

# Association of Prenatal Exposure to Air Pollution With Autism Spectrum Disorder

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## Key Points

**Question** Is prenatal exposure to air pollution a risk factor for autism spectrum disorder?

**Findings** In this population-based cohort study of 132 256 births, maternal exposure to nitric oxide during pregnancy was associated with increased risk of autism spectrum disorder in offspring.

**Meaning** Reducing exposures of pregnant women to environmental nitric oxide may be associated with a reduction in autism spectrum disorder incidence in their children.

## Abstract

**Importance** The etiology of autism spectrum disorder (ASD) is poorly understood, but prior studies suggest associations with airborne pollutants.

**Objective** To evaluate the association between prenatal exposures to airborne pollutants and ASD in a large population-based cohort.

**Design, Setting, and Participants** This population-based cohort encompassed nearly all births in Metro Vancouver, British Columbia, Canada, from 2004 through 2009, with follow-up through 2014. Children were diagnosed with ASD using a standardized assessment with the Autism Diagnostic Interview–Revised and Autism Diagnostic Observation Schedule. Monthly mean exposures to particulate matter with a diameter less than 2.5  $\mu\text{m}$  (PM<sub>2.5</sub>), nitric oxide (NO), and nitrogen dioxide (NO<sub>2</sub>) at the maternal residence during pregnancy were estimated with temporally adjusted, high-resolution land use regression models. The association between prenatal air pollution exposures and the odds of developing ASD was evaluated using logistic regression adjusted for child sex, birth month, birth year, maternal age, maternal birthplace, and neighborhood-level urbanicity and income band. Data analysis occurred from June 2016 to May 2018.

**Exposures** Mean monthly concentrations of ambient PM<sub>2.5</sub>, NO, and NO<sub>2</sub> at the maternal residence during pregnancy, calculated retrospectively using temporally adjusted, high-resolution land use regression models.

**Main Outcomes and Measures** Autism spectrum disorder diagnoses based on standardized assessment of the Autism Diagnostic Interview–Revised and Autism Diagnostic Observation Schedule. The hypothesis being tested was formulated during data collection.

**Results** In a cohort of 132 256 births, 1307 children (1.0%) were diagnosed with ASD by the age of 5 years. The final sample size for the PM<sub>2.5</sub>-adjusted model was 129 439 children, and for NO and NO<sub>2</sub>, it was 129 436 children; of these, 1276 (1.0%) were diagnosed with ASD. Adjusted odds ratios for ASD per interquartile range (IQR) were not significant for exposure to PM<sub>2.5</sub> during pregnancy (1.04 [95% CI, 0.98-1.10] per 1.5  $\mu\text{g}/\text{m}^3$  increase [IQR] in PM<sub>2.5</sub>) or NO<sub>2</sub> (1.06 [95% CI, 0.99-1.12] per 4.8 ppb [IQR] increase in NO<sub>2</sub>) but the odds ratio was significant for NO (1.07 [95% CI, 1.01-1.13] per 10.7 ppb [IQR] increase in NO). Odds ratios for male children were 1.04 (95% CI, 0.98-1.10) for PM<sub>2.5</sub>; 1.09 (95% CI, 1.02-1.15) for NO; and 1.07 (95% CI, 1.00-1.13) for NO<sub>2</sub>. For female children, they were for 1.03 (95% CI, 0.90-1.18) for PM<sub>2.5</sub>; 0.98 (95% CI, 0.83-1.13) for NO; and 1.00 (95% CI, 0.86-1.16) for NO<sub>2</sub>.

**Conclusions and Relevance** In a population-based birth cohort, we detected an association between exposure to NO and ASD but no significant association with PM<sub>2.5</sub> and NO<sub>2</sub>.

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