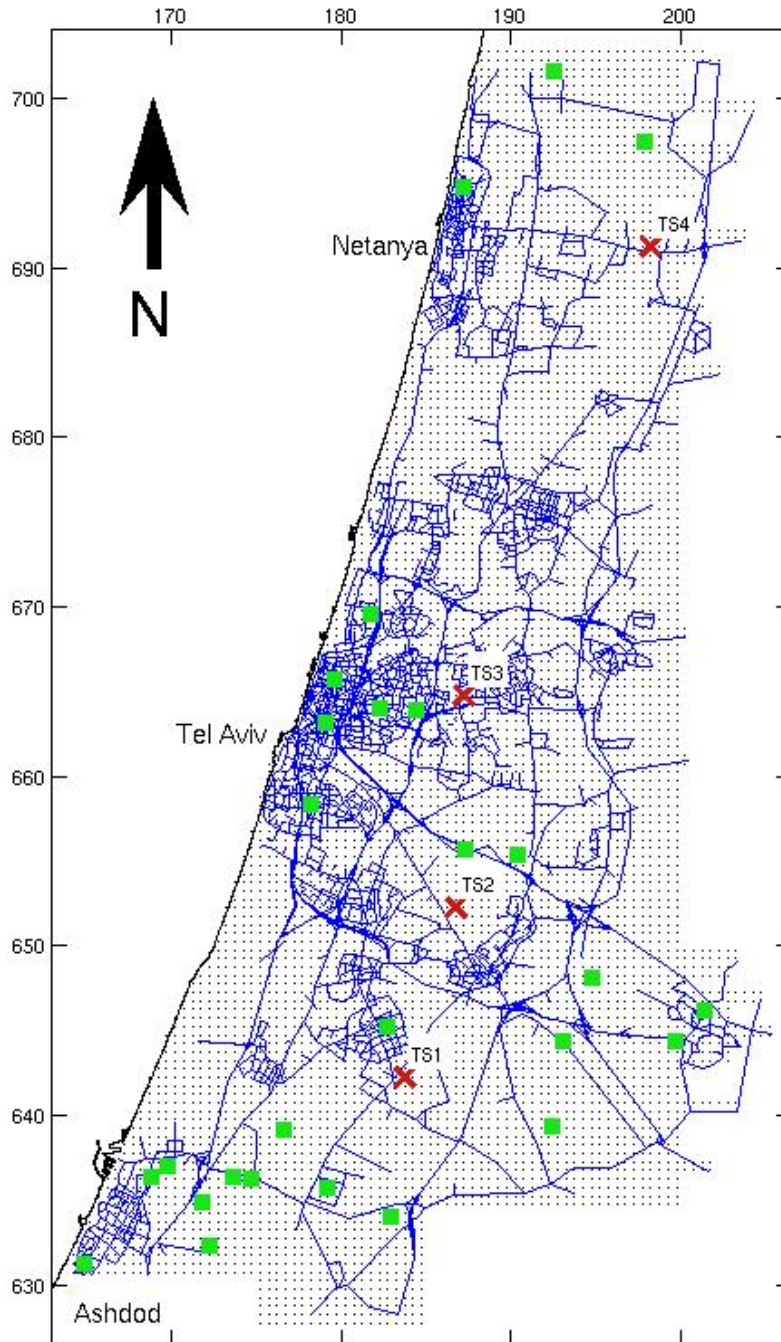


Web Figure 1: Study Area



The study area map showing the shoreline, the road network (thinned in dense areas for visual purposes), the observation locations of the nitrogen dioxide (NO₂) monitors used in the study (green squares) and the spatial 500- x 500-m grid. The four red X-marks are locations of grid points for which time series are plotted in Figure 2. The numbers on the axes are the coordinates using the Israel Transverse Mercator (New Israeli Grid) system in kilometers.

Web Appendix

Air pollution monitoring data and meteorological records used for estimating the exposure were obtained from the Technion Center of Excellence in Exposure Science and Environmental Health's air pollution monitoring database and included all data observed in Israel from 1997 to date. Data records consist of half-hourly means of the monitored variables after they pass quality assurance and quality control processes. All NO₂ records observed in general monitoring stations in the study area were used (i.e., data from road-side stations were excluded as they represent their specific locations rather than the general population exposure).

The Optimized Dispersion Model¹ was used to produce a concentration map for every daytime half hour in the working days of the study period at 500 X 500 m grid resolution. The model is a dispersion-like model that uses proxies for traffic emissions (time-of-day specific traffic volumes obtained from an independent traffic assignment model) and meteorological data as inputs, and produces concentration maps of traffic-related primary pollutants. The wind field used by the model was the half-hourly Representative Wind.² Hence, the model accounts for spatiotemporal concentration variability that results due to daily varying emissions and meteorological conditions. The model coefficients are found by fitting it to half-hourly pollutant observations, and used for obtaining the half-hourly NO₂ concentrations throughout the study area.

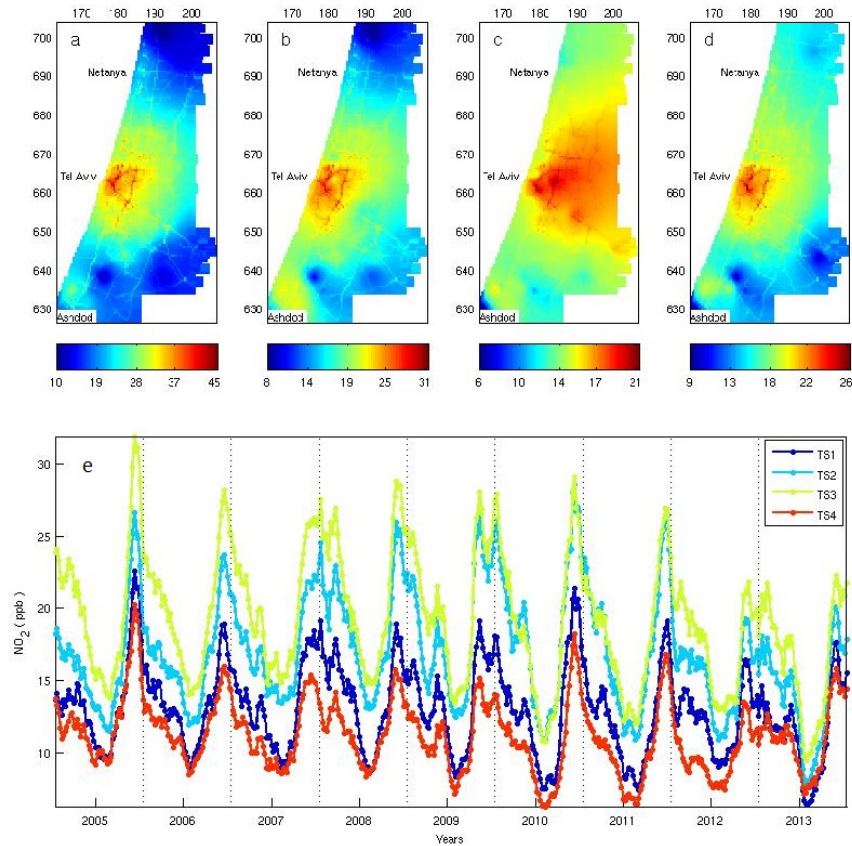
Based on the daily profile of available traffic proxies, daytime was defined as the hours between 06:00-21:00. Working days were all the Sundays to Fridays that did not fall on statutory holidays. For the nights and weekends, for which traffic volume and average vehicle speed data were not available, we calculated the concentration maps using an Inverse Distance Weighting spatial interpolation scheme^{3,4} with the power parameter selected as the one maximizing the leave-one-out cross-validation root mean squared error. The weekly traffic-related NO₂ exposure metrics at each grid point were calculated as the mean value of the half-hourly concentrations assigned to it during each of the weekly spans. For the current investigation, we used an improved version of the model in which an interpolation map of the raw observed residuals were used to obtain the residual correction.⁵ The latter was a fraction of the residuals interpolation map, with the fraction depending on the spatial autocorrelation of the residuals. Thus, random residuals were not corrected whereas spatial bias in the exposure model (if found in any of the half hourly maps) has been corrected. The cross-validated performance of the

model (based on the morning, noon and evening time points weekly averages) is $R^2 = 0.7$, mean bias = 0.16 ppb and RMSE = 3.92 ppb.

References

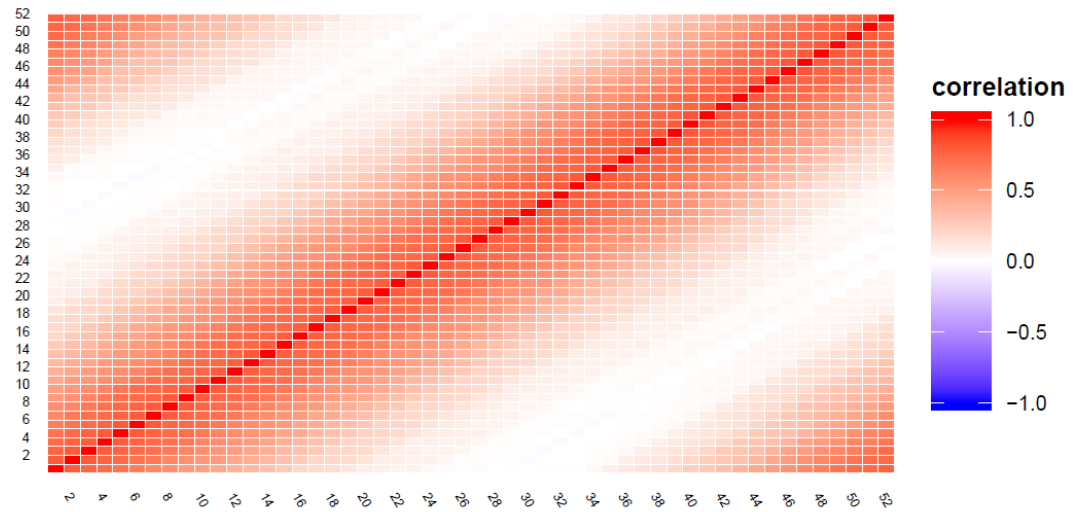
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Web Figure 2: Spatial and Temporal Variability of NO₂



Top: Weekly mean NO₂ exposure concentrations in the study area during different seasons. (a) Map for the week starting on January 8, 2005 (winter); (b) map for the week starting on April 9, 2005 (spring); (c) map for the week starting on July 9, 2005 (summer); (d) map for the week starting on October 8, 2005 (fall). Note that the color codes are different for each plot. *Bottom:* (e) Weekly NO₂ concentration time series at four grid points representing different parts of the study area during January 2005–December 2013 (dotted line represent year boundaries). The locations of these points are shown in red in Web Figure 1.

Web Figure 3: Pearson Correlations Among NO₂ Exposures During the First Year of Life



**Web Table 1: Correlation Coefficients for Correlation Among 9-Month
NO₂ Exposure Periods in the Study Population**

	Pregnancy	Postpregnancy
Prepregnancy	0.86	0.79
Pregnancy		0.88

Web Table 2: Associations Between 9-Month NO₂ Exposure Periods and Risk of Autism Spectrum Disorder

Model(s) Specifications	N (Cases, Controls)	Pregnancy^a	9 Months Postpregnancy^a
1. Unadjusted, separate models	2098, 54191	1.06 (0.99-1.13)	1.07 (0.99-1.15)
2. Adjusted, separate models ^b	2098, 54191	1.08 (1.01-1.15)	1.09 (1.02-1.18)
3. Mutually adjusted ^c	2098, 54191	0.77 (0.59-1.00)	1.40 (1.09-1.80)
4. Adjusted, separate models that also include prepregnancy exposure ^d	1721, 45449	0.83 (0.63-1.10)	1.22 (0.96-1.54)
5. With all three exposure periods ^e	1721, 45449	0.60 (0.42-0.84)	1.59 (1.18-2.15)
6. Boys only ^f	1435, 23247	0.51 (0.35-0.76)	1.63 (1.17-2.27)
7. Girls only ^f	286, 22202	1.46 (0.61-3.46)	1.17 (0.57-2.41)

a. Associations are reported as odds ratios (95% confidence interval) per pregnancy NO₂ interquartile range (5.85 ppb). Pregnancy exposure was calculated for the exact pregnancy period for each child.

b. Adjusted for: year of birth, calendar month of birth, population group, paternal age and census poverty index.

c. One model with the same adjustment as in [2], but including both exposure periods.

d. Same separate models as in [2], but adjusted also for exposure during 9 months before conception (limited to children for whom data is available for this period).

e. Same as in [3], but adjusted also for exposure during 9 months before conception (limited to children for whom data is available for this period). Results for 9 months prepregnancy: 1.11 (0.83-1.49).

f. Same as in [5], but sex-stratified. Results for 9 months prepregnancy: Boys: 1.22 (0.88-1.67), Girls: 0.75 (0.37-1.53).

Web Table 3: Associations Between 9-Month Postpregnancy NO₂ Exposure and Risk of ASD: Sensitivity Analyses

Model/Population	Cases, <i>n</i> (%)	Controls, <i>n</i> (%)	Odds Ratio (95% CI)
1. Original model ^a	1721(100)	45446 (100)	1.59 (1.18-2.15)
2. With additional adjustments ^b	1721 (100)	45446 (100)	1.53 (1.13-2.07)
3. GA between 38-41 weeks ^c	1629 (72.4)	44430 (80.3)	1.52 (1.12-2.07)
4. Excluding subjects missing GA ^c	1629 (94.6)	44430 (97.8)	1.56 (1.14-2.13)
5. Excluding subjects missing SSA ^c	1616 (94.3)	41237 (90.7)	1.47 (1.07-2.01)
6. Excluding multiple births ^c	1585 (92.3)	43077 (94.9)	1.45 (1.05-1.98)
7. Excluding Arabs and UOJ ^c	1487 (87.1)	32885 (72.2)	1.53 (1.11-2.12)
8. Excluding Arabs ^c	1657 (96.7)	42245 (92.8)	1.52 (1.12-2.07)
9. Excluding siblings with ASD ^c	1536 (89.6)	45136 (99.3)	1.52 (1.10-2.09)
10. Adjusted for GA at birth ^c	1629 (94.6)	44430 (97.8)	1.51 (1.11-2.06)
11. Adjusted for birth weight ^c	1721 (95.1)	45446 (98.5)	1.49 (1.11-2.02)

Abbreviations: ASD = autism spectrum disorder; GA = gestational age; SSA = small statistical area; UOJ = ultraorthodox Jews.

a. All odds ratios are per pregnancy NO₂ interquartile range (5.85 ppb). The original model is adjusted for year of birth, calendar month of birth, population group, father's age and census poverty index, exposure during pregnancy and exposure 9 months before pregnancy.

b. Additionally adjusted for child's sex, maternal age, maternal and paternal income levels, multiple birth, parents' immigration.

c. With same covariates like model 2.