Supplementary Online Content

Pagalan L, Bickford C, Weikum W, et al. Association of prenatal exposure to air pollution with autism spectrum disorder. *JAMA Pediatr*. Published online November 19, 2018. doi:10.1001/jamapediatrics.2018.3101.

This supplementary material has been provided by the authors to give readers

additional information about their work.

eFigure 1. Truncated land use regression model for PM$_{2.5}$ (2003) in Metro Vancouver, Canada.

The original LUR models for Metro Vancouver were developed by Henderson et al. [1] as exposure assessment tools for epidemiological applications. We extracted air pollutant concentrations from the truncated LUR models at all postal codes [2–8] within the study area and then multiplied them by the temporal factors to produce monthly air pollutant estimates across all postal codes. We then linked air pollutant estimates for each mother during each month of pregnancy using conception date, birth date, and residential postal code. Mothers in the cohort resided at 52,754 unique postal codes; out of these, we truncated 8.1% to 1.4 µg/m^3 for PM$_{2.5}$, 23 postal codes to 1.3 ppb for NO, and 138 postal codes to 6.9 ppb for NO$_2$.
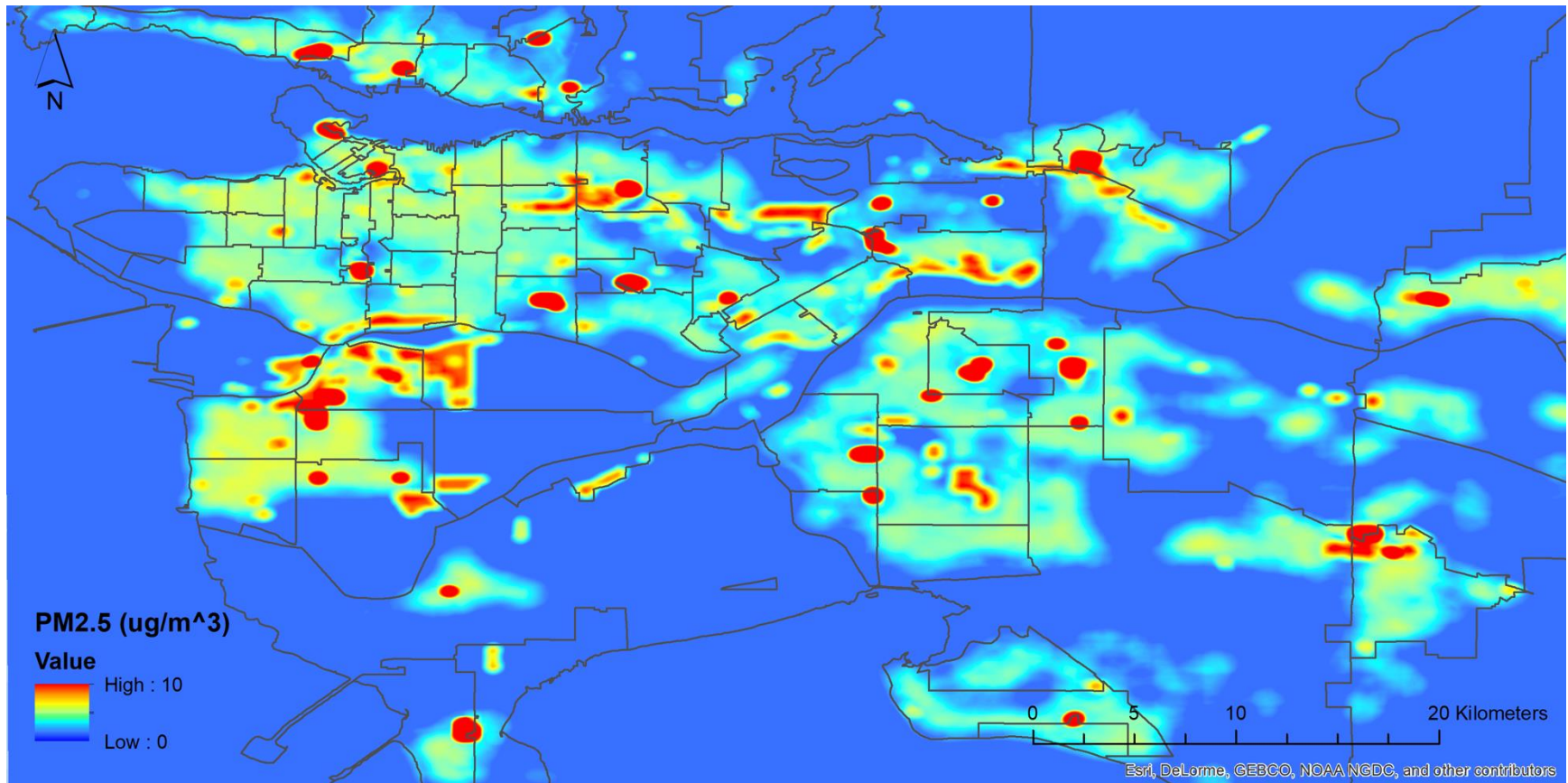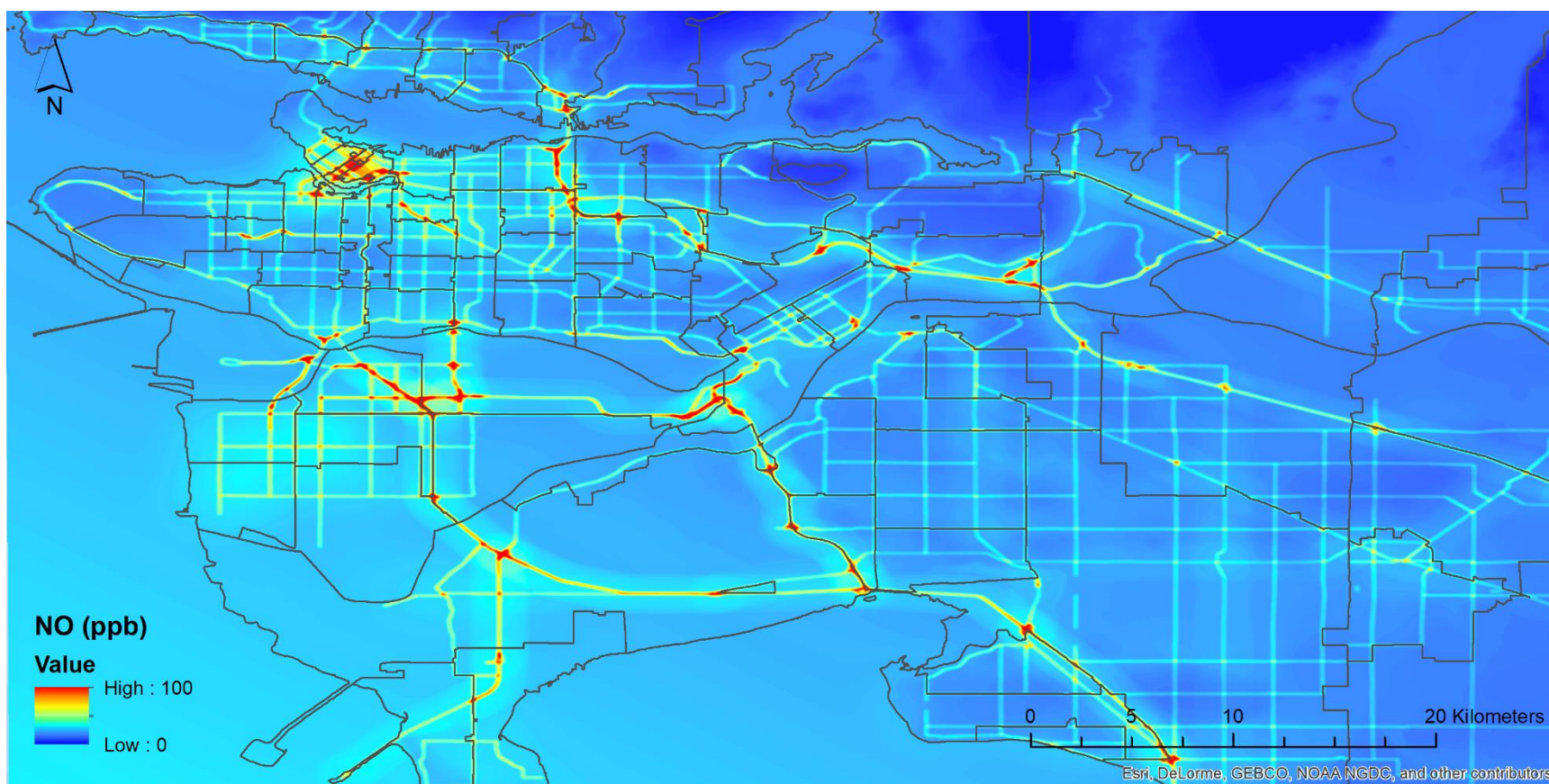
eFigure 2. Truncated land use regression model for NO (2003) in Metro Vancouver, Canada.

The original LUR models for Metro Vancouver were developed by Henderson et al. [1] as exposure assessment tools for epidemiological applications. We extracted air pollutant concentrations from the truncated LUR models at all postal codes [2-8] within the study area and then multiplied them by the temporal factors to produce monthly air pollutant estimates across all postal codes. We then linked air pollutant estimates for each mother during each month of pregnancy using conception date, birth date, and residential postal code. Mothers in the cohort resided at 52,754 unique postal codes; out of these, we truncated 8.1% to 1.4 µg/m^3 for $PM_{2.5}$, 23 postal codes to 1.3 ppb for NO, and 138 postal codes to 6.9 ppb for NO_2.
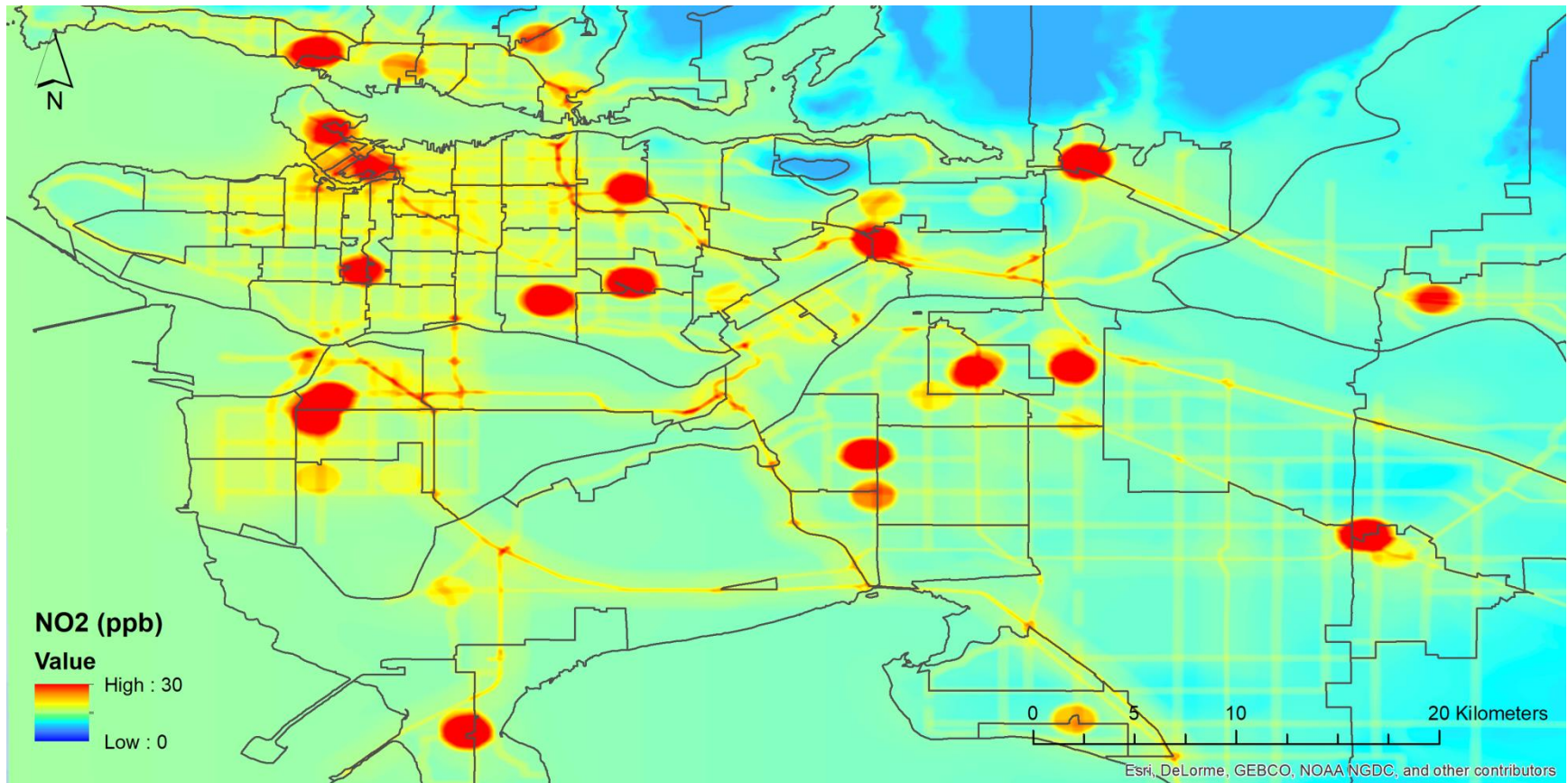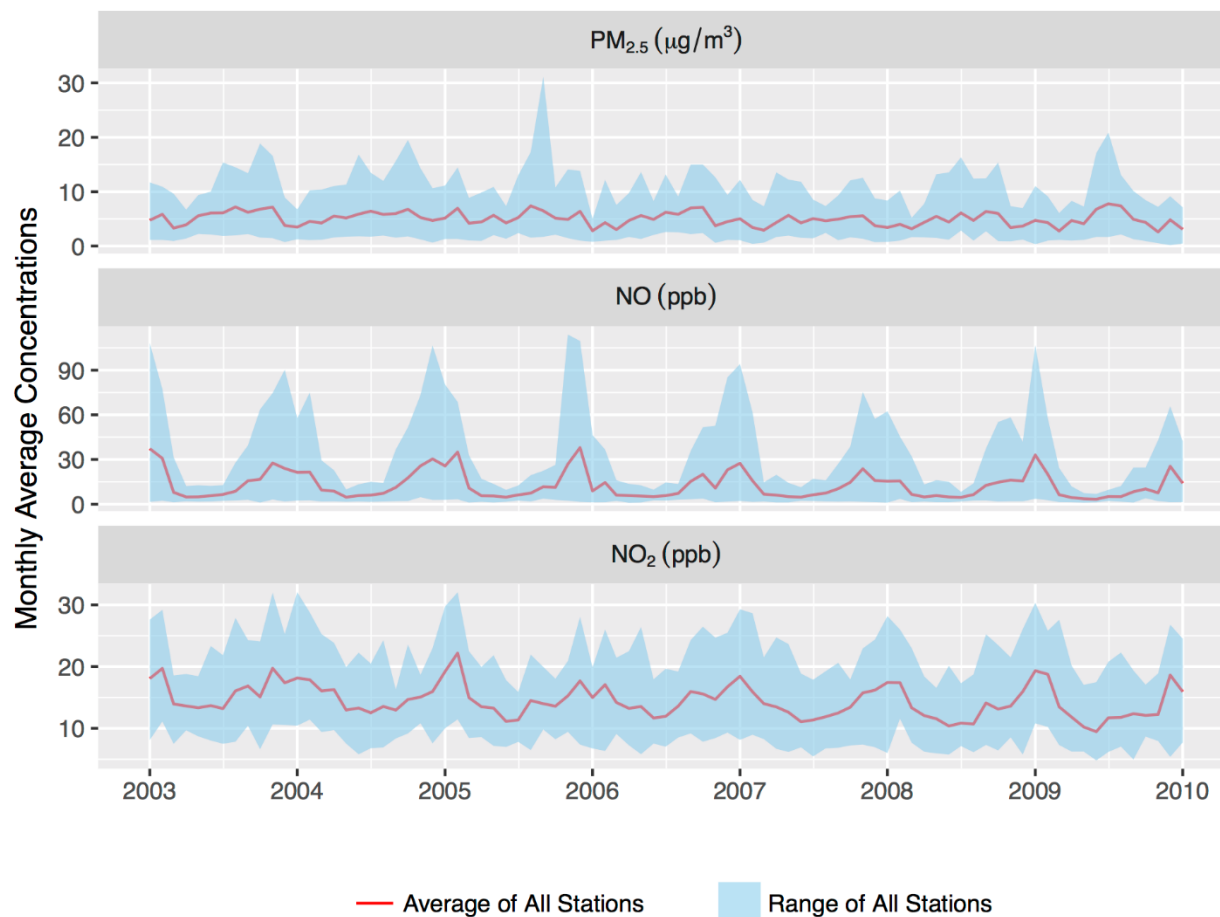
eFigure 3. Truncated land use regression model for NO₂ (2003) in Metro Vancouver, Canada.

The original LUR models for Metro Vancouver were developed by Henderson et al. [1] as exposure assessment tools for epidemiological applications. We extracted air pollutant concentrations from the truncated LUR models at all postal codes [2–8] within the study area and then multiplied them by the temporal factors to produce monthly air pollutant estimates across all postal codes. We then linked air pollutant estimates for each mother during each month of pregnancy using conception date, birth date, and residential postal code. Mothers in the cohort resided at 52,754 unique postal codes; out of these, we truncated 8.1% to 1.4 μg/m³ for $PM_{2.5}$, 23 postal codes to 1.3 ppb for NO, and 138 postal codes to 6.9 ppb for NO_2.

eFigure 4. Monthly average concentrations of PM$_{2.5}$, NO, and NO$_2$ from air quality monitoring stations in Metro Vancouver, 2003–2009.

Temporal trends in monthly average concentrations PM$_{2.5}$, NO, and NO$_2$ from air quality monitoring stations in Metro Vancouver. Annual average concentrations have decreased slightly: from an annual average of 5.7 to 5.0 μg/m^3 for PM$_{2.5}$, 16.0 to 11.0 ppb for NO, and 16.0 to 13.5 ppb for NO$_2$. Concentrations of PM$_{2.5}$ tended to be higher in summer, whereas NO and NO$_2$ concentrations were higher in winter.
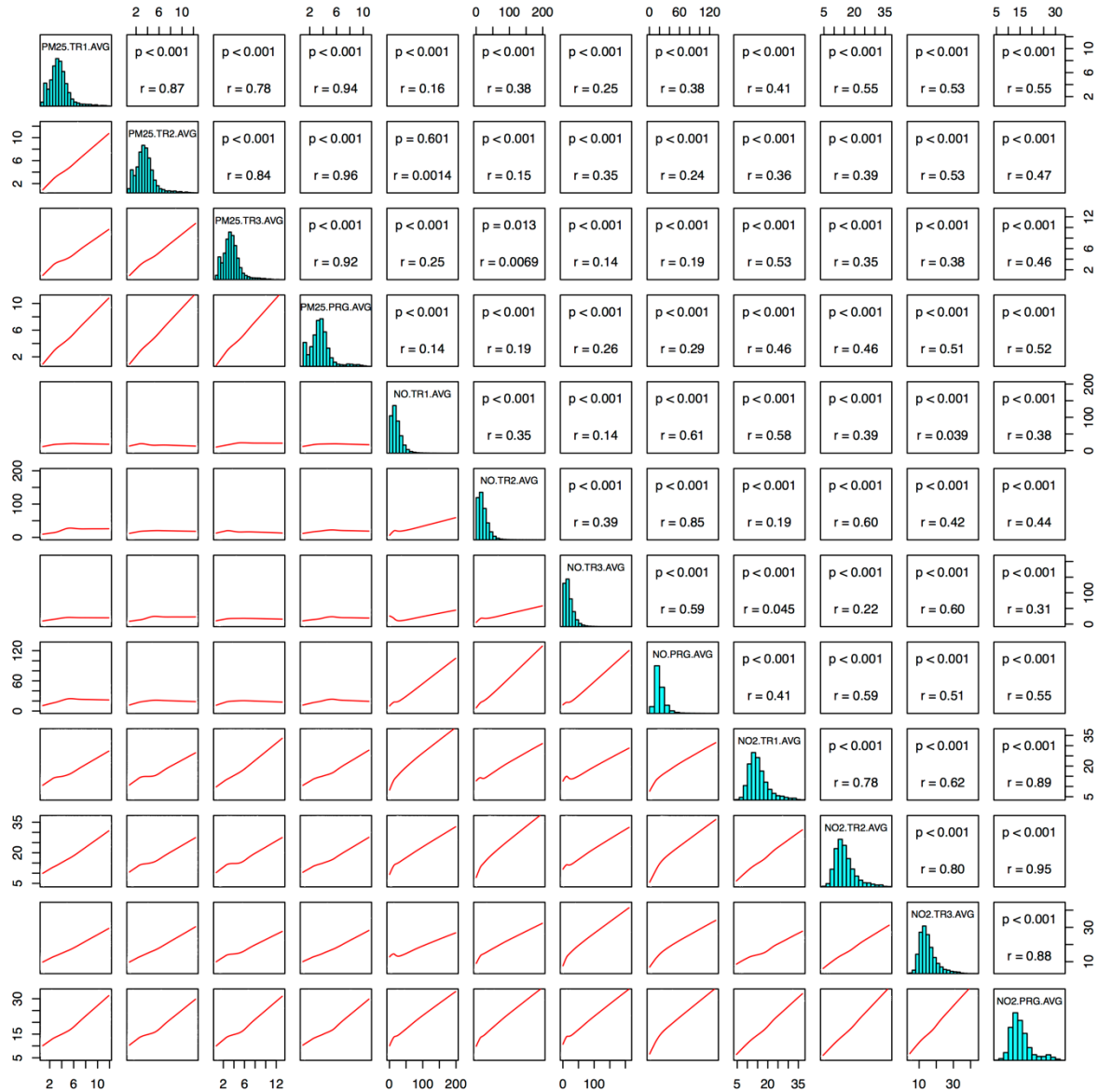
eFigure 5. Correlation matrix of air pollutant exposures across pregnancy and trimesters.

The correlation matrix shows the distribution of exposure estimates for each pollutant across four time periods (i.e. full pregnancy and trimesters 1–3) and the correlation coefficient among all pollutant and time periods pairs. NO_2 showed moderate positive correlations with both $PM_{2.5}$ and NO. Correlations across time periods within pollutants was high for $PM_{2.5}$ and NO_2. Abbreviations: PRG, full pregnancy; TR1, trimester 1; TR2, trimester 2; and TR3, trimester 3.

eFigure 6. Overall and sex-stratified odds of ASD for prenatal exposure to air pollutants during pregnancy and trimesters among children born in Metro Vancouver, Canada, between 2004–2009.
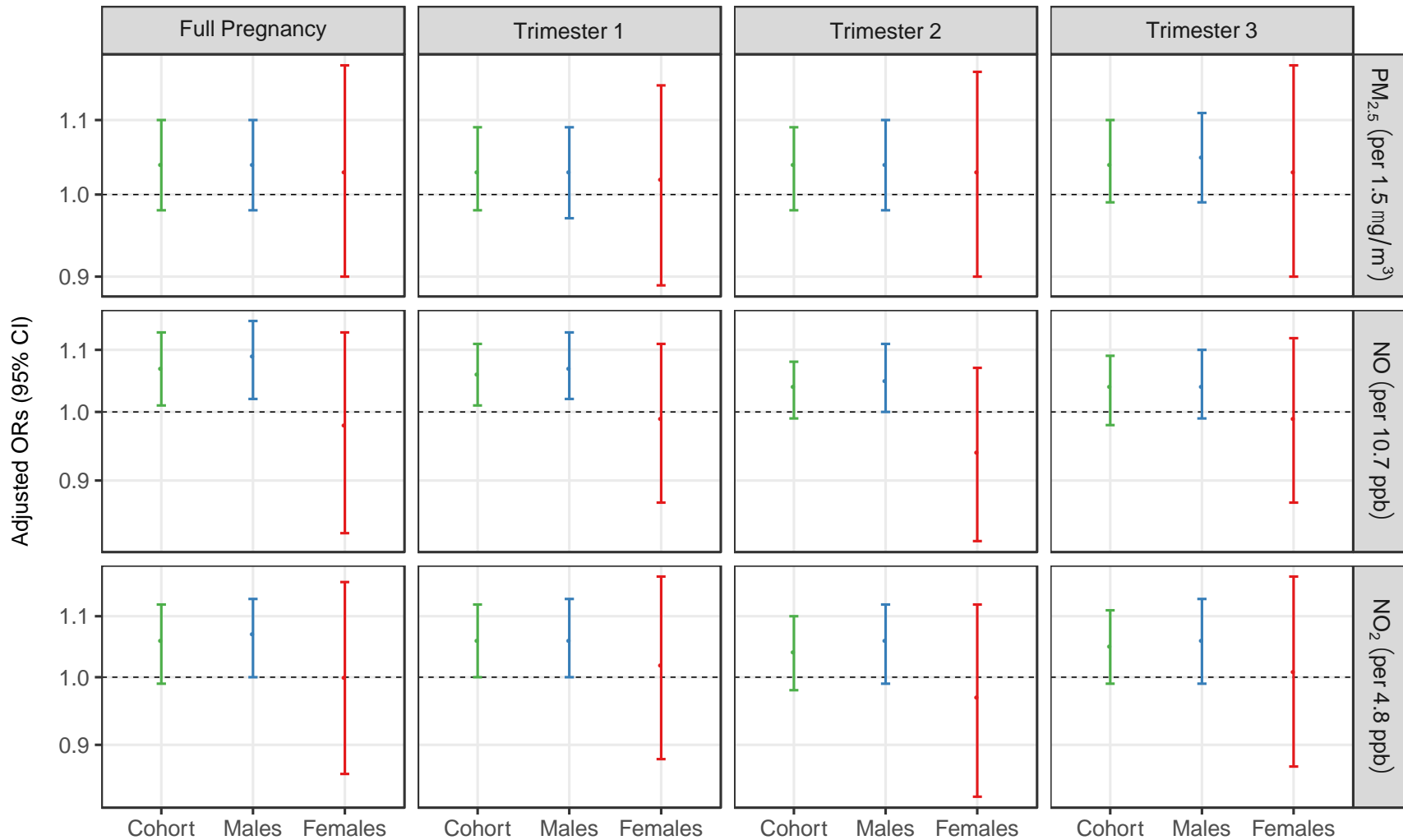
Single pollutant and single time period models adjusted for child sex, birth month, birth year, maternal age, maternal birthplace, and neighborhood-level urbanicity and income band.

eTable 1. Median monthly average prenatal exposure estimates among children born in Metro Vancouver, Canada, between 2004–2009.

Pollutant	Units	Time Period	Sample Size [a]	Median Monthly Average Exposure Estimates (IQR)	
$PM_{2.5}$	µg/m³	Full Pregnancy	131,440	3.5	(2.7, 4.2)
		Trimester 1	131,447	3.4	(2.6, 4.3)
		Trimester 2	131,640	3.4	(2.6, 4.3)
		Trimester 3	131,206	3.4	(2.5, 4.3)
NO	ppb	Full Pregnancy	131,437	18.3	(14.0, 24.7)
		Trimester 1	131,444	17.4	(10.0, 28.3)
		Trimester 2	131,637	16.6	(9.5, 27.8)
		Trimester 3	131,203	15.3	(9.1, 26.5)
NO_2	ppb	Full Pregnancy	131,437	14.3	(12.2, 17.0)
		Trimester 1	131,444	14.5	(12.1, 17.6)
		Trimester 2	131,637	14.3	(11.9, 17.5)
		Trimester 3	131,203	14.0	(11.6, 17.2)

[a] Monthly average exposure estimates based on complete monthly exposures for the period of interest. Incomplete prenatal monthly exposures, approximately 0.5–0.8% of the cohort (n = 132,256 children), are a result of postal codes retiring during the period of interest, preventing spatial referencing.

eTable 2. Sensitivity analyses of odds of ASD for prenatal exposure to air pollutants.

Pollutant	Units	Model [a]	Sample Size	Children with ASD	OR (95% CI)
$PM_{2.5}$	Per IQR (1.5 µg/m3)	Unadjusted full pregnancy model	131,440	1,300	1.08 (1.03, 1.14)
		Adjusted full pregnancy model	129,439	1,276	1.04 (0.98, 1.10)
		Adjusted full pregnancy model + gestational age	129,439	1,276	1.04 (0.99, 1.10)
		Adjusted full pregnancy model + small for gestational age	129,423	1,276	1.04 (0.98, 1.10)
		Adjusted full pregnancy model + birth weight	129,423	1,276	1.04 (0.98, 1.10)
		Adjusted full pregnancy model + multiple birth	129,439	1,276	1.04 (0.98, 1.10)
		Adjusted full pregnancy model + parity	129,438	1,276	1.03 (0.97, 1.08)
		Adjusted full pregnancy model + smoking	129,439	1,276	1.04 (0.98, 1.10)
		Adjusted full pregnancy model replacing birth month with conception month	129,439	1,276	1.04 (0.98, 1.10)
		Adjusted full pregnancy model using non-truncated, temporally adjusted LUR	129,439	1,276	1.04 (0.98, 1.09)
NO	Per IQR (10.7 ppb)	Unadjusted full pregnancy model	131,437	1,300	1.09 (1.03, 1.14)
		Adjusted full pregnancy model	129,436	1,276	1.07 (1.01, 1.13)
		Adjusted full pregnancy model + gestational age	129,436	1,276	1.07 (1.01, 1.13)
		Adjusted full pregnancy model + small for gestational age	129,420	1,276	1.07 (1.01, 1.13)
		Adjusted full pregnancy model + birth weight	129,420	1,276	1.07 (1.01, 1.13)
		Adjusted full pregnancy model + multiple birth	129,436	1,276	1.07 (1.01, 1.13)
		Adjusted full pregnancy model + parity	129,435	1,276	1.05 (0.99, 1.11)
		Adjusted full pregnancy model + smoking	129,436	1,276	1.07 (1.01, 1.13)
		Adjusted full pregnancy model replacing birth month with conception month	129,436	1,276	1.07 (1.01, 1.13)
		Adjusted full pregnancy model using non-truncated, temporally adjusted LUR	129,436	1,276	1.07 (1.01, 1.13)
NO_2	Per IQR (4.8 ppb)	Unadjusted full pregnancy model	131,437	1,300	1.11 (1.05, 1.17)
		Adjusted full pregnancy model	129,436	1,276	1.06 (0.99, 1.12)
		Adjusted full pregnancy model + gestational age	129,436	1,276	1.06 (1.00, 1.12)
		Adjusted full pregnancy model + small for gestational age	129,420	1,276	1.05 (0.99, 1.12)
		Adjusted full pregnancy model + birth weight	129,420	1,276	1.06 (0.99, 1.12)
		Adjusted full pregnancy model + multiple birth	129,436	1,276	1.06 (0.99, 1.12)
		Adjusted full pregnancy model + parity	129,435	1,276	1.03 (0.97, 1.09)
		Adjusted full pregnancy model + smoking	129,436	1,276	1.05 (0.99, 1.12)
		Adjusted full pregnancy model replacing birth month with conception month	129,436	1,276	1.06 (0.99, 1.12)
		Adjusted full pregnancy model using non-truncated, temporally adjusted LUR	129,436	1,276	1.06 (0.99, 1.12)

[a] Models adjusted for child sex, birth month, birth year, maternal age, maternal birthplace, and neighborhood-level urbanicity and income band.

eTable 3. Comparison of adjusted odds ratios between individual trimester models versus a mutually adjusted trimester model.

Pollutant	Units	Model [a]	Trimester	OR (95 %)
$PM_{2.5}$	Per IQR (1.5 µg/m³)	Adjusted trimester 1 model	Trimester 1	1.03 (0.98, 1.09)
		Adjusted trimester 2 model	Trimester 2	1.04 (0.98, 1.09)
		Adjusted trimester 3 model	Trimester 3	1.04 (0.99, 1.10)
		Adjusted model with mutually adjusted trimesters	Trimester 1	0.92 (0.79, 1.08)
			Trimester 2	1.06 (0.90, 1.24)
			Trimester 3	1.06 (0.93, 1.22)
NO	Per IQR (10.7 ppb)	Adjusted trimester 1 model	Trimester 1	1.06 (1.01, 1.11)
		Adjusted trimester 2 model	Trimester 2	1.04 (0.99, 1.08)
		Adjusted trimester 3 model	Trimester 3	1.04 (0.98, 1.09)
		Adjusted model with mutually adjusted trimesters	Trimester 1	1.06 (1.00, 1.13)
			Trimester 2	0.98 (0.91, 1.05)
			Trimester 3	1.02 (0.96, 1.09)
NO_2	Per IQR (4.8 ppb)	Adjusted trimester 1 model	Trimester 1	1.06 (1.00, 1.12)
		Adjusted trimester 2 model	Trimester 2	1.04 (0.98, 1.10)
		Adjusted trimester 3 model	Trimester 3	1.05 (0.99, 1.11)
		Adjusted model with mutually adjusted trimesters	Trimester 1	1.09 (0.93, 1.28)
			Trimester 2	0.90 (0.75, 1.09)
			Trimester 3	1.07 (0.90, 1.26)

[a] Models adjusted for child sex, birth month, birth year, maternal age, maternal birthplace, and neighborhood-level urbanicity and income band.

eReferences

1. Henderson SB, Beckerman B, Jerrett M, Brauer M. Application of land use regression to estimate long-term concentrations of traffic-related nitrogen oxides and fine particulate matter. *Environ Sci Technol*. 2007;41(7):2422-2428. doi:10.1021/es0606780

2. 2009-11-19, "Census of Canada. Postal Code Conversion File, January 2003 Postal Codes, 2001", http://hdl.handle.net.proxy.lib.sfu.ca/11272/TF2D9 V3 [Version].

3. 2009-11-19, "Census of Canada. Postal Code Conversion File, July 2004 Postal Codes, 2001", http://hdl.handle.net.proxy.lib.sfu.ca/11272/SRHXK V2 [Version].

4. 2009-11-18, "Census of Canada. Postal Code Conversion File, October 2005 Postal Codes, 2001", http://hdl.handle.net.proxy.lib.sfu.ca/11272/92QKP V3 [Version].

5. 2009-11-19, "Census of Canada. Postal Code Conversion File, September 2006 Postal Codes, 2001", http://hdl.handle.net.proxy.lib.sfu.ca/11272/HQIOQ V2 [Version].

6. 2009-11-19, "Census of Canada. Postal Code Conversion File, September 2007 Postal Codes, 2006 [2007]", http://hdl.handle.net.proxy.lib.sfu.ca/11272/PVVYH V2 [Version].

7. 2009-11-18, "Census of Canada. Postal Code Conversion File, March 2008 Postal Codes, 2006 [2008]", http://hdl.handle.net.proxy.lib.sfu.ca/11272/LNEEC V3 [Version].

8. 2010-01-28, "Census of Canada. Postal Code Conversion File, July 2009 Postal Codes, 2006 [2009]", http://hdl.handle.net.proxy.lib.sfu.ca/11272/NTC6K V3 [Version].