



Association Between Prenatal Air Pollution Exposure and Autism in Children: EPINED Study

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Abstract

Purpose Air pollutants are emerging as recognised contributing factors in the aetiology of neurodevelopmental disorders, particularly increasing the risk of autism in children. This study explored the association between prenatal exposure to air pollutants and the likelihood of developing autism, considering both autistic symptoms and diagnosed cases in a school-based population from Tarragona (Spain), a province with extensive petrochemical activity.

Methods In the first phase, parents and teachers of 3,727 children (aged 4 and 11 years) completed screening questionnaires (CAST and EDUTEA, respectively). In the second phase, 623 children were individually assessed, and diagnoses were based on DSM-5 criteria (58 children with autism and 51 with subthreshold autistic traits).

Results We performed multiple regressions, adjusting for individual, social, and family covariates. Significant associations were found between exposure to PM_{coarse} (β -0.16; CI: 0.03–0.29), NO_2 (β -0.15; CI: 0.02–0.28), and NO_x (β -0.18; CI: 0.03–0.34) and autism symptom scores reported by the teachers. Furthermore, a significant association suggests higher exposure to $PM_{2.5}$ (OR-1.66; CI: 1.03–2.65) and PM_{10} (OR-1.46; CI: 1.01–2.12) during the second trimester of pregnancy can lead to higher chances of developing autism+subthreshold autistic traits in children.

Conclusions These findings emphasise the potential impact of specific air pollutants, particularly during critical periods of pregnancy and foetal development, highlighting the need to explore further the role of air pollutants associated with the increased likelihood of autism in children.

Keywords Air pollutants · Autism · Neurodevelopmental disorder · Pregnancy · Prenatal

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Introduction

Autism is one of the early-onset neurodevelopment disorders (NDDs), causing lifelong disabilities characterised by social interaction and social communication impairments, restricted and repetitive patterns of behaviour, unusual interests or alterations in sensory reactivity (APA, 2022). The global prevalence of autism ranges from 0.6% to 1.0% (Zeidan et al., 2022; Salari et al., 2023; Talantseva et al., 2023; Issac et al., 2025). However, a recent study on autism prevalence in the United States estimated that the percentage ranges from 2.71% to 4.38% nationwide, with an average prevalence of 3.29% (Bradshaw et al., 2024). Whereas in Spain, the prevalence has been reported at 1.78% in preschool-aged (4–5 years) and 1.30% in school-aged (10–11 years) children, with an average prevalence of 1.53% (Morales Hidalgo et al., 2021). Differences in prevalence across regions or countries demonstrate sociodemographic disparities in autism diagnosis and highlight the necessity to explore and identify the underlying factors contributing to these variations (Grosvenor et al., 2024). The accurate aetiology and pathology of autism are unknown, yet genetics and environmental influences, particularly prenatal air pollution, are considered the main factors contributing significantly to the development of autism in children (Lam et al., 2016; Modabbernia et al., 2017; Pham et al., 2022). Air pollutants such as particulate matter (PM_{2.5} - aerodynamics of $\leq 2.5 \mu\text{m}$ and PM₁₀ - aerodynamics of $\leq 10 \mu\text{m}$), nitrogen dioxides (NO₂), and ozone (O₃), predominantly released from industrial activities such as heavy traffic, material handling, combustion processes, and chemical reactions, more common in petrochemical areas, have gained particular attention since they are among the major threat pollutants to public health (WHO, 2021).

Air pollution exposure at early stages of life is increasingly recognised as an important factor contributing to autism risk (Bölte et al., 2019; Pugsley et al., 2022). These airborne particles can accumulate within the placenta, impairing its growth and functionality by crossing into foetal circulation (Bongaerts et al., 2022; Liu et al., 2021). Air pollutants can directly or indirectly contribute to genomic alteration processes with the capability to evoke biological abnormalities, affecting the central nervous system and causing oxidative stress and neuro-inflammation (He et al., 2025; Kalenik et al., 2025; Pugsley et al., 2022). An increasing body of research highlights that prenatal and perinatal exposure to air pollutants increases children's vulnerability to developing autism (Bae et al., 2025; Amnuaylojaroen et al., 2024). For instance, a recent meta-analysis found that exposure to PM_{2.5} during pregnancy was associated with up to 15% increased risk of autism (Mamun et al., 2025). Furthermore, U.S. population-based studies reported that

higher prenatal exposure to PM_{2.5} can be associated with increased odds of autism (O'Sharkey et al., 2025; Volk et al., 2013). Similarly, a Swedish cohort study by Flanagan et al. (2023) found that prenatal exposure to local PM_{2.5} was associated with childhood autism. On the other hand, several studies have suggested that exposure during certain trimesters may be more harmful than others. While some authors find that maternal exposure to fine PM_{2.5} during the first and second trimesters may represent critical windows of susceptibility (Mamun et al., 2025; Rahman et al., 2022), others highlight that exposure during the third trimester is associated with an increased risk of autism in offspring (Jo et al., 2019; Raz et al., 2015).

In comparison to PM_{2.5}, evidence on other pollutants such as PM₁₀ and NO_x remains limited to support its association with the disorder (Dutheil et al., 2021). Prenatal exposure to NO_x has also been implicated in autism development (Carter et al., 2022; Oudin et al., 2019), with additional studies reporting associations for NO₂ (O'Sharkey et al., 2025; Wang et al., 2021). On the other hand, some studies from Europe support a limited or no association between prenatal PM₁₀, PM_{2.5}, and NO₂ exposure and autism or traits of autism in children (Mortamais et al., 2025; Ritz et al., 2018; Guxens et al., 2016). Additionally, only a few studies have explored the impact of exposure to O₃, but existing research suggests that higher levels of O₃ during late gestation may elevate the risk of autism (Ghassabian et al., 2025), particularly between 34 and 37 weeks (Rahman et al., 2022). One study further showed that O₃ may increase autism risk in those children with higher levels of DNA copy number variations vulnerability (Kim et al., 2017).

Tarragona, a province of Catalonia (northeastern region) in Spain, is one of southern Europe's largest hubs of petrochemical industries (Rovira et al., 2020, 2021). A previous study on the Tarragona population found an association between prenatal exposure to air pollutants and reduced motor functioning in infants (Iglesias-Vázquez et al., 2022), indicating a need to further investigate the potential association with neurodevelopmental disorders. Therefore, the present study aims to explore the association between prenatal exposure to air pollutants and the likelihood of developing autism, considering exposure during specific pregnancy trimesters as well as considering cofounders overlooked by previous studies, including parental age and parental autistic traits. We hypothesise that higher levels of prenatal exposure to selected air pollutants, originating directly from traffic and industrial emissions, or formed secondarily in the atmosphere from their precursors (PM_{2.5}, PM_{2.5abs}, PM₁₀, PM_{coarse}, NO_x, NO₂ and O₃) can be associated with a greater odd of likelihood of autism in children, after adjusting for individual, social, and family covariates.

Methods

Design and Participants

The study sample was drawn from the Neurodevelopmental Disorders Epidemiological Project (EPINED), conducted between 2014 and 2019 in the province of Tarragona (Catalonia, Spain), to study the epidemiology of autism and ADHD in the school population. The study was carried out in two phases. In the first phase, 3727 out of 6894 children recruited were screened for NDD symptoms, with the involvement of parents and teachers. Children belonged to two academic levels: the second level of preschool ($n=1802$) and the 5th grade of primary education ($n=1925$). Children who screened positive for autism ($n=281$), for ADHD, and the comparison group (without autism or ADHD risk) continued in the second phase, with a total of 781 children. In this phase, an individual assessment was conducted for the diagnosis of ADHD and/or autism based on the DSM-5 criteria. A complete diagnostic procedure can be found in Canals Sans et al. (2021) and Morales Hidalgo et al. (2021). As per the objective of our study, children diagnosed with ADHD were excluded, resulting in a final sample consisting of 623 children. These were initially divided into three groups: non-autism (no diagnosis of autism and/or ADHD), autism (meeting full DSM-5 criteria), and subthreshold autistic traits (children exhibiting autistic traits but not meeting full criteria). For certain analyses, the autism and subthreshold autistic traits groups were combined into a single group, labelled “autism + subthreshold autistic traits” (see Fig. 1). The study protocol was approved by Sant Joan University Hospital’s ethics committee (13-10-31/10proj5), and parents were thoroughly informed about the procedure and gave their consent to participate.

Outcome: Screening and Diagnosis of Autism

In the first phase, children were screened for autism manifestations using the Childhood Autism Spectrum Test (CAST), answered by the parents, and the EDUTEA, answered by the teachers. EDUTEA, consisting of 11 items, is designed to assess DSM-5 autism symptoms in the school environment (Morales-Hidalgo et al., 2017a, b; <https://psico.fcep.urv.cat/Q4/EduTEA>). Responses are scored on a Likert scale, with individual item scores ranging from 0 to 3. The total score can range from 0 to 33, with a cut-off point of ≥ 10 , indicating a potential need for further evaluation. The CAST (Scott et al., 2002) contains 36 dichotomous items, but the maximum score is 31 because six questions are based on the general development of the child, with a cut-off point of ≥ 15 in the Spanish population (Morales-Hidalgo et al., 2017b). The questionnaire is particularly useful in identifying subtle or

mild manifestations of autism in children (4–11 years). Children who scored above the cut-off on either test (EDUTEA or CAST) were considered at increased likelihood of autism and were further assessed in the second phase of the study.

In the diagnosis 2nd phase, children and their parents were individually assessed with clinical and neuropsychological tests by two professional psychiatrists and psychologists. Autism Diagnostic Observation Schedule, 2nd ed. (ADOS-2; Lord et al., 2012) was administered to the child by a trained professional. We used the ADOS score to refer to autism severity according to the criteria of Gotham et al. (2009), where scores are represented as follows: 1–3 is “non-spectrum”, 4–5 is “ASD”, and 6–10 is “autism”. The Autism Diagnostic Interview-Revised (ADI-R; Rutter et al., 2003) was administered to the parents to collect the primary symptoms of autism in their children. Both instruments provided the necessary information by meeting or surpassing the autism cut-off scores established by the ADI-R diagnostic algorithm and the ADOS-2, thereby ensuring the assessment complied with autism diagnostic criteria according to DSM-5 standards. Children who did not fully meet the diagnostic criteria but had positive screenings on tools such as CAST or EDUTEA and scored 1 or 2 points below the threshold on ADI-R and ADOS-2 were classified as having subthreshold autistic traits. The diagnosis was complemented with the assessment of neuropsychological functions and intellectual capacity by administering to the children the WPPSI-IV (for pre-schoolers) and the WISC-IV (school-age). These tests were then used to obtain scores on the intelligence quotient (IQ) (Wechsler, 2005, 2014).

Air Pollutant Exposure Measurement

Parents provided demographic information and a residential history dating back to the child’s birth to assess their exposure to air pollutants during pregnancy. The estimation of traffic-related air pollution exposure at birth home addresses was done from a Land Use Regression (LUR) model developed for the ESCAPE (European Study of Cohorts for Air Pollution Effects) project, including six air pollutants: $PM_{2.5}$ (aerodynamics of $\leq 2.5 \mu m$), PM_{10} (aerodynamics of $\leq 10 \mu m$), PM_{coarse} (aerodynamics between 2.5 and $10 \mu m$), $PM_{2.5absorbance}$ (indicator of black carbon with aerodynamics of $< 2.5 \mu m$, a component of $PM_{2.5}$), NO_2 , NO_x . Measurements of PM ($PM_{2.5}$, PM_{10}) and NO_x/NO_2 were monitored from 20 to 40 locations, respectively, across the region, conducted over two weeks per location, covering warm, cold, and intermediate temperature seasons from 2009 (Eeftens et al., 2012). PM mass between 10 and $2.5 \mu m$ (PM_{coarse}) was calculated by subtraction of $PM_{2.5}$ from PM_{10} , and $PM_{absorbance}$ was measured in the lab as part of $PM_{2.5}$ particles. O_3 estimations were used from

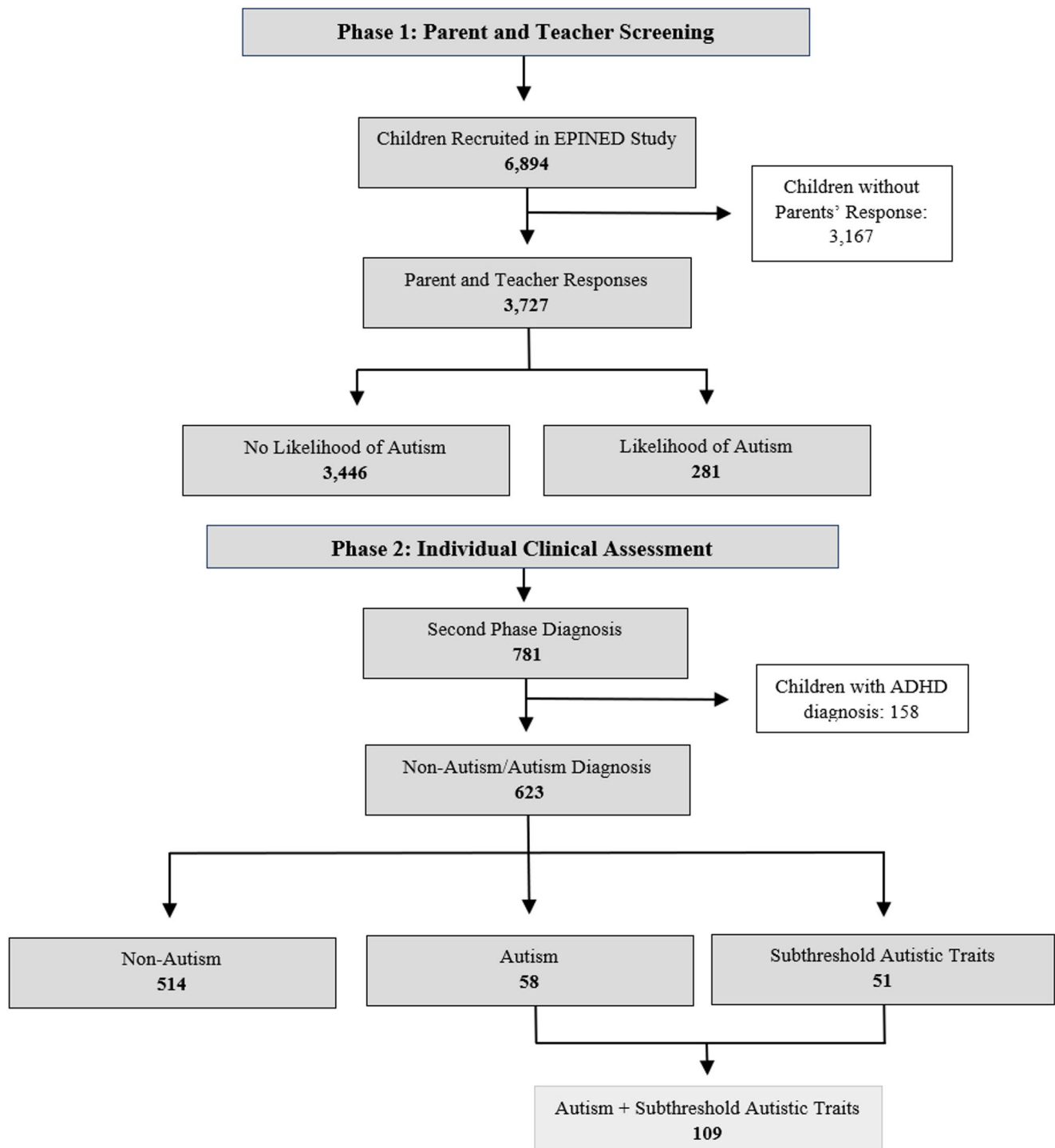


Fig. 1 Flowchart of participants included in the study

the ELAPSE (Effects of Low-Level Air Pollution: A Study in Europe) project (de Hoogh et al., 2018). The daily concentration of O_3 was derived in 2010 from the AirBase v8 dataset (EEA, 2015), calculated for an 8-hour maximum average every day in warm (April–September) and cold (January–March and October–December) seasons. From the

background monitoring and daily collected data, an estimated air pollution exposure was measured based on the residential address provided during pregnancy for each participant. A back-extrapolation method was used to estimate the average concentration for the entire pregnancy period using the average annual concentration routine from the

background monitoring sites. The LUR model generated R^2 of 75% for $PM_{2.5abs}$, 76% for PM_{coarse} , 62% for $PM_{2.5}$, 76% for PM_{10} , 69% for NO_x , 71% for NO_2 , and 69.6% for O_3 for the Catalonia region of Spain (Eeftens et al., 2012; de Hoogh et al., 2018).

Secondary Data

Additional data about the mothers' pregnancy and demographic details were collected during both the first and second phases of the study. This included information on place and date of birth of children, occupation and education of both parents which were used to calculate the socioeconomic status of the family (SES; low, medium and high) by the Catalan classification of occupation (CCO-2011), the mother and father age at the pregnancy (in years) to determine the age risk, and parental autistic traits, measured using the Autism Spectrum Quotient (AQ-short; Hoekstra et al., 2007), a 28-item questionnaire validated in Spanish (Lugo-Marín et al., 2019). Furthermore, maternal exposure to toxins during pregnancy (smoking and/or alcohol), gestational age (weeks of pregnancy), birth weight of the child used to measure small for gestational age (SGA), and maternal weight gain during pregnancy (in kg) were also recorded (Karimi et al., 2017; Lyall et al., 2017; Modabbernia et al., 2017; Wang et al., 2017), and autistic traits of parents using the Autism Spectrum Quotient. Children's characteristics included age (in years), gender (male or female), and ethnicity (Spanish or non-Spanish).

Prenatal environmental variables were also considered, including the Normalized Difference Vegetation Index (NDVI), which measures surrounding greenness (Weier & Herring, 2000). NDVI values were calculated within a 300 m buffer zone around geocoded locations. To cover the entire period, satellite images from 2009 to 2015 were sourced from the USGS website (<https://espa.cr.usgs.gov/>) and post-processed to remove non-quality pixels such as water, snow reflection, or saturated pixels. The Deprivation Index, which measures socioeconomic deprivation in Spanish census sections based on regional socioeconomic indicators, was included (Duque et al., 2021). Distance to the closest industry was calculated using the land cover classification from the Mapa de Cobertes de Sol de Catalonia (MCSC version 4; 2009). Residential area type was determined by the Instituto Nacional de Estadística (INE) classification based on population size: rural (<2000), suburban (2000–10,000), and urban (>10,000).

Statistical Analyses

Statistical analyses were performed using SPSS, while plots were created with R. The air pollutant exposure was

standardised according to the conventional units as follows: $NO_x - 20 \mu g/m^3$, NO_2 , O_3 and $PM_{10} - 10 \mu g/m^3$, $PM_{2.5}$ and $PM_{coarse} - 5 \mu g/m^3$, $PM_{2.5absorbance} - 10^{-5} m^{-1}$. Spearman's correlation test was conducted to analyse the correlation between the pollutants. Single pollutant exposure models were analysed using multiple linear regression for continuous data and logistic regression for categorical data to obtain β and odds ratios (ORs) with 95% confidence levels (CI), respectively. After an unadjusted model, three additional models were adjusted for secondary data, chosen based on the Directed Acyclic Graph (DAG) approach as well as previous research evidence (Supplementary S. Figure 1). No significant correlations were found between toxins and other secondary data.

Results

Participant's Characteristics

The descriptive characteristics of the participants, including sociodemographic data, psychological data and pregnancy and childbirth details) for Phase 1 (screening for autism symptoms) and Phase 2 (diagnosis for autism) are summarised in Table 1. In both phases, the males were significantly higher in the group's risk of autism and diagnoses. In Phase 1, the mean age was 4.20 years (SD 0.54) for preschoolers and 10.17 years (SD 0.50) for schoolers children, while in Phase 2, it was 4.63 years (SD 0.50) and 10.61 years (SD 0.61), respectively. In phase 1, most children came from medium SES households (58.3%), lived in urban residential areas (64.6%), and were of Spanish ethnicity (84.1%). In phase 2, most participants came from medium SES households (62.4%) and urban residential areas (61.5%). ADOS severity score in the autism group is in the "ASD range" as calibrated according to Gotham et al. (2009). In addition, in autism groups, ADI-R diagnostic algorithm scores exceed the cut-offs suggested for the diagnosis (ADI-R reference).

Correlation and Concentrations of Air Pollutants

Descriptive statistics and Spearman correlation details of the air pollutants are summarised in Table 2. The mean of prenatal air pollutant exposure was 14.93, 32.77, 18.69, 31.52, 52.71, and 70.07 for $PM_{2.5}$, PM_{10} , PM_{coarse} , NO_2 , NO_x , and O_3 in $\mu g/m^3$, respectively, and 1.86 for $PM_{2.5abs}$ in $10^{-5} m^{-1}$. According to the WHO (2021) annual recommended air quality guidelines for some pollutants, our median exceeds the limits. Further details of prenatal air pollutant exposure in each district of Tarragona can be found in Supplementary Table 1. Positive correlations between air pollutants ranged from 0.54 ($PM_{2.5}$ and NO_x) to the highest, 0.99 (NO_2 and

Table 1 Descriptive characteristics of participants in phases 1 and 2

Phase 1 (Symptoms)		No likelihood of Autism ^a	Likelihood of Autism ^b	Total	<i>p</i> ^{ab}
		(<i>n</i> =3446)	(<i>n</i> =281)	(<i>n</i> =3727)	
Sociodemographic data					
Age (years)		7.27±3.02	7.45±3.06	7.29±3.03	0.34
Sex	Male	46.4 (1599)	70.8 (199)	48.2 (1798)	<0.001
	Female	53.6 (1847)	29.2 (82)	51.8 (1929)	
Ethnicity	Autochthon	85.1 (2932)	72.2 (203)	84.1 (3132)	<0.001
SES	Low	15.6 (536)	28.5 (80)	16.5 (616)	<0.001
	Medium	58.2 (2007)	59.1 (166)	58.3 (2173)	
	High	24.5 (843)	12.1 (34)	23.5 (877)	
Residential area	Rural	3.9 (136)	3.9 (11)	3.9 (147)	0.99
	Suburban	31.4 (1083)	31.7 (89)	31.4 (1172)	
	Urban	64.6 (2227)	64.4 (181)	64.6 (2408)	
Autism risk assessment					
EDUTEA		(<i>n</i> =3541)	(<i>n</i> =186)	(<i>n</i> =3727)	
	SCI	1.23±2.18	13.59±4.19	1.84±3.55	<0.001
	RRB	0.25±0.69	5.15±3.27	0.50±1.45	<0.001
	Total	1.48±2.57	18.74±6.04	2.35±4.71	<0.001
CAST		(<i>n</i> =3572)	(<i>n</i> =155)	(<i>n</i> =3727)	
	Total	6.67±3.19	17.65±2.92	7.12±3.79	<0.001
Phase 2 (Diagnosis)		Non-Autism ^c	Autism ^d	Subthreshold autistic traits ^e	<i>p</i> ^{cd} , <i>p</i> ^{ce}
		(<i>n</i> =514)	(<i>n</i> =58)	(<i>n</i> =51)	
Sociodemographic data					
Age (years)		8.20±2.99	7.29±3.02	7.66±3.16	0.03, 0.22
Sex	Male	56.8 (292)	81.0 (47)	78.4 (40)	0.01, <0.001
	Female	43.2 (222)	19.0 (11)	21.6 (11)	
Ethnicity	Autochthon	82.5 (424)	79.3 (46)	88.2 (45)	0.55, 0.29
SES	Low	16.3 (84)	17.2 (10)	25.5 (13)	0.89, 0.18
	Medium	63.2 (325)	60.3 (35)	56.9 (29)	
	High	20.4 (105)	22.4 (13)	17.6 (9)	
Residential area	Rural	6.0 (31)	1.7 (1)	7.8 (4)	0.41, 0.79
	Suburban	32.7 (168)	34.5 (20)	31.4 (16)	
	Urban	61.3 (315)	63.8 (37)	60.8 (31)	
Distance to industry (km)		0.38±0.39	0.37±0.39	0.24±0.33	0.82, 0.55
Pregnancy and children's birth details					
Birth Weight (kg)		3.21±0.59	3.28±0.55	3.22±0.66	0.40, 0.62
Birth length (m)		0.50±0.21	0.49±0.03	0.49±0.03	0.69, 0.77
Small for gestational age		18.5 (95)	10.3 (6)	5.9 (3)	0.13, 0.03
Mother's age at childbirth		31.03±5.13	32.10±5.21	32.07±5.98	0.40, 0.17
Father's age at childbirth		34.14±5.33	34.69±4.54	35.37±7.44	0.67, 0.09
Mother's gestational age (weeks)		38.89±2.49	39.32±1.89	38.94±2.44	0.30, 0.94
Toxins during pregnancy	Yes	16.5 (85)	12.1 (7)	23.5 (12)	0.38, 0.21
	No	83.5 (429)	87.9 (51)	76.5 (39)	
Maternal weight gain during pregnancy (kg)		13.80±6.88	14.16±6.05	15.29±7.83	0.70, 0.15
Autism assessment					
Children					
ADI-R		(<i>n</i> =512)	(<i>n</i> =58)	(<i>n</i> =51)	
	SI	1.91±2.04	13.69±5.98	7.26±3.76	<0.001, <0.001
	SCI	1.59±1.69	10.76±3.79	5.88±3.37	<0.001, <0.001
	RRB	0.65±0.93	4.26±2.37	2.28±1.12	<0.001, <0.001
ADOS-2 Severity		(<i>n</i> =512)	(<i>n</i> =58)	(<i>n</i> =51)	
	SCI	1.83±1.31	5.32±1.97	4.17±2.12	<0.001, <0.001
	RRB	1.33±1.07	5.55±2.28	3.17±2.55	<0.001, <0.001
	Total	1.35±0.91	5.43±1.95	3.39±1.98	<0.001, <0.001
Total IQ		101.54±15.08	88.67±17.04	96.82±18.44	<0.001, 0.04
Parents AQ score					

Table 1 (continued)

Phase 2 (Diagnosis)	Non-Autism ^c (<i>n</i> = 514)	Autism ^d (<i>n</i> = 58)	Subthreshold autistic traits ^e (<i>n</i> = 51)	<i>p</i> ^{cd} , <i>p</i> ^{ce}
Mother	(<i>n</i> = 270) 53.34 ± 9.96	(<i>n</i> = 53) 50.92 ± 9.26	(<i>n</i> = 46) 54.76 ± 10.47	0.10, 0.37
Father	(<i>n</i> = 222) 54.98 ± 10.48	(<i>n</i> = 46) 58.76 ± 10.32	(<i>n</i> = 41) 57.92 ± 8.66	0.03, 0.09

Data representation: M ± SD or % (*n*). a = No likelihood of autism; b = Likelihood of autism; c = Non-autism; d = Autism; e = Subthreshold autistic traits. Significance: *pa* = comparison a vs b; *pcd* = comparison c vs d; *pce* = comparison c vs e

SES socio-economic status, *SC* social communication impairment, *RRB* restrictive/repetitive behaviour patterns, *SI* social interactions, *IQ* intelligence quotient, *Toxins* during pregnancy: alcohol and/or tobacco, *CAST* Childhood Autism Spectrum Test, *ADI-R* Autism Diagnostic Interview-Revised, *ADOS-2* Autism Diagnostic Observation Schedule, 2nd edition, *AQ* Autism Spectrum Quotient

NO_x), whereas the correlation between O₃ and others was in a negative direction, ranging from −0.48 (PM_{2.5} and O₃) and −0.32 (PM_{coarse} and O₃). Figure 2 shows the spatial distribution of geocode values in a 5 km hexagonal grid.

Association Between the Likelihood of Autism and Air Pollutants - Phase 1

Figure 3 presents the β coefficients and 95% CIs for CAST and EDUTEA scores (full β details can be found in Supplementary Table 2). A positive and significant association between PM_{coarse}, NO₂ and NO_x exposure, and EDUTEA total scores was observed. Specifically, for PM_{coarse}, the unadjusted Model 1 yielded a β of 0.21 (95% CI: 0.02–0.38), while the fully adjusted Model 3 showed a β of 0.16 (95% CI: 0.03–0.29). Similarly, significant positive associations were observed for NO₂ (β = 0.15, 95% CI: 0.02–0.28) and NO_x (β = 0.18, 95% CI: 0.03–0.34) with EDUTEA total scores. On the other hand, no significant associations were observed for CAST scores. Furthermore, across three models (unadjusted and adjusted), no significant associations were observed between the likelihood of autism risk, based on teachers' and parents' reports, and any of the analysed pollutants in association with prenatal exposure to air pollutants (full details of the ORs are provided in Supplementary Table 3).

Association Between Autism and Air Pollutants Exposure - Phase 2

Prenatal exposure data were analysed by trimester (1, 2, and 3), across four models (unadjusted and adjusted). While no significant associations were found between air pollutants and autism, positive and significant associations emerged when children with subthreshold autistic traits were included. Figure 4 (adjusted models 3 and 4) highlights that in trimester 2, specifically in model 4, exposure to PM_{2.5} showed a significant OR of 1.66 (95% CI: 1.03–2.65), and exposure to PM₁₀ showed a significant OR of 1.46 (95% CI: 1.01–2.12). The complete ORs of all models can be

found in Supplementary Tables 4 and 5. Whereas, when the overall pregnancy period was analysed, no association was observed between prenatal exposure to air pollutants and either two outcomes (autism alone or autism combined with subthreshold autistic traits) compared to non-autism, across four models. However, the ORs showed a slight increase from model 1 to model 4 for PM_{2.5} and PM₁₀, particularly when the analysis included children with subthreshold autistic traits. Other pollutants, PM_{2.5abs}, PM_{coarse}, NO₂, NO_x, and O₃, showed minimal or no association with either outcome. Complete ORs details can be found in Supplementary Table 6.

Discussion

In the present study, we explored the association between the likelihood of autism based on the symptoms assessment and autism diagnosis with prenatal air pollution exposure, such as PM_{2.5}, PM₁₀, PM_{coarse}, PM_{2.5abs}, NO_x, NO₂, and O₃. A significant association was observed between exposure to PM_{coarse}, NO₂, and NO_x and higher EDUTEA autism symptoms test scores, indicating that higher exposure to these pollutants can be associated with an increased likelihood of autism-related traits in children, based on the teacher's scored screening. Furthermore, a significant association suggests that higher exposure to PM_{2.5} and PM₁₀ during the second trimester of pregnancy can lead to a higher likelihood of developing autism in children, while no significant associations were obtained between other pollutants and the likelihood of autism.

Our findings contribute to the growing body of literature exploring the relationship between prenatal exposure to air pollutants and autism-related outcomes. Consistent with previous research, our study found each 10 $\mu\text{g}/\text{m}^3$ increase in NO₂ and 20 $\mu\text{g}/\text{m}^3$ in NO_x was associated with an increase of 0.18 and 0.15 points, respectively, in teachers' reported autism symptom scores (O'Sharkey et al., 2025; Murphy et al., 2024; Wang et al., 2021; Oudin et al., 2019; Volk et al., 2013). These changes correspond to approximately 0.55%

Table 2 Spearman correlation and descriptive statistics of air pollutants

Pollutants	WHO 2021*	Min	Max	Mean	SD	Median	IQR	PM _{2.5}	PM ₁₀	PM _{2.5,subs}	PM _{coarse}	NO ₂	NO _x	O ₃
PM _{2.5}	5	7.64	22.87	14.93	0.03	15.12	2.31	1						
PM ₁₀	15	14.48	59.32	32.77	5.64	33.03	6.18	0.63	1					
PM _{2.5,subs}	-	0.68	4.71	1.86	0.49	1.83	0.61	0.65	0.83	1				
PM _{coarse}	-	7.69	38.72	18.69	4.44	18.46	5.78	0.55	0.87	0.72	1			
NO ₂	10	1.81	77.35	31.52	13.65	30.97	16.84	0.55	0.81	0.97	0.7	1		
NO _x	-	1.47	142.78	52.71	23.76	51.55	29.52	0.54	0.81	0.97	0.71	0.99	1	
O ₃	60	43.29	101.53	70.07	9.4	68.59	11.93	-0.48	-0.42	-0.44	-0.32	-0.35	-0.34	1

Bold: Significance level $p < .001$

*WHO (2021): Annual recommended air quality guidelines

Units of measurement: PM_{2.5}, PM₁₀, PM_{coarse}, NO₂, NO_x, O₃: $\mu\text{g}/\text{m}^3$ and PM_{2.5,subs}: 10^{-5} m^{-1}

IQR Interquartile range, SD standard deviation, PM_{2.5} Particulate matter with aerodynamic diameter $\leq 2.5 \mu\text{m}$, PM₁₀ Particulate matter with aerodynamic diameter $\leq 10 \mu\text{m}$, PM_{coarse} Particulate matter $2.5\text{--}10 \mu\text{m}$, PM_{2.5,subs}: Absorbance of PM $< 2.5 \mu\text{m}$; NO₂ Nitrogen dioxide, NO_x Nitrogen oxides; O₃ Ozone

and 0.46% increases in EDUTEA scores for NO₂ and NO_x, respectively. The magnitude of these effects is modest, which is likely explained by the community-based nature of our sample, where most children had low scores and limited variability, resulting in small but consistent average increases across the distribution. Moreover, it is important to note that teacher-reported information on autism symptoms played an important role in the identification of autism in the school environment in our sample. Although both teachers' and parents' information is highly correlated with the diagnostic outcomes, however, teachers often demonstrate to have greater proficiency in recognising the social and communication skills of children when compared to the parents (Kaur et al., 2024; Morales Hidalgo et al., 2021; Morales-Hidalgo et al., 2017a). We also observed that each $5 \mu\text{g}/\text{m}^3$ in PM_{coarse} was associated with an increase of 0.16 points in these scores. To our knowledge, no prior research has specifically examined this pollutant concerning autism outcomes; therefore, it demands further investigation to validate and understand the underlying mechanisms. Evidence regarding PM_{2.5} and PM₁₀ remains mixed. Several studies report associations between prenatal exposure to these pollutants and autism diagnosis (O'Sharkey et al., 2025; Flanagan et al., 2023; Volk et al., 2013). However, in our study, the association between air pollutant exposure and autism-related symptoms reported by parents was not significant, supporting findings from Guxens et al. (2016) in several European cohorts. Regarding O₃, we did not observe a significant association with the likelihood of autism in children, consistent with Murphy et al. (2024). This contrasts with other studies suggesting that O₃ exposure may increase autism risk (Ghassabian et al., 2025; Kim et al., 2017).

Although many studies have examined exposure across the entire pregnancy, evidence suggests that risks may vary by trimester, highlighting the importance of timing in prenatal exposure; nonetheless, comparing results across trimesters is challenging due to limited data availability. For example, Raz et al. (2015) observed that in the third trimester, exposure to PM_{2.5} was associated with increased odds of autism diagnosis (OR: 1.42, CI: 1.09–1.86) compared to the first two trimesters. Furthermore, Wang et al. (2021) reported an association between NO₂ exposure and increased autism risk across all trimesters of pregnancy. Whereas, McGuinn et al. (2020) observed an association between O₃ and autism in the third trimester (OR: 1.2, CI: 1.1–1.4). Our findings on PM_{2.5} (OR: 1.66, CI: 1.03–2.65) and PM₁₀ (OR: 1.46, CI: 1.01–2.12) exposure during the second trimester align with those of Rahman et al. (2022) who found that PM_{2.5} exposure during the first two trimesters (1–27 weeks of gestation) was associated with an elevated autism risk (hazard ratio [HR]: 1.14, CI: 1.06–1.23), highlighting the importance of a pregnancy-sensitive window. Particularly,

Fig. 2 Spatial distribution of geo-code values in a 5 km hexagonal grid

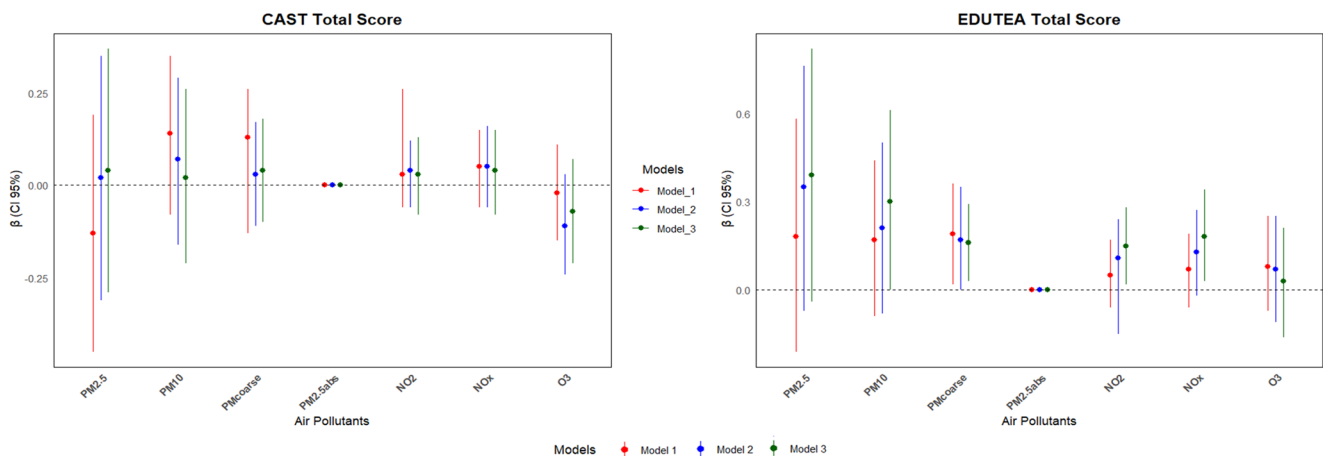
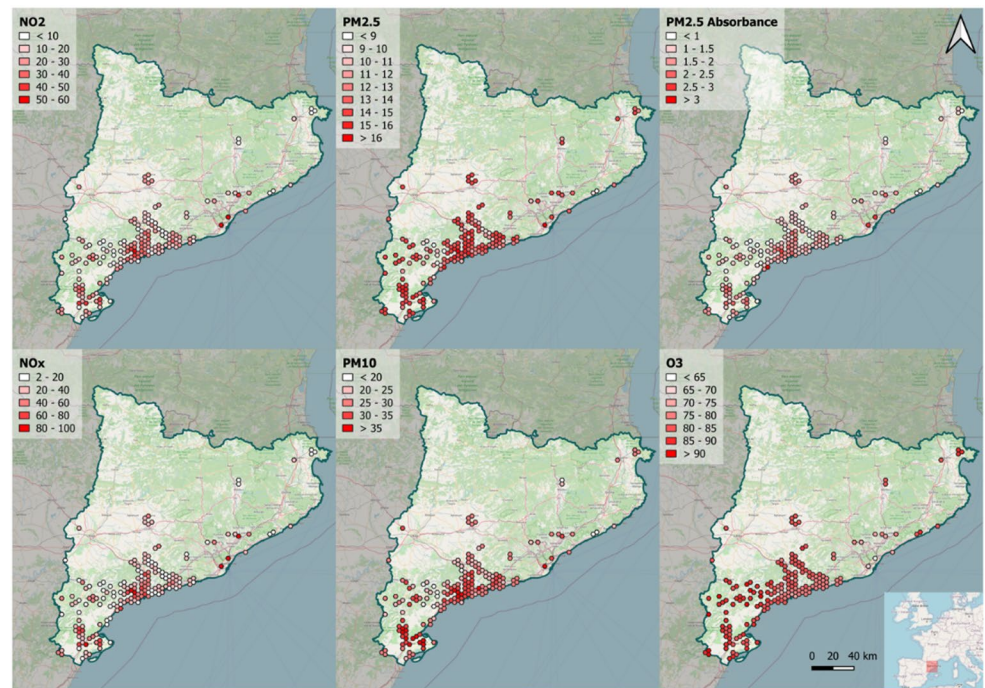


Fig. 3 Phase 1 beta coefficients and 95% confidence intervals for CAST and EDUTEA scores across models. Model 1: unadjusted; Model 2: adjusted for NDVI, deprivation index, age, sex, ethnicity and SES; Model 3: adjusted for model 2 covariables + distance to industry, type of residential area. NDVI: Normalized Difference Vegetation Index;

PM_{2.5}: Particulate matter with aerodynamic diameter ≤ 2.5 μm ; PM₁₀: Particulate matter with aerodynamic diameter ≤ 10 μm ; PM_{coarse}: Particulate matter 2.5–10 μm ; PM_{2.5abs}: Absorbance of PM < 2.5 μm ; NO₂: Nitrogen dioxide; NO_x: Nitrogen oxides; O₃: Ozone

the second trimester of the pregnancy is a window for rapid brain development, marked by the neuronal proliferation stage and axonal growth; therefore, any disruption during this phase, particularly due to fine particles from air pollutants, could interfere with the normal brain development of the foetus (Cortes-Albornoz et al., 2023). However, the findings regarding exposure to PM₁₀ require further investigation to validate the association and its effects. Notably, the effects of both PM_{2.5} and PM₁₀ remain significant in Model 4, which further adjusts for parental phenotype, suggesting

that the observed associations are driven by air pollutants independently of genetic predisposition.

Comparing data across continents, most of our findings align with some previous European studies that found no significant association between autism and air pollutants (Mortamais et al., 2025; Gong et al., 2014, 2017). In contrast, the most significant associations are obtained from other parts of the world, particularly North America, Taiwan, and Israel (O'Sharkey et al., 2025; Murphy et al., 2024; Carter et al., 2022; Wang et al., 2021; Raz et al., 2015). The inconsistencies across studies highlight the complexity of

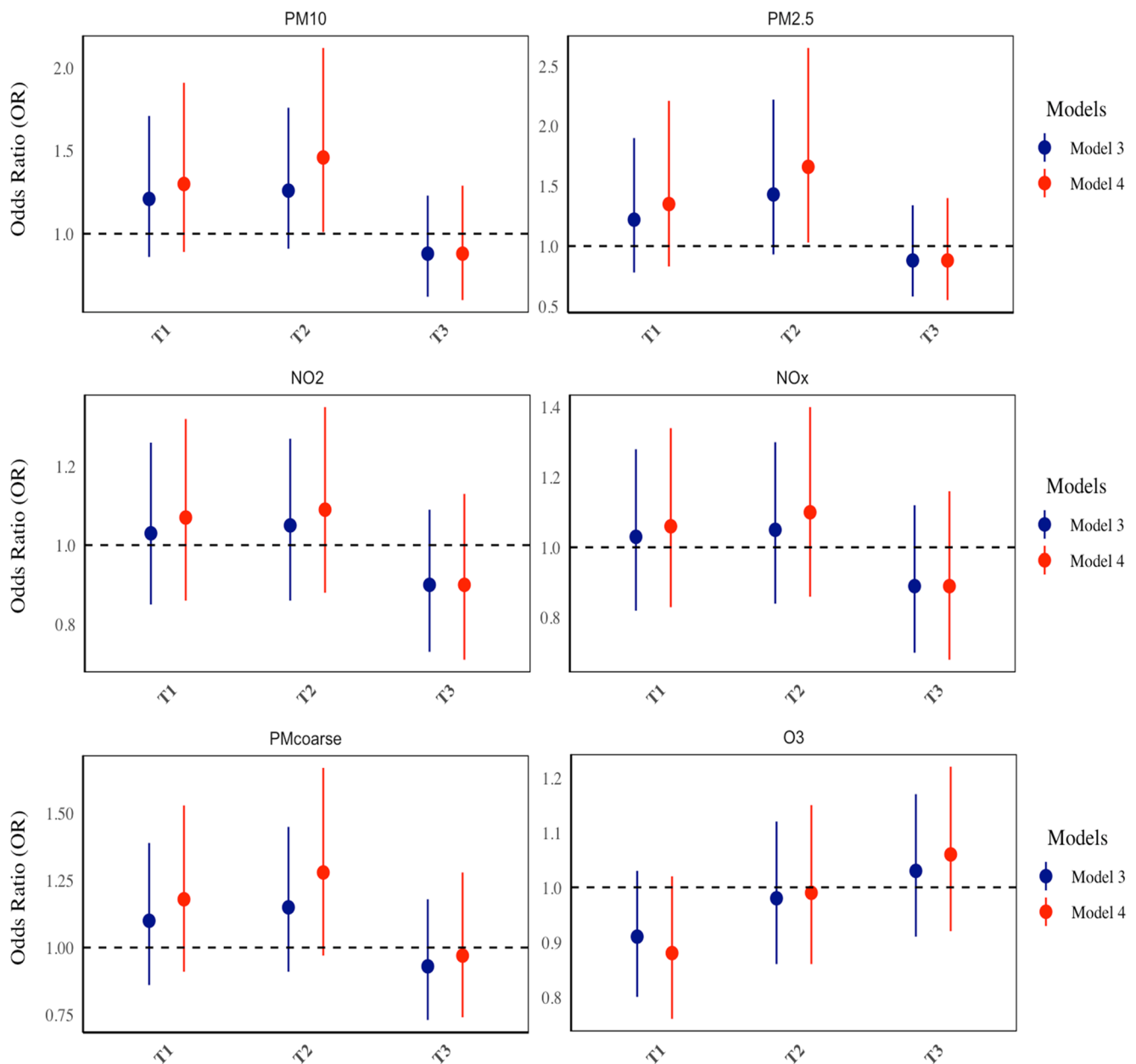


Fig. 4 Phase 2 odds ratios and 95% confidence intervals for autism and autism+subthreshold autistic traits vs. non-autism across models per trimester. Model 3: adjusted for NDVI, deprivation index, age, sex, ethnicity and SES, distance to industry, type of residential area, mother age risk, father age risk, toxins during pregnancy, low birth weight, weight gain during pregnancy, weeks of pregnancy; Model 4: adjusted

for model 3 covariables+mother-father autism risk. T1: trimester 1; T2: trimester 2; T3: trimester 3; PM_{2.5}: Particulate matter with aerodynamic diameter $\leq 2.5 \mu\text{m}$; PM₁₀: Particulate matter with aerodynamic diameter $\leq 10 \mu\text{m}$; PM_{coarse}: Particulate matter 2.5–10 μm ; PM_{2.5abs}: Absorbance of PM $< 2.5 \mu\text{m}$; NO₂: Nitrogen dioxide; NO_x: Nitrogen oxides; O₃: Ozone

disentangling the effects of pollutants on autism-related outcomes. Factors such as regional differences in airborne particle composition, standardised yet variable measures of pollutant exposure, and methodological discrepancies - including variations in data collection tools (e.g., different methods for assessing symptoms or autism diagnoses) and study designs (cohort vs. case-control), may further

contribute to variability in findings (Pagalan et al., 2019; Dutheil et al., 2021).

Certainly, genetics plays a fundamental role in the predisposition to autism; however, as observed, environmental factors, such as prenatal exposure to pollutants, can play a role in modifying gene expression and increasing the risk of autism (Kalenik et al., 2025; Love et al., 2024; Pugsley et al., 2022). In this regard, our findings are particularly relevant

given that the sample of our study comes from one of the largest petrochemical hubs in southern Europe, where children are more heavily exposed to these pollutants compared to other regions. In addition, the estimated prevalence of autism and subthreshold autistic traits in the school population of Tarragona is notably high (3.31%) (Morales Hidalgo et al., 2021), and the prevalence of autism within the health-care regions of the province of Tarragona is among the highest in our region (Catalonia, Spain) (Pérez-Crespo et al., 2019). Being in the major petrochemical area, the average air pollutant levels in our sample exceeded the WHO's recommended annual limits for several key pollutants. For example, $PM_{2.5}$, PM_{10} , NO_2 , and O_3 concentrations in our sample were 2–3 times more than those recommended by the WHO. Although our exposure assessment was an average of 9 months of pregnancy periods rather than a complete 12-month annual average as per WHO guidelines, pollutant exposure levels were consistently higher during the gestation period. This highlights the potential for increased foetal exposure to air pollution, which may have implications for neurodevelopmental outcomes, including autism risk. Authors explain that exposure to disruptive events such as environmental (air pollution) in the mid-late gestational periods, a critical window for the development of the foetus, when neurogenesis, neural circuit formation, apoptosis, synaptogenesis, migration or myelination starts to occur, can harm the neurodevelopment of the child (Andescavage et al., 2017; Konkell, 2018; Sunyer & Dadvand, 2019). Beyond these, air pollutants are also known to cause oxidative stress, hence damaging the DNA, disrupting cellular signalling pathways, and altering the brain morphometry of newborns (Bos et al., 2023; Wang et al., 2022). Disruption in any of the processes during the brain development stage of the foetus can lead to adverse outcomes, in particular to the cognitive development of the child later in life (Morgan et al., 2023; Perera et al., 2024). Henceforth, a direct link or aetiology between air pollution exposure during pregnancy and neurotoxicity remains unclear; however, such exposures, as observed and evidenced by their impact on the neurodevelopment of the foetus, may directly or indirectly contribute to the risk of autism development in children (Bae et al., 2025; He et al., 2025).

Strengths and Limitations of the Study

Our study possesses several notable strengths. First, our sample was obtained from an epidemiological study. So, we were able to analyse the association of pollutants with autism, considering not only an assessment of symptoms mostly reported by parents, but also symptoms reported by teachers, and a detailed and comprehensive assessment for autism that allows us to obtain diagnoses and syndromes

without meeting all diagnostic criteria. It also incorporated localised exposure data, reflecting regional variations in air pollution that might not align with national averages often used in larger studies. Second, our approach incorporated a comprehensive evaluation of covariates often overlooked in previous research, including parental age, parental autistic traits, and other potential confounding factors associated with both autism and air pollution. This warrants a more nuanced understanding of the interaction between these variables and pollutant exposure.

Despite its strengths, our study has certain limitations. First, our study was epidemiological rather than registry-based; therefore, the sample size was relatively small compared to previous registry-based studies. Consequently, the sample size was also smaller than that in other countries. This limitation reduced the statistical power to detect subtle effects, potentially underestimating small effect sizes and restricting the possibility of applying more advanced analyses. Second, air pollution exposure was estimated based on the mothers' residential addresses during pregnancy. This approach did not account for other significant sources of exposure, such as work-related commutes or time spent in other environments, which may have introduced some exposure misclassification. Third, the study did not account for other pollutants, such as heavy metals, persistent organic pollutants, and pesticides, which can be present in food, water, and soil and may significantly contribute to autism risk. These limitations highlight areas for improvement in future studies, such as the need for larger and more diverse samples, comprehensive tracking of individual exposure patterns, and enhanced pollutant monitoring capabilities to refine exposure estimates.

Conclusion

To summarise, our study highlights the potential role of prenatal air pollutant exposure in the development of autism in children. We found that exposure to PM_{coarse} , NO_2 , and NO_x increases the score of autism symptoms based on reports provided by teachers. At the same time, exposure to $PM_{2.5}$ and PM_{10} during the second trimester of pregnancy increased the likelihood of suffering from autism spectrum disorders, which supports the importance of a critical window for children's neurodevelopment. While most of the pollutants do not demonstrate a significant association with autism risk, these results highlight future studies to explore the role of pollutants in NDDs. It further highlights the necessity to mitigate the potential effects of air pollutants, especially in a region with high industrial or traffic emissions, to protect mothers and, as a result, children's neurodevelopment.

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Declarations

Conflict of interest The authors have no conflict of interest to declare.

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References

- Amnuaylojaroen, T., Parasin, N., & Saokaew, S. (2024). Exploring the association between early-life air pollution exposure and autism spectrum disorders in children: A systematic review and meta-analysis. *Reproductive Toxicology*, 125, Article 108582. <https://doi.org/10.1016/j.reprotox.2024.108582>
- Andescavage, N. N., du Plessis, A., McCarter, R., Serag, A., Evangelou, I., Vezina, G., Robertson, R., & Limperopoulos, C. (2017). Complex trajectories of brain development in the healthy human fetus. *Cerebral Cortex (New York N Y : 1991)*, 27(11), 5274–5283. <https://doi.org/10.1093/cercor/bhw306>
- APA (2022). *Diagnostic and statistical manual of mental disorders (5th ed., text rev.)*.
- Bae, H. J., Mony, T. J., & Park, S. J. (2025). Association between prenatal particulate matter exposure and neuropsychiatric disorders development. *Biomolecules & Therapeutics*, 33(4), 557–571. <https://doi.org/10.4062/biomolther.2025.031>
- Bölte, S., Girdler, S., & Marschik, P. B. (2019). The contribution of environmental exposure to the etiology of autism spectrum disorder. *Cellular and Molecular Life Sciences*, 76(7), 1275–1297. <https://doi.org/10.1007/s00018-018-2988-4>
- Bongaerts, E., Lecante, L. L., Bové, H., Roeflaers, M. B. J., Ameloot, M., Fowler, P. A., & Nawrot, T. S. (2022). 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. *The Lancet Planetary Health*, 6(10), e804–e811. [https://doi.org/10.1016/S2542-5196\(22\)00200-5](https://doi.org/10.1016/S2542-5196(22)00200-5)
- Bos, B., Barratt, B., Batalle, D., Gale-Grant, O., Hughes, E. J., Beevers, S., Cordero-Grande, L., Price, A. N., Hutter, J., Hajnal, J. V., Kelly, F. J., Edwards, D., A., & Counsell, S. J. (2023). Prenatal exposure to air pollution is associated with structural changes in the neonatal brain. *Environment International*, 174, 107921. <https://doi.org/10.1016/j.envint.2023.107921>
- Bradshaw, J., Eberth, J. M., Zgodic, A., Federico, A., Flory, K., & McLain, A. C. (2024). County-Level prevalence estimates of autism spectrum disorder in children in the united States. *Journal of Autism and Developmental Disorders*, 54(7), 2710–2718. <https://doi.org/10.1007/s10803-023-05920-z>
- Canals Sans, J., Morales Hidalgo, P., Roigé Castellví, J., Voltas Moreso, N., & Hernández Martínez, C. (2021). Prevalence and epidemiological characteristics of ADHD in pre-school and school age children in the province of Tarragona, Spain. *Journal of Attention Disorders*, 25(13), 1818–1833. <https://doi.org/10.1177/1087054720938866>
- Carter, S. A., Rahman, M. M., Lin, J. C., Shu, Y. H., Chow, T., Yu, X., Martinez, M. P., Eckel, S. P., Chen, J. C., Chen, Z., Schwartz, J., Pavlovic, N., Lurmann, F. W., McConnell, R., & Xiang, A. H. (2022). In utero exposure to near-roadway air pollution and autism spectrum disorder in children. *Environment International*, 158, Article 106898. <https://doi.org/10.1016/j.envint.2021.106898>
- Cortes-Albornoz, M. C., Calixto, C., Bedoya, M. A., Didier, R. A., Estroff, J. A., & Jaimes, C. (2023). Fetal brain growth in the early second trimester. *American Journal of Neuroradiology*, 44(12), 1440–1444. <https://doi.org/10.3174/ajnr.A8051>
- de Hoogh, K., Chen, J., Gulliver, J., Hoffmann, B., Hertel, O., Ketzel, M., Bauwelinck, M., van Donkelaar, A., Hvidtfeldt, U. A., Katsouyanni, K., Klompmaker, J., Martin, R. V., Samoli, E., Schwartz, P. E., Stafoggia, M., Bellander, T., Strak, M., Wolf, K., Vienneau, D., & Hoek, G. (2018). Spatial PM_{2.5}, NO₂, O₃ and BC models for Western Europe – Evaluation of spatiotemporal stability. *Environment International*, 120, 81–92. <https://doi.org/10.1016/j.envint.2018.07.036>
- Duque, I., Domínguez-Berjón, M. F., Cebrecos, A., Prieto-Salceda, M. D., Esnaola, S., Calvo Sánchez, M., & Mari-Dell'Olmo, M. (2021). Índice de privación En España Por sección censal En 2011. *Gaceta Sanitaria*, 35(2), 113–122. <https://doi.org/10.1016/j.gaceta.2019.10.008>
- Dutheil, F., Comptour, A., Morlon, R., Mermillod, M., Pereira, B., Baker, J. S., Charkhabi, M., Clinchamps, M., & Bourdel, N. (2021). Autism spectrum disorder and air pollution: A systematic review and meta-analysis. *Environmental Pollution (Barking, Essex: 1987)*, 278, Article 116856. <https://doi.org/10.1016/j.envpol.2021.116856>
- EEA (2015). *Airbase—The European Air Quality Database, Version 8 (Available)*. <http://www.eea.europa.eu/data-and-maps/data/airbase-the-european-air-quality-database8>
- Eeftens, M., Tsai, M. Y., Ampe, C., Anwander, B., Beelen, R., Bellander, T., Cesaroni, G., Cirach, M., Cyrys, J., de Hoogh, K., De Nazelle, A., de Vocht, F., Declercq, C., Dedelè, A., Eriksen, K., Galassi, C., Gražulevičienė, R., Grivas, G., Heinrich, J., & Hoek, G. (2012). Spatial variation of PM_{2.5}, PM₁₀, PM_{2.5} absorbance and PMcoarse concentrations between and within 20 European study areas and the relationship with NO₂ – Results of the

- ESCAPE project. *Atmospheric Environment*, 62, 303–317. <https://doi.org/10.1016/j.atmosenv.2012.08.038>
- Flanagan, E., Malmqvist, E., Rittner, R., Gustafsson, P., Källén, K., & Oudin, A. (2023). Exposure to local, source-specific ambient air pollution during pregnancy and autism in children: A cohort study from Southern Sweden. *Scientific Reports*, 13(1), Article 3848. <https://doi.org/10.1038/s41598-023-30877-5>
- Ghassabian, A., Dickerson, A. S., Wang, Y., Braun, J. M., Bennett, D. H., Croen, L. A., LeWinn, K. Z., Burris, H. H., Habre, R., Lyall, K., Frazier, J. A., Glass, H. C., Hooper, S. R., Joseph, R. M., Karr, C. J., Schmidt, R. J., Friedman, C., Karagas, M. R., Stroustrup, A., ... the ECHO Cohort Consortium. (2025). Prenatal Air Pollution Exposure and Autism Spectrum Disorder in the ECHO Consortium. *Environmental Health Perspectives*, <https://doi.org/10.1289/EHP16675>
- Gong, T., Almqvist, C., Bølte, S., Lichtenstein, P., Anckarsäter, H., Lind, T., Lundholm, C., & Pershagen, G. (2014). Exposure to air pollution from traffic and neurodevelopmental disorders in Swedish twins. *Twin Research and Human Genetics*, 17(6), 553–562. <https://doi.org/10.1017/thg.2014.58>
- Gong, T., Dalman, C., Wicks, S., Dal, H., Magnusson, C., Lundholm, C., Almqvist, C., & Pershagen, G. (2017). Perinatal exposure to Traffic-Related air pollution and autism spectrum disorders. *Environmental Health Perspectives*, 125(1), 119–126. <https://doi.org/10.1289/EHP118>
- Gotham, K., Pickles, A., & Lord, C. (2009). Standardizing ADOS scores for a measure of severity in autism spectrum disorders. *Journal of Autism and Developmental Disorders*, 39(5), 693–705. <https://doi.org/10.1007/s10803-008-0674-3>
- Grosvenor, L. P., Croen, L. A., Lynch, F. L., Marafino, B. J., Maye, M., Penfold, R. B., Simon, G. E., & Ames, J. L. (2024). Autism diagnosis among US children and adults, 2011–2022. *JAMA Network Open*, 7(10), Article e2442218. <https://doi.org/10.1001/jamanetworkopen.2024.42218>
- Guxens, M., Ghassabian, A., Gong, T., Garcia-Esteban, R., Porta, D., Giorgis-Allemand, L., Almqvist, C., Aranbarri, A., Beelen, R., Badaloni, C., Cesaroni, G., de Nazelle, A., Estarlich, M., Forastiere, F., Forns, J., Gehring, U., Ibarluzea, J., Jaddoe, V. W. V., Korek, M., & Sunyer, J. (2016). Air pollution exposure during pregnancy and childhood autistic traits in four European population-based cohort studies: The ESCAPE project. *Environmental Health Perspectives*, 124(1), 133–140. <https://doi.org/10.1289/ehp.1408483>
- He, Z., Song, A. Y., Schrott, R., Feinberg, J. I., Bakulski, K. M., Benke, K. S., Croen, L. A., Hertz-Picciotto, I., Schmidt, R. J., Lyall, K., Newschaffer, C. J., Fallin, M. D., Volk, H. E., & Ladd-Acosta, C. (2025). The association of prenatal ambient air pollution with placental epigenetic gestational age at birth. *Environmental Epidemiology*, 9(3), Article e384. <https://doi.org/10.1097/EE9.0000000000000384>
- Hoekstra, R. A., Bartels, M., Verweij, C. J. H., & Boomsma, D. I. (2007). Heritability of autistic traits in the general population. *Archives of Pediatrics & Adolescent Medicine*, 161(4), 372–377. <https://doi.org/10.1001/archpedi.161.4.372>
- Iglesias-Vázquez, L., Binter, A. C., Canals, J., Hernández-Martínez, C., Voltas, N., Ambrós, A., Fernández-Barrés, S., Pérez-Crespo, L., Guxens, M., & Arijia, V. (2022). Maternal exposure to air pollution during pregnancy and child's cognitive, language, and motor function: ECLIPSES study. *Environmental Research*, 212, Article 113501. <https://doi.org/10.1016/j.envres.2022.113501>
- Issac, A., Halemani, K., Shetty, A., Thimmappa, L., Vijay, V., Koni, K., Mishra, P., & Kapoor, V. (2025). The global prevalence of autism spectrum disorder in children: A systematic review and meta-analysis. *Osong Public Health and Research Perspectives*, 16(1), 3–27. <https://doi.org/10.24171/j.phrp.2024.0286>
- Jo, H., Eckel, S. P., Wang, X., Chen, J. C., Cockburn, M., Martinez, M. P., Chow, T., Molshatzki, N., Lurmann, F. W., Funk, W. E., Xiang, A. H., & McConnell, R. (2019). Sex-specific associations of autism spectrum disorder with residential air pollution exposure in a large Southern California pregnancy cohort. *Environmental Pollution (Barking, Essex: 1987)*, 254, Article 113010. <https://doi.org/10.1016/j.envpol.2019.113010>
- Kalenik, S., Zaczek, A., & Rodacka, A. (2025). Air Pollution-Induced neurotoxicity: The relationship between air Pollution, epigenetic Changes, and neurological disorders. *International Journal of Molecular Sciences*, 26(7), 3402. <https://doi.org/10.3390/ijms26073402>
- Karimi, P., Kamali, E., Mousavi, S. M., & Karahmadi, M. (2017). Environmental factors influencing the risk of autism. *Journal of Research in Medical Sciences*, 22, Article 27. <https://doi.org/10.4103/1735-1995.200272>
- Kaur, S., Morales-Hidalgo, P., Voltas, N., & Canals-Sans, J. (2024). Cluster analysis of teachers report for identifying symptoms of autism spectrum and/or attention deficit hyperactivity in school population: EPINED study. *Autism Research*, 17(5), 1027–1040. <https://doi.org/10.1002/aur.3138>
- Kim, D., Volk, H., Girirajan, S., Pendergrass, S., Hall, M. A., Verma, S. S., Schmidt, R. J., Hansen, R. L., Ghosh, D., Ludena-Rodriguez, Y., Kim, K., Ritchie, M. D., Hertz-Picciotto, I., & Selleck, S. B. (2017). The joint effect of air pollution exposure and copy number variation on risk for autism. *Autism Research*, 10(9), 1470–1480. <https://doi.org/10.1002/aur.1799>
- Konkel, L. (2018). The brain before birth: Using fMRI to explore the secrets of fetal neurodevelopment. *Environmental Health Perspectives*, 126(11), Article 112001. <https://doi.org/10.1289/EHP2268>
- Lam, J., Sutton, P., Kalkbrenner, A., Windham, G., Halladay, A., Koustas, E., Lawler, C., Davidson, L., Daniels, N., Newschaffer, C., & Woodruff, T. (2016). A systematic review and meta-analysis of multiple airborne pollutants and autism spectrum disorder. *PLoS One*, 11(9), Article e0161851. <https://doi.org/10.1371/journal.pone.0161851>
- Liu, N. M., Miyashita, L., Maher, B. A., McPhail, G., Jones, C. J. P., Barratt, B., Thangaratinam, S., Karloukovski, V., Ahmed, I. A., Aslam, Z., & Grigg, J. (2021). Evidence for the presence of air pollution nanoparticles in placental tissue cells. *Science of the Total Environment*, 751, Article 142235. <https://doi.org/10.1016/j.scitotenv.2020.142235>
- Lord, C., Rutter, M., DiLavore, P., Risi, S., Gotham, K., & Bishop, S. (2012). Autism diagnostic observation schedule (2nd edition (ADOS-2)). Western Psychological Corporation.
- Love, C., Sominsky, L., O'Hely, M., Berk, M., Vuillermin, P., & Dawson, S. L. (2024). Prenatal environmental risk factors for autism spectrum disorder and their potential mechanisms. *BMC Medicine*, 22(1), Article 393. <https://doi.org/10.1186/s12916-024-03617-3>
- Lugo-Marín, J., Díez-Villoria, E., Magán-Maganto, M., Pérez-Méndez, L., Alviani, M., de la Fuente-Portero, J. A., & Canal-Bedia, R. (2019). Spanish validation of the autism quotient short form questionnaire for adults with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, 49(11), 4375–4389. <https://doi.org/10.1007/s10803-019-04127-5>
- Lyall, K., Croen, L., Daniels, J., Fallin, M. D., Ladd-Acosta, C., Lee, B. K., Park, B. Y., Snyder, N. W., Schendel, D., Volk, H., Windham, G. C., & Newschaffer, C. (2017). The changing epidemiology of autism spectrum disorders. *Annual Review of Public Health*, 38(1), 81–102. <https://doi.org/10.1146/annurev-publhea-10-031816-044318>
- Mamun, M. A., Al-Mamun, F., Roy, N., Raquib, A., Kaggwa, M. M., Almerab, M. M., Gozal, D., & Hossain, M. S. (2025). Preconception and gestational versus postnatal exposure to air pollutants

- and risk of autism spectrum disorder: A systematic review and meta-analysis. *International Archives of Occupational and Environmental Health*, 98(1), 33–57. <https://doi.org/10.1007/s00420-024-02112-9>
- McGuinn, L. A., Windham, G. C., Kalkbrenner, A. E., Bradley, C., Di, Q., Croen, L. A., Fallin, M. D., Hoffman, K., Ladd-Acosta, C., Schwartz, J., Rappold, A. G., Richardson, D. B., Neas, L. M., Gammon, M. D., Schieve, L. A., & Daniels, J. L. (2020). Early life exposure to air pollution and autism spectrum disorder: Findings from a multisite case-control study. *Epidemiology*, 31(1), 103–114. <https://doi.org/10.1097/EDE.0000000000001109>
- Modabbernia, A., Velthorst, E., & Reichenberg, A. (2017). Environmental risk factors for autism: An evidence-based review of systematic reviews and meta-analyses. *Molecular Autism*, 8(1), Article 13. <https://doi.org/10.1186/s13229-017-0121-4>
- Morales Hidalgo, P., Voltas Moreso, N., & Canals Sans, J. (2021). Autism spectrum disorder prevalence and associated sociodemographic factors in the school population: Epined study. *Autism*, 25(7), 1999–2011. <https://doi.org/10.1177/13623613211007717>
- Morales-Hidalgo, P., Hernández-Martínez, C., Voltas, N., & Canals, J. (2017a). Edutea: A DSM-5 teacher screening questionnaire for autism spectrum disorder and social pragmatic communication disorder. *International Journal of Clinical and Health Psychology*, 17(3), 269–281. <https://doi.org/10.1016/j.ijchp.2017.05.002>
- Morales-Hidalgo, P., Roigé-Castellví, J., Vigil-Colet, A., & Canals Sans, J. (2017b). The childhood autism spectrum test (CAST): Spanish adaptation and validation. *Autism Research: Official Journal of the International Society for Autism Research*, 10(9), 1491–1498. <https://doi.org/10.1002/aur.1793>
- Morgan, Z. E. M., Bailey, M. J., Trifonova, D. I., Naik, N. C., Patterson, W. B., Lurmann, F. W., Chang, H. H., Peterson, B. S., Goran, M. I., & Alderete, T. L. (2023). Prenatal exposure to ambient air pollution is associated with neurodevelopmental outcomes at 2 years of age. *Environmental Health*, 22, Article 11. <https://doi.org/10.1186/s12940-022-00951-y>
- Mortamais, M., Ongono, J. S., Michelon, C., Hough, I., Seyve, E., Kloog, I., Zaros, C., Charles, M. A., Lepeule, J., & Baghdadli, A. (2025). Prenatal exposure to ambient particulate matter and autism spectrum disorder in children, a case control study in France. *Journal of Autism and Developmental Disorders*. <https://doi.org/10.1007/s10803-025-06795-y>
- Murphy, M. S. Q., Abdulaziz, K. E., Lavigne, É., Erwin, E., Guo, Y., Dingwall-Harvey, A. L. J., Stieb, D., Walker, M. C., Wen, S. W., & Shin, H. H. (2024). Association between prenatal air pollutant exposure and autism spectrum disorders in young children: A matched case-control study in Canada. *Environmental Research*, 261, Article 119706. <https://doi.org/10.1016/j.envres.2024.119706>
- O'Sharkey, K., Mitra, S., Chow, T., Paik, S., Thompson, L., Su, J., Cockburn, M., & Ritz, B. (2025). 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). *Environment International*, 201, Article 109562. <https://doi.org/10.1016/j.envint.2025.109562>
- Oudin, A., Frondelius, K., Haglund, N., Källén, K., Forsberg, B., Gustafsson, P., & Malmqvist, E. (2019). Prenatal exposure to air pollution as a potential risk factor for autism and ADHD. *Environment International*, 133, Article 105149. <https://doi.org/10.1016/j.envint.2019.105149>
- Pagalan, L., Bickford, C., Weikum, W., Lanphear, B., Brauer, M., Lanphear, N., Hanley, G. E., Oberlander, T. F., & Winters, M. (2019). Association of prenatal exposure to air pollution with autism spectrum disorder. *JAMA Pediatrics*, 173(1), 86–92. <https://doi.org/10.1001/jamapediatrics.2018.3101>
- Perera, F. P., Miao, Y., Ross, Z., Rauh, V., Margolis, A., Hoepner, L., Riley, K. W., Herbstman, J., & Wang, S. (2024). Prenatal exposure to air pollution during the early and middle stages of pregnancy is associated with adverse neurodevelopmental outcomes at ages 1 to 3 years. *Environmental Health*, 23(1), Article 95. <https://doi.org/10.1186/s12940-024-01132-9>
- Pérez-Crespo, L., Prats-Urbe, A., Tobias, A., Duran-Tauleria, E., Coronado, R., Hervás, A., & Guxens, M. (2019). Temporal and geographical variability of prevalence and incidence of autism spectrum disorder diagnoses in children in Catalonia, Spain. *Autism Research*, 12(11), 1693–1705. <https://doi.org/10.1002/aur.2172>
- Pham, C., Symeonides, C., O'Hely, M., Sly, P. D., Knibbs, L. D., Thomson, S., Vuillermin, P., Saffery, R., & Ponsonby, A. L. (2022). Early life environmental factors associated with autism spectrum disorder symptoms in children at age 2 years: A birth cohort study. *Autism*, 26(7), 1864–1881. <https://doi.org/10.1177/13623613211068223>
- Pugsley, K., Scherer, S. W., Bellgrove, M. A., & Hawi, Z. (2022). Environmental exposures associated with elevated risk for autism spectrum disorder may augment the burden of deleterious de novo mutations among probands. *Molecular Psychiatry*, 27(1), 710–730. <https://doi.org/10.1038/s41380-021-01142-w>
- Rahman, M. M., Shu, Y. H., Chow, T., Lurmann, F. W., Yu, X., Martinez, M. P., Carter, S. A., Eckel, S. P., Chen, J. C., Chen, Z., Levitt, P., Schwartz, J., McConnell, R., & Xiang, A. H. (2022). Prenatal exposure to air pollution and autism spectrum disorder: Sensitive windows of exposure and sex differences. *Environmental Health Perspectives*, 130(1), Article 017008. <https://doi.org/10.1289/EHP9509>
- Raz, R., Roberts, A. L., Lyall, K., Hart, J. E., Just, A. C., Laden, F., & Weisskopf, M. G. (2015). Autism spectrum disorder and particulate matter air pollution before, during, and after pregnancy: A nested case-control analysis within the nurses' health study II cohort. *Environmental Health Perspectives*, 123(3), 264–270. <https://doi.org/10.1289/ehp.1408133>
- Ritz, B., Liew, Z., Yan, Q., Cuia, X., Virk, J., Ketzler, M., & Raaschou-Nielsen, O. (2018). Air pollution and autism in Denmark. *Environmental Epidemiology*, 2(4), Article e028. <https://doi.org/10.1097/EE9.0000000000000028>
- Rovira, J., Domingo, J. L., & Schuhmacher, M. (2020). Air quality, health impacts and burden of disease due to air pollution (PM10, PM2.5, NO2 and O3): Application of AirQ+ model to the camp de Tarragona County (Catalonia, Spain). *The Science of the Total Environment*, 703, Article 135538. <https://doi.org/10.1016/j.scitotenv.2019.135538>
- Rovira, J., Nadal, M., Schuhmacher, M., & Domingo, J. L. (2021). Environmental impact and human health risks of air pollutants near a large chemical/petrochemical complex: Case study in Tarragona, Spain. *Science of the Total Environment*, 787, Article 147550. <https://doi.org/10.1016/j.scitotenv.2021.147550>
- Rutter, M., Le Couteur, A., & Lord, C. (2003). *ADI-R: Autism Diagnostic Interview-Revised (ADI-R)*. Western Psychological Services.
- Salari, N., Ghasemi, H., Abdoli, N., Rahmani, A., Shiri, M. H., Hashemian, A. H., Akbari, H., & Mohammadi, M. (2023). The global prevalence of ADHD in children and adolescents: A systematic review and meta-analysis. *Italian Journal of Pediatrics*, 49(1), Article 48. <https://doi.org/10.1186/s13052-023-01456-1>
- Scott, F. J., Baron-Cohen, S., Bolton, P., & Brayne, C. (2002). The CAST (Childhood asperger syndrome test): Preliminary development of a UK screen for mainstream primary-school-age children. *Autism*, 6(1), 9–31. <https://doi.org/10.1177/1362361302006001003>
- Sunyer, J., & Dadvand, P. (2019). Pre-natal brain development as a target for urban air pollution. *Basic & Clinical Pharmacology & Toxicology*, 125(Suppl 3), 81–88. <https://doi.org/10.1111/bcpt.13226>

- Talantseva, O. I., Romanova, R. S., Shurdova, E. M., Dolgorukova, T. A., Sologub, P. S., Titova, O. S., Kleeva, D. F., & Grigorenko, E. L. (2023). The global prevalence of autism spectrum disorder: A three-level meta-analysis. *Frontiers in Psychiatry*. <https://doi.org/10.3389/fpsyt.2023.1071181>
- Volk, H. E., Lurmann, F., Penfold, B., Hertz-Picciotto, I., & McConnell, R. (2013). Traffic-related air pollution, particulate matter, and autism. *JAMA Psychiatry*, 70(1), 71–77. <https://doi.org/10.1001/jamapsychiatry.2013.266>
- Wang, C., Geng, H., Liu, W., & Zhang, G. (2017). Prenatal, perinatal, and postnatal factors associated with autism: A meta-analysis. *Medicine*, 96(18), Article e6696. <https://doi.org/10.1097/MD.0000000000006696>
- Wang, S. Y., Cheng, Y. Y., Guo, H. R., & Tseng, Y. C. (2021). Air pollution during pregnancy and childhood autism spectrum disorder in Taiwan. *International Journal of Environmental Research and Public Health*, 18(18), 9784. <https://doi.org/10.3390/ijerph18189784>
- Wang, Y., Perera, F., Guo, J., Riley, K. W., Durham, T., Ross, Z., Ananth, C. V., Baccarelli, A., Wang, S., & Herbstman, J. B. (2022). A methodological pipeline to generate an epigenetic marker of prenatal exposure to air pollution indicators. *Epigenetics*, 17(1), 32–40. <https://doi.org/10.1080/15592294.2021.1872926>
- Wechsler, D. (2005). *Wechsler intelligence scale for Children—Fourth edition*. TEA Ediciones.
- Wechsler, D. (2014). *Wechsler preschool and primary scale of intelligence* (4th ed.). Pearson C & T Assessment.
- Weier, J., & Herring, D. (2000). *Measuring Vegetation (NDVI & EVI)*. NASA Earth Observatory. <https://earthobservatory.nasa.gov/features/MeasuringVegetation>
- WHO (2021). WHO global air quality guidelines: Particulate matter (PM_{2.5} and PM₁₀), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide. <https://www.who.int/publications-detail-redirection/9789240034228>
- Zeidan, J., Fombonne, E., Scora, J., Ibrahim, A., Durkin, M. S., Saxena, S., Yusuf, A., Shih, A., & Elsabbagh, M. (2022). Global prevalence of autism: A systematic review update. *Autism Research*, 15(5), 778–790. <https://doi.org/10.1002/aur.2696>

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