**−0.55 (-0.83, -0.26)**	**<0.001**	**−0.53 (-0.80, -0.26)**	**<0.001**	**−0.65 (-0.89, -0.41)**	**<0.001**	−0.09 (−0.32, 0.14)	0.435	**−0.52 (-0.77, -0.26)**	**<0.001**	−0.27 (−0.54, 0.01)	0.056
	2	**−0.99 (-1.50, -0.48)**	**<0.001**	**−0.96 (-1.45, -0.48)**	**<0.001**	**−1.18 (-1.61, -0.75)**	**<0.001**	−0.17 (−0.57, 0.24)	0.426	**−0.93 (-1.39, -0.48)**	**<0.001**	−0.48 (−0.97, 0.00)	0.052
	3	**−1.41 (-2.14, -0.69)**	**<0.001**	**−1.38 (-2.07, -0.69)**	**<0.001**	**−1.69 (-2.30, -1.08)**	**<0.001**	−0.24 (−0.82, 0.34)	0.424	**−1.34 (-1.98, -0.69)**	**<0.001**	−0.69 (−1.38, 0.00)	0.051
PM_{10}	Overall	0.25 (−0.19, 0.69)	0.260	**−0.62 (-1.04, -0.21)**	**0.003**	**−0.53 (-0.90, -0.16)**	**0.004**	−0.28 (−0.63, 0.07)	0.123	**−0.41 (-0.80, -0.01)**	**0.042**	**−0.95 (-1.37, -0.53)**	**<0.001**
	1	0.12 (−0.08, 0.31)	0.239	**−0.29 (-0.48, -0.11)**	**0.002**	**−0.25 (-0.41, -0.08)**	**0.003**	−0.13 (−0.29, 0.03)	0.107	**−0.19 (-0.37, -0.01)**	**0.034**	**−0.45 (-0.63, -0.26)**	**<0.001**
	2	0.26 (−0.15, 0.67)	0.219	**−0.64 (-1.03, -0.25)**	**0.001**	**−0.54 (-0.88, -0.20)**	**0.001**	−0.28 (−0.61, 0.05)	0.092	**−0.41 (-0.78, -0.05)**	**0.027**	**−0.97 (-1.36, -0.58)**	**<0.001**
	3	0.39 (−0.23, 1.01)	0.216	**−0.97 (-1.56, -0.38)**	**0.001**	**−0.82 (-1.34, -0.31)**	**0.001**	−0.43 (−0.92, 0.07)	0.090	**−0.63 (-1.19, -0.08)**	**0.026**	**−1.48 (-2.07, -0.89)**	**<0.001**
PM_{coarse}	Overall	0.05 (−0.62, 0.72)	0.878	**−1.02 (-1.66, -0.38)**	**0.001**	**−1.66 (-2.21, -1.10)**	**<0.001**	0.12 (−0.41, 0.66)	0.651	**−0.61 (-1.21, -0.01)**	**0.045**	−0.52 (−1.16, 0.12)	0.113
	1	0.02 (−0.28, 0.32)	0.873	**−0.48 (-0.76, -0.19)**	**0.001**	**−0.78 (-1.03, -0.53)**	**<0.001**	0.06 (−0.18, 0.30)	0.637	**−0.29 (-0.55, -0.02)**	**0.037**	−0.24 (−0.53, 0.04)	0.098
	2	0.05 (−0.57, 0.68)	0.868	**−1.04 (-1.64, -0.45)**	**<0.001**	**−1.69 (-2.21, -1.17)**	**<0.001**	0.13 (−0.37, 0.63)	0.622	**−0.62 (-1.18, -0.06)**	**0.029**	−0.53 (−1.13, 0.07)	0.084
	3	0.08 (−0.87, 1.03)	0.867	**−1.59 (-2.49, -0.68)**	**<0.001**	**−2.57 (-3.36, -1.79)**	**<0.001**	0.19 (−0.56, 0.95)	0.619	**−0.95 (-1.79, -0.10)**	**0.028**	−0.80 (−1.71, 0.10)	0.082
$PM_{2.5abs}$	Overall	**−0.96 (-1.58, -0.34)**	**0.002**	**−1.28 (-1.87, -0.69)**	**0.001**	**−1.87 (-2.38, -1.35)**	**<0.001**	0.22 (−0.28, 0.72)	0.386	**−0.94 (-1.50, -0.39)**	**<0.001**	−0.50 (−1.09, 0.09)	0.098
	1	**−0.45 (-0.73, -0.17)**	**0.001**	**−0.60 (-0.86, -0.34)**	**<0.001**	**−0.87 (-1.11, -0.64)**	**<0.001**	0.10 (−0.12, 0.32)	0.365	**−0.44 (-0.69, -0.19)**	**<0.001**	−0.23 (−0.50, 0.03)	0.084
	2	**−0.98 (-1.57, -0.40)**	**<0.001**	**−1.31 (-1.86, -0.76)**	**<0.001**	**−1.91 (-2.39, -1.42)**	**<0.001**	0.22 (−0.24, 0.69)	0.345	**−0.96 (-1.48, -0.45)**	**<0.001**	−0.51 (−1.07, 0.04)	0.071
	3	**−1.50 (-2.38, -0.62)**	**<0.001**	**−1.99 (-2.83, -1.16)**	**<0.001**	**−2.90 (-3.63, -2.17)**	**<0.001**	0.34 (−0.36, 1.04)	0.341	**−1.47 (-2.25, -0.68)**	**<0.001**	−0.78 (−1.61, 0.06)	0.069
NO_x	Overall	−0.59 (−1.23, 0.05)	0.071	**−1.38 (-1.98, -0.77)**	**<0.001**	**−2.27 (-2.81, -1.74)**	**<0.001**	−0.14 (−0.65, 0.37)	0.588	**−1.25 (-1.82, -0.67)**	**<0.001**	−0.06 (−0.67, 0.55)	0.851
	1	−0.21 (−0.44, 0.02)	0.068	**−0.49 (-0.71, -0.28)**	**<0.001**	**−0.82 (-1.01, -0.63)**	**<0.001**	−0.05 (−0.23, 0.13)	0.583	**−0.45 (-0.65, -0.24)**	**<0.001**	−0.02 (−0.24, 0.20)	0.850
	2	**−0.61 (-1.19, -0.02)**	**0.042**	**−1.41 (-1.97, -0.86)**	**<0.001**	**−2.33 (-2.82, -1.85)**	**<0.001**	−0.14 (−0.61, 0.32)	0.541	**−1.28 (-1.80, -0.76)**	**<0.001**	−0.06 (−0.62, 0.50)	0.833
	3	**−0.99 (-1.92, -0.05)**	**0.039**	**−2.29 (-3.18, -1.40)**	**<0.001**	**−3.79 (-4.57, -3.01)**	**<0.001**	−0.24 (−0.98, 0.51)	0.536	**−2.08 (-2.91, -1.24)**	**<0.001**	−0.10 (−0.99, 0.80)	0.831
NO_2	Overall	−0.43 (−0.97, 0.12)	0.126	**−1.11 (-1.63, -0.59)**	**<0.001**	**−2.00 (-2.45, -1.55)**	**<0.001**	−0.12 (−0.56, 0.31)	0.580	**−1.04 (-1.52, -0.55)**	**<0.001**	0.04 (−0.48, 0.56)	0.880
	1	−0.15 (−0.35, 0.04)	0.122	**−0.40 (-0.58, -0.21)**	**<0.001**	**−0.72 (-0.88, -0.56)**	**<0.001**	−0.04 (−0.20, 0.11)	0.575	**−0.37 (-0.55, -0.20)**	**<0.001**	0.01 (−0.17, 0.20)	0.879
	2	−0.44 (−0.93, 0.06)	0.084	**−1.14 (-1.61, -0.66)**	**<0.001**	**−2.05 (-2.46, -1.64)**	**<0.001**	−0.13 (−0.52, 0.27)	0.532	**−1.06 (-1.51, -0.62)**	**<0.001**	0.04 (−0.43, 0.51)	0.865

(*continued on next page*)

Table 3 (*continued*)

Pollutants	Trimesters	VCI	*p*	FRI	*p*	WMI	*p*	PSI	*p*	FSIQ	*p*	VAI	*p*
		β *(CI 95%)*		β *(CI 95%)*		β *(CI 95%)*		β *(CI 95%)*		β *(CI 95%)*		β *(CI 95%)*	
	3	−0.71 (−1.51, 0.09)	0.081	**−1.85 (-2.60, -1.09)**	**<0.001**	**−3.33 (-3.99, -2.67)**	**<0.001**	−0.20 (−0.84, 0.43)	0.528	**−1.73 (-2.44, -1.02)**	**<0.001**	0.07 (−0.69, 0.83)	0.863
O_3	Overall	0.30 (−0.01, 0.62)	0.061	**0.31 (0.01, 0.61)**	**0.044**	**0.41 (0.14, 0.68)**	**0.002**	0.24 (−0.02, 0.49)	0.070	**0.38 (0.09, 0.66)**	**0.009**	0.29 (−0.01, 0.59)	0.062
	1	**0.15 (0.00, 0.30)**	**0.050**	**0.15 (0.01, 0.29)**	**0.035**	**0.20 (0.08, 0.33)**	**0.001**	0.12 (−0.00, 0.24)	0.056	**0.18 (0.05, 0.32)**	**0.006**	**0.14 (0.00, 0.28)**	**0.050**
	2	**0.31 (0.01, 0.61)**	**0.042**	**0.32 (0.03, 0.60)**	**0.029**	**0.42 (0.17, 0.67)**	**0.001**	0.24 (−0.00, 0.48)	0.051	**0.38 (0.12, 0.65)**	**0.004**	**0.29 (0.01, 0.58)**	**0.043**
	3	**0.47 (0.02, 0.91)**	**0.041**	**0.48 (0.05, 0.90)**	**0.028**	**0.63 (0.25, 1.00)**	**0.001**	0.36 (−0.01, 0.72)	0.051	**0.57 (0.18, 0.97)**	**0.004**	**0.44 (0.02, 0.87)**	**0.041**

Models were adjusted for the child's sex, family socio-economic status, maternal alcohol or tobacco consumption during pregnancy, gestational weight gain, small-for-gestational-age status, normalised difference vegetation index and deprivation index.

Abbreviations: VCI: Verbal Comprehension Index; FRI: Fluid Reasoning Index; WMI: Working Memory Index; PSI: Processing Speed Index; FSIQ: Full Scale IQ; VAI: Vocabulary Acquisition Index; $PM_{2.5}$: Particulate matter with aerodynamic diameter ≤2.5 μm; PM_{10}: Particulate matter with aerodynamic diameter ≤10 μm; PM_{coarse}: Particulate matter 2.5–10 μm; $PM_{2.5abs}$: Absorbance of PM < 2.5 μm; NO_2: Nitrogen dioxide; NO_x: Nitrogen oxides; O_3: Ozone.

4. Discussion

In this study, we investigated the association between prenatal exposure to multiple air pollutants and cognitive performance in both preschool-aged and school-aged children. By examining a broad developmental window and several pollutants, particularly $PM_{2.5}$, $PM_{2.5abs}$, NO_x, NO_2, and to a lesser extent PM_{10}, PM_{coarse}, the study highlights that higher prenatal exposure to particulate matter and nitrogen oxides is associated with poorer cognitive performance, particularly affecting verbal comprehension, perceptual or fluid reasoning, working memory, and FSIQ. While single-pollutant models identified stronger associations in the third trimester of pregnancy, mixture analyses highlighted that the relative contributions of pollutants varied across trimesters, with PMs contributing more to earlier stages and O_3 and other pollutants contributing more prominently at later stages. Although most mixture estimates were not statistically significant except for verbal comprehension in school-aged children, these findings suggest that considering pollutant mixtures provides complementary insight into the complexity of prenatal exposure patterns beyond individual pollutant effects.

4.1. Cognitive effects in preschool- vs. school-aged children

Among preschool-aged children, higher prenatal exposure to $PM_{2.5}$, PM_{10}, $PM_{2.5abs}$, PM_{coarse}, NO_x and NO_2 was associated with lower scores on several WPPSI-IV domains, particularly fluid reasoning, working memory and full-scale IQ. These results are in line with previous cohorts showing that prenatal PM_{10}, $PM_{2.5}$ and NO_2 are associated with poorer cognitive and executive function in early childhood, including lower IQ, memory and attentional performance (Loftus et al., 2019; Chiu et al., 2016, 2023; Guilbert et al., 2023). Authors have found that prenatal $PM_{2.5}$ exposure during specific gestational windows was associated with poor performance in memory and attention domains at early school ages, with evidence of sensitive windows during pregnancy (Chiu et al., 2016; Hsu et al., 2024). Similar associations for NO_2 have been reported for psychomotor development and attention (Shang et al., 2020). Consistent with earlier studies, we also observed a significant association between $PM_{2.5}$, $PM_{2.5abs}$, NO_x exposure and the verbal comprehension index, indicating lower vocabulary-related skills in preschool-aged children (Volk et al., 2021). Nevertheless, these associations should be interpreted cautiously and examined further.

In school-aged children, we observed that prenatal $PM_{2.5}$, $PM_{2.5abs}$, PM_{coarse}, NO_x and NO_2 remained associated with lower verbal comprehension and full-scale IQ scores on the WISC-IV, indicating that detrimental effects of prenatal air pollution may persist into later childhood rather than dissipating over time. This persistence is consistent with recent studies showing that prenatal $PM_{2.5}$ exposure predicts lower IQ and processing speed (Holm et al., 2023) and cognitive performance at 6-10 years of age, and with systematic reviews linking early-life $PM_{2.5}$ to lasting cognitive impacts (X. Zhang et al., 2022). On the other hand, a study found that higher exposure to PM_{coarse} was associated with fewer attention problems (Kusters et al., 2022). Furthermore, we observed subtle associations between $PM_{2.5abs}$, PM_{coarse}, NO_x and NO_2 and perceptual reasoning and working memory, whereas few comparable associations were observed in school-aged children; therefore, these results should be interpreted with caution (Volk et al., 2021).

In contrast to other pollutants, O_3 showed positive associations with cognitive performance in preschool-aged children. In our data, O_3 was negatively correlated with traffic-related pollutants (PM and NO_x), consistent with atmospheric "NO titration" in high-traffic areas (Tobías et al., 2020; Zhan et al., 2025). This inverse spatial association has been widely noted and may lead to apparently protective associations with ozone when O_3 functions as a proxy for reduced traffic-related pollution, rather than reflecting beneficial exposure per se. The absence of O_3 associations in school-aged children, combined with the strong negative impacts of PM and NO_x, supports the interpretation that positive O_3 associations reflect negative confounding or mixture collinearity, not true neuroprotective effects (Kusters et al., 2022).

4.2. Sensitive windows of prenatal exposure

In contrast to previous studies, which typically identify the first or second trimester as the most vulnerable period (Perera et al., 2024; Tokuda et al., 2023), we found that prenatal exposure to individual pollutants in the third trimester had the strongest impact across both age groups. Our results are consistent with Hsu et al. (2024) who reported that substantial $PM_{2.5}$ exposure in late gestation (30-40 weeks) can affect the neurodevelopment of children. Throughout the middle to late stages of pregnancy, neuro-apoptosis, a normal, programmed cell death involved in neural differentiation, takes place. There is evidence that neuroinflammation brought on by air pollution can interfere with this process (Tau and Peterson, 2010). Accordingly, our findings indicate that exposure during mid-to-late pregnancy may interfere with processes of fetal brain development in this period, subsequently affecting

Table 4
Cognitive Performance by Prenatal Air Pollution Exposure from WISC-IV in school-aged children.

Pollutants	Trimesters	VCI	*p*	PRI	*p*	WMI	*p*	PSI	*p*	FSIQ	*p*
		β *(CI 95%)*		β *(CI 95%)*		β *(CI 95%)*		β *(CI 95%)*		β *(CI 95%)*	
$PM_{2.5}$	Overall	**−1.12 (-1.53, -0.72)**	**<0.001**	−0.26 (−0.72, 0.19)	0.256	0.30 (−0.12, 0.73)	0.163	**−0.64 (-1.05, -0.23)**	**0.002**	**−0.58 (-1.02, -0.15)**	**0.001**
	1	**−0.63 (-0.85, -0.41)**	**<0.001**	−0.15 (−0.39, 0.10)	0.236	0.17 (−0.06, 0.40)	0.145	**−0.36 (-0.58, -0.14)**	**0.001**	**−0.33 (-0.56, -0.10)**	**0.005**
	2	**−1.14 (-1.53, -0.75)**	**<0.001**	−0.27 (−0.70, 0.17)	0.228	0.31 (−0.10, 0.71)	0.138	**−0.65 (-1.04, -0.26)**	**0.001**	**−0.60 (-1.01, -0.18)**	**0.004**
	3	**−1.64 (-2.19, -1.08)**	**<0.001**	−0.38 (−1.00, 0.24)	0.225	0.44 (−0.14, 1.02)	0.136	**−0.93 (-1.49, -0.37)**	**0.001**	**−0.85 (-1.44, -0.26)**	**0.004**
PM_{10}	Overall	**−0.56 (-0.87, -0.26)**	**<0.001**	−0.33 (−0.67, 0.01)	0.054	0.13 (−0.19, 0.45)	0.421	−0.19 (−0.50, 0.11)	0.214	−0.29 (−0.61, 0.03)	0.079
	1	**−0.26 (-0.40, -0.13)**	**<0.001**	**−0.16 (-0.31, 0.00)**	**0.043**	0.06 (−0.08, 0.20)	0.400	−0.09 (−0.23, 0.05)	0.194	−0.14 (−0.28, 0.01)	0.066
	2	**−0.57 (-0.86, -0.29)**	**<0.001**	**−0.34 (-0.66, -0.02)**	**0.035**	0.13 (−0.16, 0.43)	0.380	−0.20 (−0.49, 0.09)	0.175	−0.30 (−0.60, 0.01)	0.055
	3	**−0.87 (-1.30, -0.45)**	**<0.001**	**−0.52 (-0.99, -0.04)**	**0.033**	0.20 (−0.25, 0.65)	0.376	−0.30 (−0.74, 0.13)	0.172	−0.45 (−0.91, 0.01)	0.053
PM_{coarse}	Overall	**−1.67 (-2.17, -1.18)**	**<0.001**	**−0.85 (-1.40, -0.29)**	**0.003**	−0.51 (−1.03, 0.01)	0.054	−0.12 (−0.62, 0.39)	0.649	**−0.97 (-1.50, -0.45)**	**<0.001**
	1	**−0.78 (-1.01, -0.56)**	**<0.001**	**−0.40 (-0.64, -0.15)**	**0.001**	**−0.24 (-0.47, -0.01)**	**0.043**	−0.05 (−0.28, 0.17)	0.634	**−0.46 (-0.69, -0.22)**	**<0.001**
	2	**−1.71 (-2.17, -1.24)**	**<0.001**	**−0.87 (-1.38, -0.35)**	**0.001**	**−0.52 (-1.01, -0.04)**	**0.035**	−0.12 (−0.59, 0.35)	0.619	**−1.00 (-1.49, -0.50)**	**<0.001**
	3	**−2.60 (-3.30, -1.90)**	**<0.001**	**−1.32 (-2.10, -0.53)**	**0.001**	**−0.79 (-1.53, -0.06)**	**0.033**	−0.18 (−0.89, 0.53)	0.617	**−1.51 (-2.26, -0.77)**	**<0.001**
$PM_{2.5abs}$	Overall	**−2.08 (-2.56, -1.61)**	**<0.001**	−0.51 (−1.04, 0.03)	0.062	−0.48 (−0.98, 0.02)	0.058	−0.18 (−0.66, 0.30)	0.460	**−1.06 (-1.57, -0.55)**	**<0.001**
	1	**−0.97 (-1.19, -0.76)**	**<0.001**	−0.24 (−0.47, 0.00)	0.051	**−0.23 (-0.45, 0.00)**	**0.047**	−0.09 (−0.30, 0.13)	0.441	**−0.50 (-0.72, -0.27)**	**<0.001**
	2	**−2.13 (-2.57, -1.68)**	**<0.001**	**−0.52 (-1.01, -0.02)**	**0.041**	**−0.49 (-0.96, -0.03)**	**0.038**	−0.19 (−0.64, 0.27)	0.421	**−1.08 (-1.56, -0.60)**	**<0.001**
	3	**−3.23 (-3.91, -2.56)**	**<0.001**	**−0.79 (-1.54, -0.03)**	**0.040**	**−0.75 (-1.46, -0.04)**	**0.037**	−0.28 (−0.96, 0.40)	0.417	**−1.64 (-2.36, -0.93)**	**<0.001**
NO_x	Overall	**−2.31 (-2.76, -1.85)**	**<0.001**	**−0.63 (-1.14, -0.12)**	**0.015**	**−0.53 (-1.01, -0.06)**	**0.028**	−0.25 (−0.71, 0.21)	0.292	**−1.19 (-1.68, -0.71)**	**<0.001**
	1	**−0.83 (-0.99, -0.67)**	**<0.001**	**−0.23 (-0.41, -0.05)**	**0.014**	**−0.19 (-0.36, -0.02)**	**0.027**	−0.09 (−0.25, 0.07)	0.287	**−0.43 (-0.60, -0.26)**	**<0.001**
	2	**−2.36 (-2.78, -1.95)**	**<0.001**	**−0.65 (-1.11, -0.18)**	**0.006**	**−0.55 (-0.98, -0.11)**	**0.013**	−0.26 (−0.68, 0.17)	0.235	**−1.22 (-1.66, -0.78)**	**<0.001**
	3	**−3.84 (-4.50, -3.18)**	**<0.001**	**−1.05 (-1.80, -0.31)**	**0.005**	**−0.89 (-1.59, -0.19)**	**0.012**	−0.41 (−1.09, 0.26)	0.230	**−1.99 (-2.70, -1.28)**	**<0.001**
NO_2	Overall	**−2.02 (-2.41, -1.63)**	**<0.001**	**−0.52 (-0.96, -0.09)**	**0.019**	**−0.42 (-0.83, -0.01)**	**0.047**	−0.19 (−0.58, 0.21)	0.357	**−1.00 (-1.42, -0.59)**	**<0.001**
	1	**−0.73 (-0.86, -0.59)**	**<0.001**	**−0.19 (-0.34, -0.03)**	**0.017**	**−0.15 (-0.30, 0.00)**	**0.044**	−0.07 (−0.21, 0.07)	0.351	**−0.36 (-0.51, -0.21)**	**<0.001**
	2	**−2.07 (-2.42, -1.72)**	**<0.001**	**−0.54 (-0.93, -0.14)**	**0.008**	**−0.43 (-0.80, -0.05)**	**0.025**	−0.19 (−0.55, 0.17)	0.299	**−1.03 (-1.41, -0.65)**	**<0.001**
	3	**−3.37 (-3.93, -2.80)**	**<0.001**	**−0.87 (-1.51, -0.23)**	**0.007**	**−0.69 (-1.29, -0.09)**	**0.023**	−0.31 (−0.89, 0.27)	0.293	**−1.67 (-2.28, -1.06)**	**<0.001**
O_3	Overall	−0.14 (−0.35, 0.07)	0.184	0.09 (−0.15, 0.32)	0.463	−0.02 (−0.24, 0.20)	0.881	−0.01 (−0.22, 0.20)	0.907	−0.03 (−0.25, 0.19)	0.798
	1	−0.07 (−0.17, 0.03)	0.165	0.04 (−0.07, 0.15)	0.443	−0.01 (−0.11, 0.09)	0.876	−0.01 (−0.11, 0.09)	0.903	−0.01 (−0.12, 0.09)	0.789
	2	−0.15 (−0.34, 0.05)	0.150	0.09 (−0.13, 0.31)	0.426	−0.02 (−0.22, 0.19)	0.872	−0.01 (−0.21, 0.19)	0.899	−0.03 (−0.24, 0.18)	0.781
	3	−0.22 (−0.51, 0.08)	0.148	0.13 (−0.19, 0.46)	0.423	−0.03 (−0.33, 0.28)	0.871	−0.02 (−0.32, 0.28)	0.898	−0.04 (−0.36, 0.27)	0.780

Models were adjusted for the child's sex, family socio-economic status, maternal alcohol or tobacco consumption during pregnancy, gestational weight gain, small-for-gestational-age status, normalised difference vegetation index and deprivation index.
Abbreviations: VCI: Verbal Comprehension Index; PRI: Perceptual Reasoning Index; WMI: Working Memory Index; PSI: Processing Speed Index; FSIQ: Full Scale IQ; $PM_{2.5}$: Particulate matter with aerodynamic diameter ≤2.5 μm; PM_{10}: Particulate matter with aerodynamic diameter ≤10 μm; PM_{coarse}: Particulate matter 2.5–10 μm; $PM_{2.5abs}$: Absorbance of PM < 2.5 μm; NO_2: Nitrogen dioxide; NO_x: Nitrogen oxides; O_3: Ozone.

cognitive functioning.

Notably, the critical window showed modest change when considering the combined effect of the pollutants. In school-aged children, the second trimester emerged as most strongly associated with deficits in verbal comprehension. This suggests that while individual pollutants may primarily affect late gestation processes, co-exposure may contribute to earlier neurodevelopmental processes. Previous studies have highlighted second-trimester sensitivity for specific pollutants and cognitive domains (Guilbert et al., 2023; Lertxundi et al., 2019; Morgan et al., 2023), but these findings were based on single-pollutant analyses. In contrast, the mixture effect observed by Chiu et al. (2023) indicated an association across the entire pregnancy. Taken together, these results



Fig. 2. Weighted quantile sum by prenatal air pollutants and trimesters - WPPSI-IV.

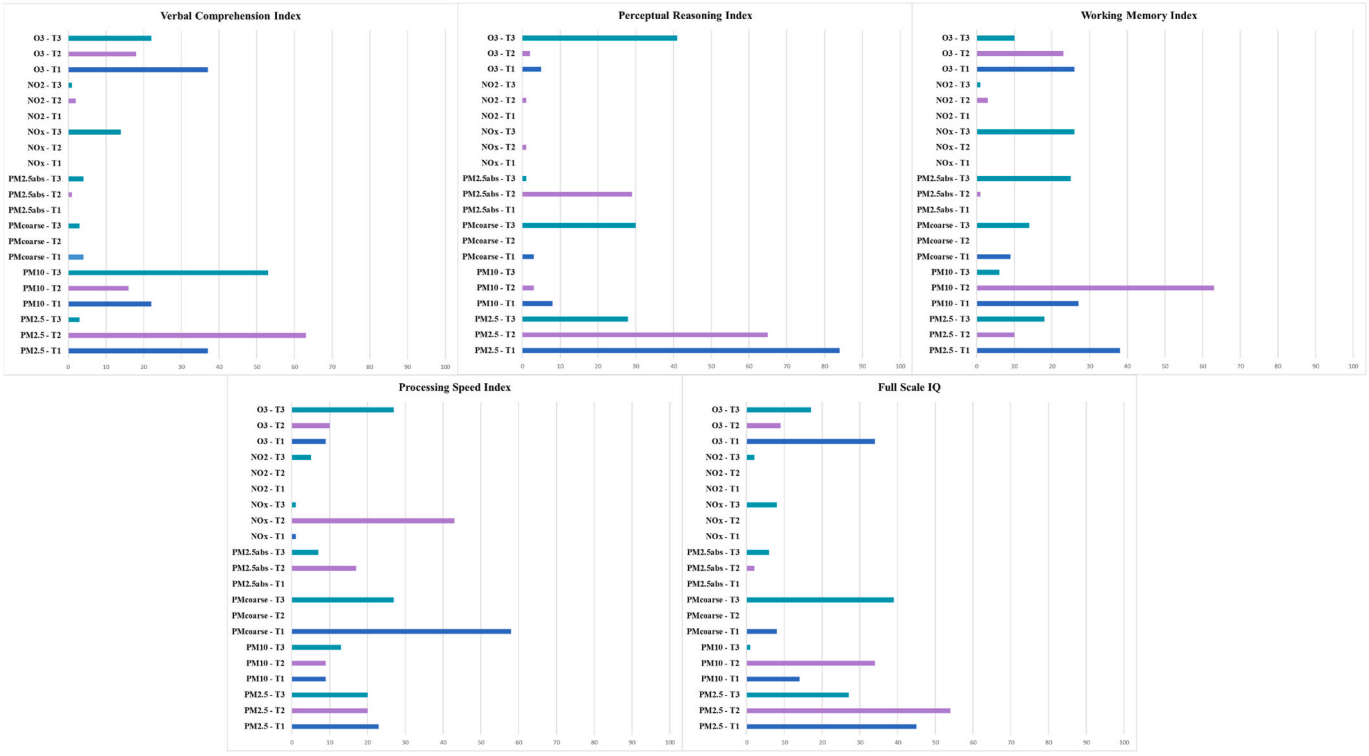


Fig. 3. Weighted quantile sum by prenatal air pollutants and trimesters - WISC-IV.

suggest that combined exposures may produce additive or synergistic effects, emphasising the complex, time-sensitive nature of prenatal vulnerability that single-pollutant studies may not fully capture. However, the trimester-specific effect of combined pollutants needs to be further investigated to clarify the mechanisms and timing of such combined effects.

4.3. Mixture effects of air pollutants

The WQS mixture analyses showed that particulate matter, particularly $PM_{2.5}$ and PM_{10}, was the main contributor to reduced cognitive performance across both age groups, with $PM_{2.5}$ exerting the strongest contribution in the first trimester and PM_{10} dominating in the third trimester. These findings reinforce those that fine and coarse particles, especially those associated with traffic emissions, may represent harmful components of the prenatal pollution mixture. O_3 also received substantial weights in some trimesters, especially for perceptual reasoning and full-scale IQ, but this is likely due to its inverse correlation with traffic-related pollutants rather than a true adverse effect, as suggested by its positive or null associations in single-pollutant models. The contributions of NO_2 and NO_x were consistently small, reflecting their high collinearity with PM fractions, which caused PM to absorb most of the mixture weight.

The WQS mixture analyses provided additional insight into the relative contributions of pollutants within the exposure mixture. In preschool-aged children, particulate matter, particularly $PM_{2.5}$, contributed more strongly to early pregnancy, especially for working memory and reasoning domains, whereas in later pregnancy, O_3 showed larger relative contributions across multiple cognitive domains. In school-aged children, $PM_{2.5}$ remained a major contributor in early and mid-pregnancy, particularly for verbal comprehension and perceptual reasoning, while contributions in late pregnancy were more distributed across pollutants, including PM_{10}, PM_{coarse}, and O_3. These findings indicate that the relative importance of pollutants within the mixture varies across gestation and cognitive domains, rather than being driven by a single pollutant across all periods (Dou et al., 2025; Sukumaran et al., 2024). The prominent role of O_3 in late pregnancy likely reflects its inverse correlation with traffic-related pollutants, rather than a direct effect, as suggested by its null or inconsistent associations in single-pollutant models. Although most mixture estimates were not statistically significant, the WQS results, except for verbal comprehension in school-aged children in the second trimester of pregnancy, complement the single-pollutant analyses by providing insight into how correlated exposures may jointly contribute to cognitive outcomes across gestation.

Several associations were null or inconsistent across pollutants, cognitive domains, and developmental stages, with particularly weak or absent findings for processing speed and largely non-significant mixture estimates. These inconsistencies may reflect domain-specific sensitivity, variability in exposure timing, limited statistical power, or measurement imprecision. Additionally, the high correlation among pollutants complicates the disentangling of independent effects. Differences between DLM and WQS results likely stem from their distinct modelling approaches: DLMs capture week-specific associations and sensitive windows, whereas standard WQS relies on trimester-averaged exposures and does not account for temporal correlations (Gasparrini, 2011; Tanner et al., 2019). As such, these methods provide complementary insights and are not expected to yield directly comparable estimates.

4.4. Strengths and limitations

This study has several notable strengths, including the assessment of cognitive performance at two developmental stages, preschool and school age, using standardised and validated instruments (WPPSI-IV and WISC-IV), which strengthens the comparability and developmental relevance of the findings. The use of high-resolution prenatal exposure estimates and pollutant standardisation across conventional units enhances the precision and interpretability of effect sizes. Furthermore, by examining trimester-specific windows of susceptibility and multi-pollutant mixture effects, the study provides a comprehensive evaluation of prenatal air pollution impacts on child neurodevelopment. However, the study's observational design cannot eliminate the possibility of residual confounding, and some degree of exposure misclassification may persist despite high spatial resolution. Prenatal air pollution exposure was estimated using the maternal residential address at birth, without accounting for potential residential mobility or time spent in other environments, such as the workplace or during commuting, which may have introduced non-differential exposure misclassification, particularly affecting trimester-specific estimates. Given the large number of statistical tests performed, the possibility of chance findings cannot be excluded, and results should be interpreted with caution. An additional limitation is the generalizability of the findings. The analytic sample was derived from a cohort of children with symptoms/diagnosis of ADHD and/or autism and may not be fully representative of the general population. Furthermore, the unexpected positive associations for O_3 likely reflect collinearity with traffic-related pollutants, complicating the interpretation of ozone's role within the mixture. As one of the first studies to explore trimester-specific combined effects of multiple pollutants, our findings highlight the need for further research to confirm and extend these results.

5. Conclusion

This study provides evidence that prenatal exposure to air pollutants, particularly fine and coarse particulate matter ($PM_{2.5}$, PM_{10}, $PM_{2.5abs}$, PM_{coarse}) and nitrogen oxides (NO_x, NO_2), can be associated with lower full-scale IQ and other aspects of cognitive performance in children, detectable both in preschool and school age. Single-pollutant analyses suggested stronger associations in late pregnancy, whereas mixture analyses indicated that the relative contributions of pollutants varied across gestation, with more modest and less consistent combined effects. The consistent pattern of negative associations underscores that prenatal air pollution may impact on cognitive performance and IQ, independent of other developmental factors. These findings emphasise the need for public health measures to reduce maternal exposure to air pollution during pregnancy and for further research to clarify the underlying mechanisms and critical windows of vulnerability.

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CRediT authorship contribution statement

Sharanpreet Kaur: Formal analysis, Writing – original draft, Writing – review & editing. **Josefa Canals-Sans:** Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Supervision, Writing – review & editing. **Carmen Hernández-Martínez:** Data curation. **Mònica Guxens:** Conceptualization, Funding acquisition, Investigation.

Declaration of competing interest

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

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2026.124908.

Data availability

The data that has been used is confidential.

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