Epidemiology of ASD
A Survey of Out-of-Pocket Expenditures for Children with Autism Spectrum Disorder in Israel

Raanan Raz · Liat Lerner-Geva · Odelia Leon · Gabriel Chodick · Lidia V. Gabis

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### Table 2  Treatment Utilization and Yearly Out-of-Pocket Costs (USD) by Category

<table>
<thead>
<tr>
<th>Treatment category</th>
<th>Proportion of subjects (%)</th>
<th>Proportion of cost (%)</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABA/DIR</td>
<td>17</td>
<td>25</td>
<td>2,067</td>
<td>6,513</td>
</tr>
<tr>
<td>Endorsed allied-medical therapies</td>
<td>96</td>
<td>25</td>
<td>2,034</td>
<td>3,403</td>
</tr>
<tr>
<td>Personal aide</td>
<td>42</td>
<td>16</td>
<td>1,297</td>
<td>3,709</td>
</tr>
<tr>
<td>Allied-medical pending endorsement therapies</td>
<td>90</td>
<td>11</td>
<td>945</td>
<td>1,655</td>
</tr>
<tr>
<td>Others</td>
<td>11</td>
<td>5</td>
<td>401</td>
<td>3,648</td>
</tr>
<tr>
<td>Other allied-medical therapies</td>
<td>17</td>
<td>5</td>
<td>394</td>
<td>2,005</td>
</tr>
<tr>
<td>Other complementary/alternative remedies</td>
<td>16</td>
<td>4</td>
<td>331</td>
<td>1,244</td>
</tr>
<tr>
<td>Food supplements</td>
<td>25</td>
<td>3</td>
<td>207</td>
<td>705</td>
</tr>
<tr>
<td>Health promotion program</td>
<td>10</td>
<td>2</td>
<td>176</td>
<td>533</td>
</tr>
<tr>
<td>Other group interventions</td>
<td>11</td>
<td>2</td>
<td>151</td>
<td>913</td>
</tr>
<tr>
<td>Neuropsychological medications</td>
<td>22</td>
<td>2</td>
<td>129</td>
<td>374</td>
</tr>
<tr>
<td>Pedagogic interventions</td>
<td>10</td>
<td>1</td>
<td>107</td>
<td>536</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100</strong></td>
<td><strong>100</strong></td>
<td><strong>8,239</strong></td>
<td><strong>11,642</strong></td>
</tr>
</tbody>
</table>

*ABA* applied behavioral analysis, *DIR* developmental, individual difference, relationship-based model, *SD* standard deviation

![Graph showing average annual out-of-pocket expenditures (USD) per child, by treatment category. Error bars represent 95% confidence interval. USD US Dollars, ABA Applied Behavioral Analysis, DIR Developmental, Individual difference, Relationship-based model.](image-url)

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Fig. 1  Cumulative incidence of ASD and non-ASD child disability benefits at NII at age 8 in the total population born in Israel 1992–2003 by birth year, as a percentage of 1992 cumulative incidence. ASD Autism spectrum disorders; NII National Insurance Institute of Israel

Fig. 2  Male:Female ratio of autism spectrum disorders cases at age 8, total population born in Israel, 1992–2003
Fig. 3 Cumulative incidence of Autism spectrum disorders in the total population born in Israel, 1992–2009. Different lines represent different birth cohorts, and are ordered from darkest to brightest. The birth cohort is noted at the end of each line, where the data for that year ends. The age of the children (cohort age) is indicated on the x-axis.
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

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Background: Autism spectrum disorder (ASD) is a developmental disorder with increasing prevalence worldwide, yet has unclear etiology.

Objective: We explored the association between maternal exposure to particulate matter (PM) air pollution and odds of ASD in her child.

Methods: We conducted a nested case–control study of participants in the Nurses’ Health Study II (NHS II), a prospective cohort of 116,430 U.S. female nurses recruited in 1989, followed by biennial mailed questionnaires. Subjects were NHS II participants’ children born 1990–2002 with ASD (n = 245), and children without ASD (n = 1,522) randomly selected using frequency matching for birth years. Diagnosis of ASD was based on maternal report, which was validated against the Autism Diagnostic Interview-Revised in a subset. Monthly averages of PM with diameters ≤ 2.5 μm (PM2.5) and 2.5–10 μm (PM10-2.5) were predicted from a spatiotemporal model for the continental United States and linked to residential addresses.

Results: PM2.5 exposure during pregnancy was associated with increased odds of ASD, with an adjusted odds ratio (OR) for ASD per interquartile range (IQR) higher PM2.5 (4.42 μg/m3) of 1.57 (95% CI: 1.22, 2.03) among women with the same address before and after pregnancy (160 cases, 986 controls). Associations with PM2.5 exposure 9 months before or after the pregnancy were weaker in independent models and null when all three time periods were included, whereas the association with the 9 months of pregnancy remained (OR = 1.63; 95% CI: 1.08, 2.47). The association between ASD and PM2.5 was stronger for exposure during the third trimester (OR = 1.42 per IQR increase in PM2.5; 95% CI: 1.09, 1.86) than during the first two trimesters (ORs = 1.06 and 1.00) when mutually adjusted. There was little association between PM10-2.5 and ASD.

Conclusions: Higher maternal exposure to PM2.5 during pregnancy, particularly the third trimester, was associated with greater odds of a child having ASD.

Citation: Raz R, Roberts AL, Lyall K, Hart JE, Just AC, Laden F, Weisskopf MG. 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. Environ Health Perspect 123:264–270; http://dx.doi.org/10.1289/ehp.1408133

Methods

Participants. The study population included offspring of participants in NHS II, a prospective cohort of 116,430 U.S. female nurses 25–43 years of age when recruited in 1989, followed biennially (Solomon et al. 1997). NHS II participants originally were recruited from 14 states in all regions of the continental United States, but they now reside in all 50 states. The study was approved by the Partners Health Care Institutional Review Board and complied with all applicable U.S. regulations; return of completed questionnaires constituted consent to participate.

In 2005, NHS II participants were asked whether any of their children had been diagnosed with autism, Asperger’s syndrome, or “other autism spectrum,” and 839 women replied affirmatively. In 2007, we initiated a follow-up genotyping study to identify genetic factors associated with ASD.
Figure 1. ORs (95% CIs) for ASD by quartile of PM exposure. ORs are adjusted for child sex, year of birth, month of birth, maternal age at birth, paternal age at birth, and census income. There were 245 cases and 1,522 controls in analyses using pre- and postpregnancy addresses. Prepregnancy address is the last known residential address before conception. Postpregnancy address is the first known residential address after birth. Nonmovers are those participants for whom prepregnancy and postpregnancy addresses were the same [cases = 160 (65%), controls = 986 (65%)]. $p$-Trend, $p$-values from models of exposures as continuous variables. The number of cases (including movers) by quartiles from low to high: 45, 66, 66, 68; controls: 397, 376, 375, 374. PM$_{2.5}$ quartile ranges (µg/m$^3$): 5.24–12.3, 12.4–14.5, 14.6–16.7, 16.7–30.8; PM$_{10-2.5}$ quartile ranges (µg/m$^3$): 1.9–6.7, 6.8–8.9, 9–11.9, 12–49.4.
Figure 2. ORs for ASD with exposure to particulate matter during pregnancy trimesters. ORs are adjusted for child sex, year of birth, month of birth, maternal age at birth, paternal age at birth, and census income. The analyses are limited to nonmovers only (i.e., those for whom prepregnancy and postpregnancy addresses were the same). Cases, $n = 160$, controls $n = 986$. 
Original Contribution

Geographic Patterns of Autism Spectrum Disorder Among Children of Participants in Nurses’ Health Study II

Kate Hoffman, Marc G. Weisskopf, Andrea L. Roberts, Raanan Raz, Jaime E. Hart, Kristen Lyall, Elin M. Hoffman, Francine Laden, and Verónica M. Vieira*

* Correspondence to Dr. Verónica M. Vieira, Program in Public Health, AIRB 2042, 653 East Peltason Drive, University of California, Irvine, CA 92697 (e-mail: vvieira@uci.edu).

Initially submitted July 11, 2016; accepted for publication November 22, 2016.
Figure 2. Geographic distribution of the risk of diagnosis with autism spectrum disorder at birth addresses across the continental United States for children born to women participating in Nurses' Health Study II, 1989–1999. The figure shows lower confidence estimates (A), point estimates (B), and upper confidence estimates (C), adjusted for child’s sex, mother’s age at child’s birth, birth year, and census-tract median income, using optimal span size of 0.70. Black contour bands indicate statistically significant areas of increased or decreased risk.

*Am J Epidemiol.* 2017;186(7):834–842
Original Contribution

Traffic-Related Air Pollution and Autism Spectrum Disorder: A Population-Based Nested Case-Control Study in Israel

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Initially submitted March 31, 2017; accepted for publication August 2, 2017.
Figure 1. Associations between exposure to nitrogen dioxide during pregnancy and during the 9 months after birth and risk of autism spectrum disorder among children born in central coastal Israel during 2005–2009. Odds ratios show the risk of autism spectrum disorder per interquartile-range increment (5.85 ppb) in nitrogen dioxide exposure. A) Results from 2 separate models, each adjusted for year of birth, calendar month of birth, population group, paternal age, and census poverty index. B) Results from 1 model, with mutual adjustment for both exposure periods in addition to all of the covariates listed above. Bars, 95% confidence intervals.

Figure 2. Results from a distributed-lag model representing polynomial time-dependent associations between weekly nitrogen dioxide exposure and risk of autism spectrum disorder among children born in central coastal Israel during 2005–2009. The black line represents the time-varying function estimating risk of autism spectrum disorder with weekly exposures during 38 weeks of pregnancy (left) and the first 38 weeks of life (right), and the gray area around it represents its 95% confidence interval. These results are from a nonlinear distributed-lag model with 7 degrees of freedom. A linear association was assumed between the exposure and the outcome at each time point. Results were adjusted for year of birth, calendar month of birth, population group, paternal age, and census poverty index.
Commentary

Live-Birth Bias and Observed Associations Between Air Pollution and Autism

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Initially submitted April 10, 2018; accepted for publication August 1, 2018.
A shared mechanism leading to depletion of susceptibles

Directed Acyclic Graph (DAG)

$U$
(e.g. some genetic sensitivity to oxidative stress)

Prenatal biological process (e.g. oxidative stress) at $t_1$

Traffic-related air pollution

Prenatal biological process (e.g. oxidative stress) at $t_2$

Fetal Loss

ASD
How plausible are the assumptions?  
The role of oxidative stress

Relative Risk = $\frac{\frac{3}{320}}{\frac{4}{360}} = 0.84$
Scenario 2: Conditioning on a collider

- How plausible are the assumptions?
- What can U be?
פרויקטים נוספים
בעבודה בהקשר ל- ASD

• משקל לידה ושובוע הרינו שלילדה ומנבאים ל- ASD, לפי קבוצת משקל לידה והשורשים של ההורים.

• שעורים הער.testing מערביים בישראל, לפי קבוצת אוכלוסייה, הקישר לחקר החלקกะ של ההורים

• התפלגות מרחבית של ASD בישראל

• שינוי בהכנסות ההורים לאחר אבחון ASD

• השפעה של חשיפה לסטרס במהלך מלחמת לבנון השנייה על היארעות אוטיזם

• זיהום אוויר ואוטיזם – חומר חלקיקי

(PM) ה küיקום

• השפעה על היארעות אוטיסם

• מהו אוטיסם ואוטיסם – חומת ה-

(ויקי PM)
תודה רבה