APPENDICES AVAILABLE ON THE HEI WEBSITE

Special Report 23
Systematic Review and Meta-analysis of Selected Health Effects of Long-Term Exposure to Traffic-Related Air Pollution

HEI Panel on the Health Effects of Long-Term Exposure to Traffic-Related Air Pollution

Chapter 12: Traffic-Related Air Pollution and Neurodevelopmental Outcomes

These Appendices were reviewed solely for spelling, grammar, and cross-references to the main text. They have not been formatted or fully edited by HEI. This document was part of the HEI Panel’s review process.

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Appendices Chapter 12: Additional Tables and Figure
Traffic-Related Air Pollution and Neurodevelopmental Outcomes

Appendix 12A  
Cognitive Function

Appendix 12B  
Attention Deficit Hyperactivity Disorder (ADHD) Diagnosis and Related Behaviors

Appendix 12C  
Autism Spectrum Disorder (ASD) Diagnosis and Related Behaviors

Appendix 12D  
References for Studies Included in the Literature Review of Neurodevelopmental Outcomes
## Appendix 12A Cognitive function

Table 12A-1. Key study characteristics of studies included in the literature review for cognitive function in children – pollutants and indirect traffic measures (N=30).

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name</th>
<th>Location</th>
<th>Study Design</th>
<th>Study period</th>
<th>Sample size</th>
<th>Exposure Window</th>
<th>Age at outcome (yrs)</th>
<th>Exposure Assessment</th>
<th>Pollutant(s)</th>
<th>Neuropsychological test(s)</th>
<th>Cognitive Domain(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basagaña 2016</td>
<td>BREATHE</td>
<td>Barcelona, Spain</td>
<td>Cohort</td>
<td>2012–2013</td>
<td>2,618</td>
<td>Average in year of assessment</td>
<td>Mean 8.5</td>
<td>Traffic-specific source apportionment</td>
<td>PM_{2.5} road dust, PM_{1.5} traffic</td>
<td>Attentional Network Task, n-back test</td>
<td>Attention (1-year change), Working memory (1-year change)</td>
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<tr>
<td>Chiu 2013</td>
<td>MISSEB</td>
<td>Boston, Massachusetts, United States</td>
<td>Cohort</td>
<td>1986–1998</td>
<td>174</td>
<td>Birth to assessment</td>
<td>9 to 11</td>
<td>LUR</td>
<td>BC</td>
<td>Conners Continuous Performance Test</td>
<td>Attention, response inhibition</td>
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<tr>
<td>Clark 2012</td>
<td>RANCH UK</td>
<td>London, United Kingdom</td>
<td>Cross-sectional</td>
<td>2002</td>
<td>719</td>
<td>Annual average at assessment</td>
<td>9 to 10</td>
<td>LUR</td>
<td>NO_{2}</td>
<td>Suffolk Reading Scale 2, Child Memory Scale, The Search and Memory Task</td>
<td>Reading comprehension, working memory, memory</td>
</tr>
<tr>
<td>Cowell 2015</td>
<td>ACCESS</td>
<td>Boston, Massachusetts, United States</td>
<td>Cohort</td>
<td>2002–2015</td>
<td>258</td>
<td>Entire pregnancy</td>
<td>6</td>
<td>LUR</td>
<td>BC</td>
<td>Wide Range Assessment of Memory and Learning</td>
<td>Memory</td>
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<tr>
<td>Forns 2017</td>
<td>BREATHE</td>
<td>Barcelona, Spain</td>
<td>Cohort</td>
<td>2012–2015</td>
<td>1,439</td>
<td>8.5</td>
<td>8.5 and 11.4</td>
<td>Surface monitoring</td>
<td>PM_{2.5}, traffic, EC, NO_{2}, PNC</td>
<td>n-back test</td>
<td>Working memory (3.5-year change)</td>
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<tr>
<td>Freire 2010</td>
<td>INMA</td>
<td>Granada, Spain</td>
<td>Cross-sectional</td>
<td>2000–2006</td>
<td>210</td>
<td>Average in year of assessment</td>
<td>4</td>
<td>LUR</td>
<td>NO_{2}</td>
<td>McCarthy Scales of Children’s Abilities</td>
<td>General, verbal, perceptual-performance, and quantitative cognition; memory</td>
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<tr>
<td>Fuertes 2016</td>
<td>GINIplus, LISAplus</td>
<td>Multiple cities, Germany</td>
<td>Cohort</td>
<td>1995–2013</td>
<td>4,745</td>
<td>Annual average at birth, 10 and 15</td>
<td>10 and 15</td>
<td>LUR</td>
<td>PM_{2.5}, abs, NO_{2}, PM_{10} mass, PM_{2.5} mass</td>
<td>Parent and self-reported questionnaire</td>
<td>Dyslexia condition or symptoms</td>
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<td>Gonzalez-Casanova 2018</td>
<td>POSGRAD</td>
<td>Mexico City, Mexico</td>
<td>Cohort</td>
<td>2005–2014</td>
<td>718</td>
<td>Entire pregnancy</td>
<td>1, 1.5, 5, and 7</td>
<td>LUR</td>
<td>Benzene, NO_{2}, NO_{x}</td>
<td>Composite of Bayley Scales of Infant Development II, McCarthy Scales of Children’s Abilities, Wechsler Abbreviated Scale of Intelligence</td>
<td>General cognitive development (over 6 years)</td>
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<td>Guxens 2012</td>
<td>INMA</td>
<td>Multiple cities, Spain</td>
<td>Cohort</td>
<td>2002–2010</td>
<td>1,854</td>
<td>Entire pregnancy</td>
<td>14 months</td>
<td>LUR</td>
<td>Benzene, NO_{2}</td>
<td>Bayley Scales of Infant Development</td>
<td>Infant cognition</td>
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<td>Guxens 2014</td>
<td>ESCAPE</td>
<td>Multiple cities, multiple countries</td>
<td>Cohort</td>
<td>2000–2011</td>
<td>9,482</td>
<td>Entire pregnancy</td>
<td>1 to 6</td>
<td>Distance or density, LUR</td>
<td>PM_{2.5}, abs, NO, NO_{x}, PM_{10} mass, PM_{2.5} mass, PM_{coarse} mass, traffic density</td>
<td>Composite of Bayley Scales of Infant Development I, II &amp; III, McArthur Communicative Development Inventory, Denver Developmental Screening Test II, McCarthy Scales of Children’s Abilities</td>
<td>General cognition, verbal cognition</td>
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<tr>
<td>Reference</td>
<td>Study Name</td>
<td>Location</td>
<td>Study Design</td>
<td>Study period</td>
<td>Sample size</td>
<td>Exposure Window</td>
<td>Age at outcome (yrs)</td>
<td>Exposure Assessment</td>
<td>Pollutant(s)</td>
<td>Neuropsychological test(s)</td>
<td>Cognitive Domain(s)</td>
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<td>Generation R</td>
<td>Rotterdam, The Netherlands</td>
<td>Cohort</td>
<td>2002–2012</td>
<td>783</td>
<td>Entire pregnancy</td>
<td>6 to 10</td>
<td>LUR</td>
<td>PM$<em>{2.5}$ abs, PM$</em>{2.5}$ mass, PM$_{10}$ mass</td>
<td>Developmental Neuropsychological Assessment</td>
<td>Attention, response inhibition, memory</td>
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<td>Ha 2019</td>
<td>Upstate KIDS</td>
<td>Multiple cities, United States</td>
<td>Cohort</td>
<td>2008–2013</td>
<td>5,825</td>
<td>Entire pregnancy, Birth to 3</td>
<td>8 months, 1, 1.5, 2, 2.5, and 3</td>
<td>Distance or density</td>
<td>Traffic distance</td>
<td>Ages and Stages Questionnaire</td>
<td>Communication, personal-social functioning, and problem-solving ability</td>
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<td>Project Viva</td>
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<td>Cohort</td>
<td>1999–20120</td>
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<td>Third trimester, birth to 6, year before assessment</td>
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<td>EC, PM$_{2.5}$ traffic density, traffic distance,</td>
<td>Kaufman Brief Intelligence Test, Wide Range Assessment of Memory and Learning</td>
<td>Verbal cognition, nonverbal cognition, memory</td>
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<td>1,212</td>
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<td>BC, PM$_{10}$, traffic density, traffic distance,</td>
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<td>Quito Child Health</td>
<td>Quito, Ecuador</td>
<td>Cross-sectional</td>
<td>2016</td>
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<td>8 to 14</td>
<td>Distance or density</td>
<td>Traffic distance</td>
<td>Behavioral Assessment and Research System</td>
<td>Attention, working memory, memory</td>
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<td>Kicinski 2015</td>
<td>Flemish Environmental Health Cohort</td>
<td>Flanders, Belgium</td>
<td>Cross-sectional</td>
<td>2008–2011</td>
<td>606</td>
<td>Average at assessment</td>
<td>15</td>
<td>Distance or density</td>
<td>Traffic density</td>
<td>Neurobehavioral Evaluation System -3</td>
<td>Attention, memory</td>
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<td>INMA Gipuzkoa</td>
<td>Gipuzkoa, Spain</td>
<td>Cohort</td>
<td>2006–2010</td>
<td>438</td>
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<td>15 months</td>
<td>LUR</td>
<td>Benzene, NO$_x$</td>
<td>Bayley Scales of Infant Development</td>
<td>Infant cognition</td>
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<td>Multiple cities, Spain</td>
<td>Cohort</td>
<td>2004–2014</td>
<td>1,119</td>
<td>Entire pregnancy</td>
<td>4 to 6</td>
<td>LUR</td>
<td>NO$<em>x$, PM$</em>{2.5}$ mass</td>
<td>McCarthy Scales of Children’s Abilities</td>
<td>General, verbal, perceptual-performance, and quantitative cognition, memory</td>
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<td>Loftus 2019</td>
<td>CANDLE</td>
<td>Shelby County, Tennessee, United States</td>
<td>Cohort</td>
<td>2006–2017</td>
<td>905</td>
<td>Entire pregnancy</td>
<td>4 to 6</td>
<td>Distance or density, LUR</td>
<td>NO$<em>x$, PM$</em>{10}$ mass, traffic distance</td>
<td>Stanford Binet Intelligence Scales, edition S</td>
<td>General, verbal and quantitative cognition</td>
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<td>Lubczyńska 2017</td>
<td>ESCAPE</td>
<td>Multiple cities, multiple countries</td>
<td>Cohort</td>
<td>2000–2011</td>
<td>7,426</td>
<td>Annual average at birth</td>
<td>1 to 9</td>
<td>LUR, traffic-specific source apportionment</td>
<td>PM$<em>{2.5}$, Cu, PM$</em>{2.5}$ Fe, PM$_{2.5}$ Zn, traffic PCA component</td>
<td>Composite of multiple tests</td>
<td>General, verbal and nonverbal cognition</td>
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<td>Mortamais 2017</td>
<td>BREATHE</td>
<td>Barcelona, Spain</td>
<td>Cohort</td>
<td>2012–2014</td>
<td>242</td>
<td>Average in year before assessment</td>
<td>8 to 12 (mean 9)</td>
<td>Surface monitoring</td>
<td>Benez(a)pyrene</td>
<td>Attentional Network Test</td>
<td>Attention (1-year change)</td>
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<tr>
<td>Porta 2016</td>
<td>GASPII</td>
<td>Rome, Italy</td>
<td>Cohort</td>
<td>2003–2011</td>
<td>474</td>
<td>Annual average at birth</td>
<td>7</td>
<td>Distance or density, LUR</td>
<td>NO$_x$, traffic density</td>
<td>Wechsler Intelligence Scale for Children-III</td>
<td>General, verbal, and perceptual-performance cognition</td>
</tr>
<tr>
<td>Reference</td>
<td>Study Name</td>
<td>Location</td>
<td>Study Design</td>
<td>Study period</td>
<td>Sample size</td>
<td>Study period</td>
<td>Sample size</td>
<td>Exposure Window</td>
<td>Age at outcome (yrs)</td>
<td>Exposure Assessment</td>
<td>Pollutant(s)</td>
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<td>Pujol 2016</td>
<td>BREATHE</td>
<td>Barcelona, Spain</td>
<td>Cohort</td>
<td>2012–2013</td>
<td>2,827</td>
<td>Annual average at assessment</td>
<td>8 to 12 (mean 9)</td>
<td>Surface monitoring</td>
<td>PM$_{2.5}$, Cu</td>
<td>Attentional Network Test</td>
<td>Attention (1-year change)</td>
</tr>
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<td>Rivas 2019</td>
<td>BREATHE</td>
<td>Barcelona, Spain</td>
<td>Cohort</td>
<td>2012–2013</td>
<td>2,221</td>
<td>Entire pregnancy, birth to 1, entire pregnancy to 7</td>
<td>7 to 10 (mean 8.5)</td>
<td>LUR</td>
<td>PM$_{2.5}$ mass</td>
<td>Attentional Network Test, n-back test</td>
<td>Attention, working memory (1-year change)</td>
</tr>
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<td>Saenen 2016</td>
<td>COGNAC</td>
<td>Flanders, Belgium</td>
<td>Cohort</td>
<td>2011–2014</td>
<td>310</td>
<td>Year before assessment</td>
<td>10</td>
<td>Distance or density, LUR</td>
<td>BC, PM$<em>{10}$ mass, PM$</em>{2.5}$ mass, traffic density</td>
<td>Stroop Test, Neurobehavioral Evaluation System: Continuous Performance Test, Digit Span Forward and Backward Tests, Digit-Symbol Test, and Pattern Comparison Test</td>
<td>Executive function, attention, working memory, memory</td>
</tr>
<tr>
<td>Sentis 2017</td>
<td>INMA</td>
<td>Multiple cities, Spain</td>
<td>Cohort</td>
<td>2003–2013</td>
<td>1,298</td>
<td>Entire pregnancy, birth to assessment</td>
<td>4 to 5</td>
<td>LUR</td>
<td>NO$_x$</td>
<td>Kiddie-Conners Continuous Performance Test</td>
<td>Attention, response inhibition</td>
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<td>Suglia 2008</td>
<td>MISSEB</td>
<td>Boston, Massachusetts, United States</td>
<td>Cohort</td>
<td>1986–2001</td>
<td>218</td>
<td>Birth to assessment</td>
<td>8 to 11, mean 9.7</td>
<td>LUR</td>
<td>BC</td>
<td>Kaufman Brief Intelligence Test, Wide Range Assessment of Memory and Learning</td>
<td>General, verbal and nonverbal cognition, memory</td>
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<td>Sunyer 2015</td>
<td>BREATHE</td>
<td>Barcelona, Spain</td>
<td>Cohort</td>
<td>2012–2013</td>
<td>2,715</td>
<td>Annual average at assessment</td>
<td>9</td>
<td>Distance or density, surface monitoring</td>
<td>EC, NO$_x$, PNC 10–700 nm, traffic density</td>
<td>Attentional Network Test, n-back test</td>
<td>Attention (1-year change), working memory (1-year change)</td>
</tr>
<tr>
<td>van Kempen 2012</td>
<td>RANCH</td>
<td>Netherlands</td>
<td>Cross-sectional</td>
<td>2002</td>
<td>485</td>
<td>Annual average at assessment</td>
<td>10</td>
<td>LUR</td>
<td>NO$_x$</td>
<td>Neurobehavioral Evaluation System: Simple Reaction Time Test, Switching Attention Test, Symbol Digit Substitution Test, Digit Memory Span Test</td>
<td>Attention, working memory, memory</td>
</tr>
<tr>
<td>Wang 2017</td>
<td>RFAB</td>
<td>Los Angeles, California, United States</td>
<td>Cohort</td>
<td>1990–2015</td>
<td>1,042</td>
<td>Average in year before assessment</td>
<td>9 to 11, 18 to 20</td>
<td>Dispersion / CTM</td>
<td>NO$_x$</td>
<td>Wechsler Abbreviated Scale of Intelligence</td>
<td>General, verbal, and perceptual-performance cognition</td>
</tr>
</tbody>
</table>

1 For studies using a cohort recruited at prenatal/birth, where prenatal/early covariates were included in analysis, study period starts at prenatal/birth recruitment and ends at last year of child’s assessment. For cohort studies of school-age children (e.g. BREATHE), period starts at recruitment and ends when cognitive assessment ends. For case control studies, period is period of case identification, even if perinatal/early life covariates are included. For cross-sectional studies, period is period of recruitment and assessment.

2 Sex was both in all studies.

3 Composite of Bayley Scales of Infant Development I and II, Denver Developmental Screening Test II, Hamburg Wechsler Intelligenztest für Kinder - IV, McArthur Communicative Development Inventory, Minnesota Infant Development Inventory, McCarthy Scales of Children’s Abilities; De Snijders-Oomen Niet-verbale Intelligenietest-Revisie, Wechsler Intelligence Scale for Children.
### Table 12A-2. Associations of PM$_{2.5}$ mass with cognitive function.

<table>
<thead>
<tr>
<th>Reference/Study Name</th>
<th>Location</th>
<th>Study period</th>
<th>Sample size</th>
<th>Mean or median exposure$^a$</th>
<th>Cognitive Domain(s)</th>
<th>Neuropsychologic al test(s)</th>
<th>Exposure Window</th>
<th>Age at outcome (years)</th>
<th>Outcome (direction$^b$)</th>
<th>Effect measure</th>
<th>Effect Estimate (95% CI)$^c$</th>
<th>Increment</th>
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<tr>
<td>Fuertes 2016 GINIplus, LISAplus</td>
<td>Multiple cities, Germany</td>
<td>1995–2013</td>
<td>4,745</td>
<td>13.3 13.2</td>
<td>Dyslexia</td>
<td>Parent questionnaire</td>
<td>Annual average at birth</td>
<td>10 and 15</td>
<td>Dyslexia (+)</td>
<td>Odds ratio</td>
<td>1.01 (0.82 to 1.25)</td>
<td>1.08 (0.95 to 1.23)</td>
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<tr>
<td>Guxens 2014 ESCAPE</td>
<td>Multiple cities, multiple countries</td>
<td>2000–2011</td>
<td>9,482</td>
<td>13.4 to 22.3</td>
<td>General cognition</td>
<td>Composite$^b$</td>
<td>Entire pregnancy</td>
<td>1 to 6</td>
<td>General cognition (-)</td>
<td>Incidence rate ratio</td>
<td>0.09 (–2.95 to 3.12)</td>
<td>–0.64 (–1/64 to 0.36)</td>
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<tr>
<td>Guxens 2018 Generation R</td>
<td>Rotterdam, The Netherlands</td>
<td>2002–2012</td>
<td>783</td>
<td>20.2</td>
<td>Attention</td>
<td>Developmental Neuropsychologic al Assessment</td>
<td>Entire pregnancy</td>
<td>6 to 10</td>
<td>Auditory attention: correct responses (-)</td>
<td>Incidence rate ratio</td>
<td>1.00 (0.99 to 1.01)</td>
<td>0.98 (0.92 to 1.03)</td>
</tr>
</tbody>
</table>

$^a$ Mean or median exposure to PM$_{2.5}$.

$^b$ Cognitive domain(s) and neuropsychologic al test(s).

$^c$ Effect estimates and 95% confidence intervals (CI).
### Chapter 12 Appendices

<table>
<thead>
<tr>
<th>Harris</th>
<th>Project Viva</th>
<th>Boston, Massachusetts, United States</th>
<th>1999–2010</th>
<th>960</th>
<th>12.3</th>
<th>Verbal cognition</th>
<th>Kaufman Brief Intelligence Test</th>
<th>Third trimester</th>
<th>6 to 10 (mean 8.0)</th>
<th>Verbal IQ (–)</th>
<th>Mean difference</th>
<th>–0.1 (–1.3 to 1.2)</th>
<th>3.8 µg/m³</th>
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<td>Non-verbal cognition</td>
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<td></td>
<td>Non-verbal IQ (–)</td>
<td>–0.2 (–1.8 to 1.5)</td>
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<td>Verbal cognition</td>
<td>Birth to 6 years</td>
<td>Verbal IQ (–)</td>
<td>0.7 (–0.4 to 1.7)</td>
<td>2.1 µg/m³</td>
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<td>Non-verbal cognition</td>
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<td></td>
<td>Non-verbal IQ (–)</td>
<td>1.1 (–0.2 to 2.5)</td>
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<td>Verbal cognition</td>
<td>Year before assessment</td>
<td>Verbal IQ (–)</td>
<td>1.1 (0.0 to 2.2)</td>
<td>2.5 µg/m³</td>
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<td>Non-verbal cognition</td>
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<td></td>
<td></td>
<td>Non-verbal IQ (–)</td>
<td>0.7 (–0.8 to 2.1)</td>
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<tr>
<td></td>
<td>Memory</td>
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<td></td>
<td>Memory</td>
<td>Third trimester</td>
<td>Design Memory (–)</td>
<td>–0.1 (–0.3 to 0.2)</td>
<td>3.8 µg/m³</td>
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<td></td>
<td>Wide Range Assessment of Memory and Learning</td>
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<td></td>
<td>Picture Memory (–)</td>
<td>0.1 (–0.2 to 0.4)</td>
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<td></td>
<td>Birth to 6 years</td>
<td>Design Memory (–)</td>
<td>–0.2 (–0.4 to 0.1)</td>
<td>2.1 µg/m³</td>
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<td></td>
<td>Picture Memory (–)</td>
<td>0.1 (–0.1 to 0.4)</td>
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<td></td>
<td>Year before assessment</td>
<td>Design Memory (–)</td>
<td>–0.1 (–0.4 to 0.1)</td>
<td>2.5 µg/m³</td>
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<td></td>
<td>Picture Memory (–)</td>
<td>0.0 (–0.2 to 0.3)</td>
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<td></td>
<td></td>
<td>Executive function</td>
<td>Third trimester</td>
<td>7.7</td>
<td>Global Executive Function (+)</td>
<td>–1.2 to 0.9</td>
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<td></td>
<td></td>
<td>Behavioral Regulation Index (+)</td>
<td>0.2 (–0.8 to 1.3)</td>
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<td></td>
<td>Metacognition Index (+)</td>
<td>–0.3 (–1.4 to 0.8)</td>
<td></td>
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<td></td>
<td></td>
<td>Birth to 3</td>
<td>Global Executive Function (+)</td>
<td>0.3 (–0.6 to 1.2)</td>
<td>2.2 µg/m³</td>
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</tbody>
</table>

**Note:** The table above presents data on cognitive and executive function measures across different time points and contexts, including mean differences in IQ and executive function scores, with a focus on the impact of environmental factors such as lead exposure. The data is sourced from the Project Viva study conducted in Boston, Massachusetts, United States, from 1999–2010.
<table>
<thead>
<tr>
<th>Behavior problems</th>
<th>Third trimester</th>
<th>Total difficulties (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 6</td>
<td>Behavioral Regulation Index (+) 0.4 (–0.5 to 1.3)</td>
<td>2.1 µg/m³</td>
</tr>
<tr>
<td></td>
<td>Metacognition Index (+) 0.2 (–0.7 to 1.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Global Executive Function (+) 0.5 (–0.5 to 1.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Behavioral Regulation Index (+) 0.7 (–0.2 to 1.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metacognition Index (+) 0.3 (–0.7 to 1.3)</td>
<td></td>
</tr>
<tr>
<td>Average in year before assessment</td>
<td>Global Executive Function (+) 0.2 (–0.8 to 1.1)</td>
<td>2.5 µg/m³</td>
</tr>
<tr>
<td></td>
<td>Behavioral Regulation Index (+) 0.1 (–0.9 to 1.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metacognition Index (+) 0.1 (–0.8 to 1.1)</td>
<td></td>
</tr>
<tr>
<td>Behavior problems</td>
<td>Strengths and Difficulties Questionnaire (teacher report)</td>
<td></td>
</tr>
<tr>
<td>Third trimester</td>
<td>Total difficulties (+) 0.3 (–0.3 to 0.9)</td>
<td>3.8 µg/m³</td>
</tr>
<tr>
<td>Birth to 3</td>
<td>Behavioral Regulation Index (+) 0.1 (–0.4 to 0.6)</td>
<td>2.2 µg/m³</td>
</tr>
<tr>
<td>Birth to 6</td>
<td>Metacognition Index (+) 0.1 (–0.4 to 0.6)</td>
<td>2.1 µg/m³</td>
</tr>
<tr>
<td>Average in year before assessment</td>
<td>Global Executive Function (+) 0.1 (–0.5 to 0.6)</td>
<td>2.5 µg/m³</td>
</tr>
<tr>
<td>Behavior problems</td>
<td>Strengths and Difficulties Questionnaire (parent report)</td>
<td></td>
</tr>
<tr>
<td>Third trimester</td>
<td>Total difficulties (+) –0.3 (–0.7 to 0.1)</td>
<td>3.8 µg/m³</td>
</tr>
<tr>
<td>Birth to 3</td>
<td>Behavioral Regulation Index (+) 0.0 (–0.4 to 0.3)</td>
<td>2.2 µg/m³</td>
</tr>
<tr>
<td>Birth to 6</td>
<td>Metacognition Index (+) –0.1 (–0.5 to 0.3)</td>
<td>2.1 µg/m³</td>
</tr>
<tr>
<td>Study</td>
<td>Location</td>
<td>Methods</td>
</tr>
<tr>
<td>-------</td>
<td>----------</td>
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</tr>
<tr>
<td>Lertxundi 2019</td>
<td>INMA Multiple cities, Spain</td>
<td>2004-2014</td>
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<tr>
<td>Rivas 2019</td>
<td>BREATHE Barcelona, Spain</td>
<td>2012-2013</td>
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<tr>
<td>Saenen 2016</td>
<td>COGNAC Flanders, Belgium</td>
<td>2011-2014</td>
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</tbody>
</table>
### Working Memory

<table>
<thead>
<tr>
<th>Test</th>
<th>Digit Span Test</th>
<th>Digit Span Backward (+)</th>
<th>0.06 (–0.07 to 0.18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NES3: Pattern Comparison Test</td>
<td>Pattern comparison latency (+)</td>
<td>0.05 (–0.09 to 0.19)</td>
<td></td>
</tr>
<tr>
<td>NES3: Digit Symbol Test</td>
<td>Digit symbol latency (+)</td>
<td>2.1 (–0.65 to 4.91)</td>
<td></td>
</tr>
<tr>
<td>NES3: Digit Span Test</td>
<td>Digit span forward (+)</td>
<td>–0.03 (–0.15 to 0.10)</td>
<td></td>
</tr>
</tbody>
</table>

### Memory

| Test                              |  |
|-----------------------------------|  |
| NES3: Digit Span Test             |  |
| NES3: Pattern Comparison Test     |  |
| NES3: Digit Symbol Test           |  |

### Notes

1. Study design is cohort for all studies.
2. Unit in the increment column. Exposure assessment in all studies is LUR.
3. A negative direction (−) means that a lower score indicates poorer cognitive function or greater cognitive difficulty; a positive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive difficulty. Ratio measures (RRs, ORs, IRRs) >1.0 indicate higher risk for the outcome.
4. Dark orange = evidence of association with poorer cognition; Light orange = suggestive evidence of association with poorer cognition. Dark blue = evidence of association with better cognition; Light blue = suggestive evidence of association with better cognition.
6. NES3 is Neurobehavioral Evaluation System 3.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name¹</th>
<th>Location</th>
<th>Study period</th>
<th>Sample size</th>
<th>Pollutant</th>
<th>Mean or median exposure ²</th>
<th>Cognitive Domain(s)</th>
<th>Neuropsychological test(s)</th>
<th>Exposure Window</th>
<th>Age at outcome (yrs)</th>
<th>Outcome (direction)³</th>
<th>Effect measure</th>
<th>Effect Estimate (95% CI)⁴</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fuertes 2016</td>
<td>GINIplus, LiSAplus</td>
<td>Multiple cities, Germany</td>
<td>1995–2013</td>
<td>4,745</td>
<td>PM₁₀ mass</td>
<td>20.4 South, 25.2 North</td>
<td>Dyslexia</td>
<td>Parent questionnaire</td>
<td>Annual average at birth</td>
<td>10 and 15</td>
<td>Dyslexia (+)</td>
<td>Odds ratio</td>
<td>1.12 (0.98 to 1.27)</td>
<td>3.0 µg/m³ South, 1.5 µg/m³ North</td>
</tr>
<tr>
<td>Guxens 2014</td>
<td>ESCAPE</td>
<td>Multiple cities, multiple countries</td>
<td>2000–2011</td>
<td>9,482</td>
<td>PM₁₀ mass</td>
<td>33 to 42</td>
<td>General cognition</td>
<td>Composite³</td>
<td>Entire pregnancy</td>
<td>1 to 6</td>
<td>General cognition (–)</td>
<td>Mean difference</td>
<td>0.75 (–1.72 to 3.21)</td>
<td>10 µg/m³</td>
</tr>
<tr>
<td>Guxens 2018</td>
<td>Generation R</td>
<td>Rotterdam, The Netherlands</td>
<td>2002–2012</td>
<td>783</td>
<td>PM粗粒 mass</td>
<td>11.8</td>
<td>Attention</td>
<td>Developmental Neuropsychological Assessment</td>
<td>Entire pregnancy</td>
<td>6 to 10</td>
<td>Auditory attention task: omission errors (+)</td>
<td>Incidence rate ratio</td>
<td>0.98 (0.92 to 1.05)</td>
<td>5 µg/m³</td>
</tr>
<tr>
<td>Reference</td>
<td>Study Name¹</td>
<td>Location</td>
<td>Study period</td>
<td>Sample size</td>
<td>Pollutant</td>
<td>Mean or median exposure²</td>
<td>Cognitive Domain(s)</td>
<td>Neuropsychological test(s)</td>
<td>Exposure Window</td>
<td>Age at outcome (yrs)</td>
<td>Outcome (direction³)</td>
<td>Effect measure</td>
<td>Effect Estimate (95% CI)⁴</td>
<td>Increment</td>
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<tr>
<td>Loftus 2019</td>
<td>CANDLE</td>
<td>Shelby County, Tennessee, United States</td>
<td>2006–2017</td>
<td>905</td>
<td>PM₁₀ mass</td>
<td>20.88 General cognition</td>
<td>Stanford Binet Intelligence Scales, edition 5</td>
<td>Entire pregnancy</td>
<td>4 to 6</td>
<td>Full Scale IQ (–)</td>
<td>Mean difference</td>
<td>–2.44 (–4.80 to –0.09)</td>
<td>5 µg/m³</td>
<td></td>
</tr>
<tr>
<td>Saenen 2016</td>
<td>COGNAC</td>
<td>Flanders, Belgium</td>
<td>2011–2014</td>
<td>310</td>
<td>PM₁₀ mass</td>
<td>21.3 Executive function</td>
<td>Stroop Test</td>
<td>Average in year before assessment</td>
<td>10</td>
<td>Selective attention (+)</td>
<td>Mean difference</td>
<td>76.5 (29.3 to 123.6)</td>
<td>1.61 µg/m³</td>
<td></td>
</tr>
</tbody>
</table>

¹Study design is cohort for all studies
²Unit in the increment column. Exposure assessment in all studies is LUR.
³A negative direction (–) means that a lower score indicates poorer cognitive function or greater cognitive difficulty; a positive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive difficulty. Ratio measures (RRs, ORs, IRRs) >1.0 indicate higher risk for the outcome.
⁴Dark orange=evidence of association with poorer cognition; Light orange=suggestive evidence of association with poorer cognition; Dark blue=evidence of association with better cognition; Light blue=suggestive evidence of association with better cognition.
⁵Composite of Bayley Scales of Infant Development I, II & III, McArthur Communicative Development Inventory, Denver Developmental Screening Test II, McCarthy Scales of Children’s Abilities.
⁶NES3 is Neurobehavioral Evaluation System 3.
Table 12A-4. Associations of PM components with cognitive function.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name¹</th>
<th>Location</th>
<th>Study period</th>
<th>Sample size</th>
<th>Pollutant</th>
<th>Mean or median exposure²</th>
<th>Cognitive Domain(s)</th>
<th>Neuropsychological test(s)</th>
<th>Exposure Window</th>
<th>Age at outcome (years)</th>
<th>Outcome (direction⁴)</th>
<th>Effect measure</th>
<th>Effect Estimate (95% CI)⁴</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basagaña 2016</td>
<td>BREATH</td>
<td>Barcelona, Spain</td>
<td>2012–2013</td>
<td>2,618</td>
<td>PM₂.₅ dust</td>
<td>1.1</td>
<td>Attention</td>
<td>Attentional Network Task</td>
<td>n-back test</td>
<td>Annual average at assessment</td>
<td>Hit rate standard error (1-year change) (+) 2-back detectability (1-year change) (–) 3-back detectability (1-year change) (–)</td>
<td>Mean difference</td>
<td>2.0 (–0.6 to 4.6)</td>
<td>1.2 µg/m³</td>
</tr>
<tr>
<td>PM₂.₅ traffic</td>
<td>5.2</td>
<td>Attention</td>
<td>Attentional Network Task</td>
<td>n-back test</td>
<td>Hit reaction standard error (1-year change) (+) 2-back detectability (1-year change) (–) 3-back detectability (1-year change) (–)</td>
<td>Mean difference</td>
<td>3.5 (0.9 to 6.1)</td>
<td>2.7 µg/m³</td>
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</tr>
<tr>
<td>Forns 2017</td>
<td>BREATH</td>
<td>Barcelona, Spain</td>
<td>2012–2015</td>
<td>1,439</td>
<td>PM₂.₅ traffic</td>
<td>Working memory</td>
<td>n-back test</td>
<td>Annual average at first assessment</td>
<td>8.5 and 11.4</td>
<td>3-back detectability (3.5 year change) (–)</td>
<td>Mean difference</td>
<td>–2.30 (–3.65 to 0.96)</td>
<td>2.7 µg/m³</td>
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<tr>
<td>Lubczyńska 2017</td>
<td>ESCAPE</td>
<td>Multiple cities, multiple countries</td>
<td>2000–2011</td>
<td>7,426</td>
<td>PM₂.₅ Cu</td>
<td>4.95–12.85</td>
<td>General cognition</td>
<td>Multiple tests³</td>
<td>Annual average at birth</td>
<td>1 to 9</td>
<td>General cognitive function (–) Verbal intelligence (–) Non-verbal intelligence (–)</td>
<td>Mean difference</td>
<td>–1.68 (–5.08 to 1.72)</td>
<td>5 ng/m³</td>
</tr>
<tr>
<td>PM₂.₅ Fe</td>
<td>127–251</td>
<td>General cognition</td>
<td>Verbal cognition Nonverbal cognition</td>
<td></td>
<td>General cognitive function (–) Verbal intelligence (–) Non-verbal intelligence (–)</td>
<td></td>
<td>Mean difference</td>
<td>–1.26 (–3.21 to 0.70)</td>
<td>100 ng/m³</td>
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<tr>
<td>PM₂.₅ Zn</td>
<td>19.42–37.53</td>
<td>General cognition</td>
<td>Verbal cognition Nonverbal cognition</td>
<td></td>
<td>General cognitive function (–) Verbal intelligence (–) Non-verbal intelligence (–)</td>
<td></td>
<td>Mean difference</td>
<td>–0.66 (–1.87 to 0.55)</td>
<td>10 ng/m³</td>
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</table>
## Chapter 12 Appendices

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name</th>
<th>Location</th>
<th>Study period</th>
<th>Sample size</th>
<th>Pollutant</th>
<th>Mean or median exposure</th>
<th>Cognitive Domain(s)</th>
<th>Neuropsychological test(s)</th>
<th>Exposure Window</th>
<th>Age at outcome (years)</th>
<th>Outcome (direction)</th>
<th>Effect measure</th>
<th>Effect Estimate (95% CI)</th>
<th>Increment</th>
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</thead>
<tbody>
<tr>
<td>Pujol 2016 BREATH</td>
<td>Barcelona, Spain</td>
<td>2012–2013</td>
<td>2,827 PM$_{2.5}$ Cu</td>
<td>8.7</td>
<td>Attention</td>
<td>Attentional Network Test</td>
<td>Annual average at assessment</td>
<td>8 to 12 (mean 9)</td>
<td>Hit reaction time (1-year change) (+)</td>
<td>Mean difference</td>
<td>4.7 (1.8 to 7.5)</td>
<td>3.4 (1.4 to 5.5)</td>
<td>1 ng/m$^3$</td>
<td></td>
</tr>
</tbody>
</table>

1. Study design is cohort for all studies
2. Unit in the increment column. Exposure assessment is LUR except for Basagaña, 2016 and Lubczyńska, 2017 (traffic-specific source apportionment) and Forns, 2017 and Pujol, 2016 (surface monitoring)
3. A negative direction (–) means that a lower score indicates poorer cognitive function or greater cognitive difficulty; a positive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive difficulty. Ratio measures (RRs, ORs, IRRs) >1.0 indicate higher risk for the outcome.
4. Dark orange=evidence of association with poorer cognition; Light orange=suggestive evidence of association with poorer cognition; Dark blue=evidence of association with better cognition; Light blue=suggestive evidence of association with better cognition.
5. Composite of Bayley Scales of Infant Development I and II, Denver Developmental Screening Test II, Hamburg Wechsler Intelligenztest für Kinder - IV, McArthur Communicative Development Inventory, Minnesota Infant Development Inventory, McCarthy Scales of Children's Abilities; De Snijders-Oomen Niet-verbale Intelligentietest-Revisie, Wechsler Intelligence Scale for Children.
Table 12A-5. Associations of UFP measured as PNC 10-700 nm with cognitive function.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name</th>
<th>Location</th>
<th>Study period</th>
<th>Sample size</th>
<th>Mean or median exposure</th>
<th>Cognitive Domain(s)</th>
<th>Neuropsychological test(s)</th>
<th>Exposure Window</th>
<th>Age at outcome (yrs)</th>
<th>Outcome (direction$^3$)</th>
<th>Effect measure</th>
<th>Effect Estimate (95% CI)$^4$</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forns 2017</td>
<td>BREATHE</td>
<td>Barcelona, Spain</td>
<td>2012–2015</td>
<td>1,439</td>
<td>21,935</td>
<td>Working memory</td>
<td>n-back test</td>
<td>Annual average in year of first assessment (8.5)</td>
<td>8.5 and 11.4</td>
<td>3-back detectability (3.5-year change) (–)</td>
<td>Mean difference</td>
<td>–3.75 (–5.68 to –1.83)</td>
<td>12,770 particles/cm$^3$</td>
</tr>
<tr>
<td>Sunyer 2015</td>
<td>BREATHE</td>
<td>Barcelona, Spain</td>
<td>2012–2013</td>
<td>2,715</td>
<td>14,407</td>
<td>Attention</td>
<td>Attentional Network Task</td>
<td>Annual average in year of assessment</td>
<td>9</td>
<td>Hit reaction time standard error (1-year change) (+)</td>
<td>Mean difference</td>
<td>3.9 (0.31 to 7.6)</td>
<td>6,110 particles/cm$^3$</td>
</tr>
</tbody>
</table>

$^1$Study design is cohort for all studies

$^2$Unit in the increment column. Exposure assessment is surface monitoring.

$^3$A negative direction (–) means that a lower score indicates poorer cognitive function or greater cognitive difficulty; a positive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive difficulty. Ratio measures (RRs, ORs, IRRs) >1.0 indicate higher risk for the outcome.

$^4$Dark orange=evidence of association with poorer cognition; Light orange=suggestive evidence of association with poorer cognition; Dark blue=evidence of association with better cognition; Light blue=suggestive evidence of association with better cognition.
## Table 12A-6. Associations of benzene with cognitive function.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name¹</th>
<th>Location</th>
<th>Study period</th>
<th>Sample size</th>
<th>Mean or median exposure²</th>
<th>Cognitive Domain(s)</th>
<th>Neuropsychological test(s)</th>
<th>Exposure Window</th>
<th>Age at outcome (yrs)</th>
<th>Outcome (direction³)</th>
<th>Effect measure</th>
<th>Effect Estimate (95% CI)⁴</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonzalez-Casanova 2018</td>
<td>POSGRAD</td>
<td>Mexico City, Mexico</td>
<td>2005–2014</td>
<td>718</td>
<td>2.3</td>
<td>General cognition</td>
<td>Composite⁵</td>
<td>Entire pregnancy</td>
<td>1, 1.5, 5, and 7</td>
<td>Low vs. positive cognitive development (−)</td>
<td>Odds ratio</td>
<td>1.00 (0.96 to 1.04)</td>
<td>2.6 µg/m³⁶</td>
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</tr>
<tr>
<td>Guxens 2012</td>
<td>INMA</td>
<td>Multiple cities, Spain</td>
<td>2002–2010</td>
<td>1,854</td>
<td>1.5</td>
<td>Infant cognition</td>
<td>Bayley Scales of Infant Development</td>
<td>Entire pregnancy</td>
<td>14 months</td>
<td>Infant cognition (−)</td>
<td>Mean difference</td>
<td>−3.57 (−3.69 to 0.56)</td>
<td>doubling</td>
</tr>
<tr>
<td>Lertxundi 2015</td>
<td>INMA Gipuzkoa</td>
<td>Gipuzkoa, Spain</td>
<td>2006–2010</td>
<td>438</td>
<td>0.86</td>
<td>Infant cognition</td>
<td>Bayley Scales of Infant Development</td>
<td>Entire pregnancy</td>
<td>13 to 18 months (mean 15 months)</td>
<td>Infant cognition (−)</td>
<td>Mean difference</td>
<td>−2.35 (90% CI: −8.46 to 3.75)</td>
<td>1 µg/m³⁶</td>
</tr>
</tbody>
</table>

¹Study design is cohort for all studies
²Unit in the increment column. Exposure assessment for all studies is LUR.
³A negative direction (−) means that a lower score indicates poorer cognitive function or greater cognitive difficulty; a positive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive difficulty. Ratio measures (RRs, ORs, IRRs) >1.0 indicate higher risk for the outcome.
⁴Dark orange=evidence of association with poorer cognition; Light orange=suggestive evidence of association with poorer cognition; Dark blue=evidence of association with better cognition; Light blue=suggestive evidence of association with better cognition.
⁵Composite of Bayley Scales of Infant Development II, McCarthy Scales of Children’s Abilities, Wechsler Abbreviated Scale of Intelligence.

## Table 12A-7. Associations of PAH (measured as benzo[a]pyrene) with cognitive function.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name¹</th>
<th>Location</th>
<th>Study period</th>
<th>Sample size</th>
<th>Mean or median exposure²</th>
<th>Cognitive Domain(s)</th>
<th>Neuropsychological test(s)</th>
<th>Exposure Window</th>
<th>Age at outcome (yrs)</th>
<th>Outcome (direction³)</th>
<th>Effect measure</th>
<th>Effect Estimate (95% CI)⁴</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortamais 2017</td>
<td>BREATHE</td>
<td>Barcelona, Spain</td>
<td>2012–2014</td>
<td>242</td>
<td>99</td>
<td>Attention</td>
<td>Attentional Network Test</td>
<td>Year before assessment</td>
<td>8 to 12 (mean 9)</td>
<td>Hit reaction time standard error (1-year change) (+)</td>
<td>Mean difference</td>
<td>3.9 (−5.9 to 13.7)</td>
<td>67 pg/m³⁸</td>
</tr>
</tbody>
</table>

¹Study design is cohort for all studies
²Unit in the increment column. Exposure assessment is surface monitoring.
³A negative direction (−) means that a lower score indicates poorer cognitive function or greater cognitive difficulty; a positive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive difficulty. Ratio measures (RRs, ORs, IRRs) >1.0 indicate higher risk for the outcome.
⁴Dark orange=evidence of association with poorer cognition; Light orange=suggestive evidence of association with poorer cognition; Dark blue=evidence of association with better cognition; Light blue=suggestive evidence of association with better cognition.
Table 12A-8. Associations of indirect traffic measures (density, distance) with cognitive function.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name1</th>
<th>Location</th>
<th>Study period</th>
<th>Sample size</th>
<th>Traffic measure</th>
<th>Cognitive Domain(s)</th>
<th>Neuropsychological test(s)</th>
<th>Exposure Window</th>
<th>Age at outcome (years)</th>
<th>Outcome (direction2)</th>
<th>Effect measure</th>
<th>Effect Estimate (95% CI)3</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guxens 2014</td>
<td>ESCAPE</td>
<td>Multiple cities, multiple countries</td>
<td>2000–2011</td>
<td>9,482</td>
<td>Density</td>
<td>Verbal cognition</td>
<td>Composite6</td>
<td>Entire pregnancy</td>
<td>1 to 6</td>
<td>Language development (−)</td>
<td>Mean difference</td>
<td>−0.04 (−0.62 to 0.54)</td>
<td>4,000 vehicle-km/day on major roads &lt;100m</td>
</tr>
<tr>
<td>Ha 2019</td>
<td>Upstate KIDS</td>
<td>Multiple cities, United States</td>
<td>2008–2013</td>
<td>5,825</td>
<td>Distance</td>
<td>General cognition</td>
<td>Ages and Stages Questionnaire</td>
<td>Birth to 3</td>
<td>8 months, 1, 1.5, 2, 2.5, and 3</td>
<td>Failure to meet developmental milestones by age 3y (&gt;2 SD below mean) (+)</td>
<td>Relative risk</td>
<td>1.18 (0.75 to 1.86), 1.20 (0.77 to 1.86)</td>
<td>&lt;50 vs. &gt;1,000 m, 50-100 vs. &gt;1,000 m to major road</td>
</tr>
<tr>
<td>Harris 2015</td>
<td>Project Viva</td>
<td>Boston, Massachusetts, United States</td>
<td>1999–2010</td>
<td>1,101</td>
<td>Density</td>
<td>Verbal cognition</td>
<td>Kaufman Brief Intelligence Test</td>
<td>At birth</td>
<td>6 to 10 (mean 8.0)</td>
<td>Verbal IQ (−)</td>
<td>Mean difference</td>
<td>0.3 (−0.3 to 0.8)</td>
<td>1.6 ln(vehicle-km/day) on roads &lt;100m</td>
</tr>
</tbody>
</table>

1. Study Name: ESCAPE, Upstate KIDS, Project Viva
2. Direction: (−) decrease, (+) increase
3. Effect Estimate: Mean difference
4. Increment: 4,000 vehicle-km/day on major roads <100m, <50 vs. >1,000 m, 50-100 vs. >1,000 m to major road
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name(^1)</th>
<th>Location</th>
<th>Study period</th>
<th>Sample size</th>
<th>Traffic measure</th>
<th>Cognitive Domain(s)</th>
<th>Neuropsychological test(s)</th>
<th>Exposure Window</th>
<th>Age at outcome (years)</th>
<th>Outcome (direction(^2))</th>
<th>Effect measure</th>
<th>Effect Estimate (95% CI)(^3)</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harris 2016</td>
<td>Project Viva</td>
<td>Boston, Massachusetts, United States</td>
<td>1999–2010</td>
<td>1,212</td>
<td>Density</td>
<td>Executive function</td>
<td>Behavior Rating Inventory of Executive Function (Teacher rated)</td>
<td>At birth</td>
<td>7.7</td>
<td>Global Executive Function (+)</td>
<td>Mean difference</td>
<td>−0.1 (−0.6 to 0.4)</td>
<td>1425 vehicle-km/day on roads &lt;100 m</td>
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<td></td>
<td>Verbal IQ (−)</td>
<td>1.1 (0.0 to 2.2)</td>
<td>1.8 ln(vehicle-km/day) on roads &lt;100 m</td>
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<td>Non-verbal IQ (−)</td>
<td>1.1 (−0.4 to 2.5)</td>
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<td></td>
<td>Design Memory (−)</td>
<td>0.1 (−0.1 to 0.4)</td>
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<td>Picture Memory (−)</td>
<td>0.0 (−0.3 to 0.3)</td>
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<td></td>
<td>Verbal IQ (−)</td>
<td>−3.6 (−8.0 to 0.8)</td>
<td>&lt;50 vs. &gt;200 m to major road</td>
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<td>Non-verbal IQ (−)</td>
<td>−7.3 (−12.9 to −1.7)</td>
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<td></td>
<td>Design Memory (−)</td>
<td>−0.1 (−1.1 to 0.9)</td>
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<td></td>
<td>Picture Memory (−)</td>
<td>−0.4 (−1.5 to 0.6)</td>
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<td>Verbal IQ (−)</td>
<td>1.0 (−4.0 to 6.0)</td>
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<td></td>
<td>Non-verbal IQ (−)</td>
<td>−5.6 (−11.9 to 0.8)</td>
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<td></td>
<td>Design Memory (−)</td>
<td>0.2 (−0.9 to 1.3)</td>
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<td></td>
<td>Picture Memory (−)</td>
<td>0.2 (−1.0 to 1.4)</td>
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</tr>
</tbody>
</table>

\(^1\) Harris, A. C., Chung, T., Källen, K., Brusilow, S. W., & Samolitis, S. (2016). \(^2\) Antecedent cognitive measures: executive function. \(^3\) Logarithmic (ln) transformation of continuous exposure variable.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name</th>
<th>Location</th>
<th>Sample size</th>
<th>Traffic measure</th>
<th>Cognitive Domain(s)</th>
<th>Neuropsychological test(s)</th>
<th>Exposure Window</th>
<th>Age at outcome (years)</th>
<th>Outcome (direction)</th>
<th>Effect</th>
<th>Effect Estimate (95% CI)</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Distance</td>
<td></td>
<td></td>
<td></td>
<td>At midchildhood</td>
<td>Global Executive Function (+)</td>
<td>0.2 (-0.3 to 0.8)</td>
<td>0.6 (0.1 to 1.1)</td>
<td>1.2 (-3.1 to 5.5)</td>
<td>1,425 vehicle-km/day on roads &lt;100 m</td>
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<td></td>
<td>At birth</td>
<td>Behavioral Regulation Index (+)</td>
<td>-0.0 (-0.5 to 0.5)</td>
<td>-0.0 (-0.7 to 7.8)</td>
<td>1.8 (-2.6 to 6.3)</td>
<td>&lt;50 vs. &gt;200 m to major road</td>
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<td></td>
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<td></td>
<td></td>
<td>At midchildhood</td>
<td>Metacognition Index (+)</td>
<td>2.7 (-1.6 to 7.1)</td>
<td>3.5 (-0.7 to 7.8)</td>
<td>1.2 (-3.1 to 5.5)</td>
<td>1,241 vehicle-km/day on roads &lt;100 m</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Density</td>
<td>Behavior problems</td>
<td>Strengths and Difficulties Questionnaire (teacher report)</td>
<td>At birth</td>
<td>Total difficulties (+)</td>
<td>0.0 (-0.3 to 0.3)</td>
<td>0.1 (-0.2 to 0.3)</td>
<td>1.5 (-1.0 to 3.9)</td>
<td>0.1 (-2.4 to 2.5)</td>
<td>&lt;50 vs. &gt;200 m to major road</td>
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<td></td>
<td></td>
<td></td>
<td>At midchildhood</td>
<td>Global Executive Function (+)</td>
<td>0.1 (-0.1 to 0.3)</td>
<td>0.1 (-0.1 to 0.3)</td>
<td>0.9 (-0.6 to 2.5)</td>
<td>1,425 vehicle-km/day on roads &lt;100 m</td>
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<td></td>
<td></td>
<td></td>
<td>At birth</td>
<td>Behavioral Regulation Index (+)</td>
<td>1.5 (-1.0 to 3.9)</td>
<td>1.5 (-1.0 to 3.9)</td>
<td>0.9 (-0.6 to 2.5)</td>
<td>&lt;50 vs. &gt;200 m to major road</td>
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<tr>
<td></td>
<td></td>
<td>Distance</td>
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<td></td>
<td>At midchildhood</td>
<td>Metacognition Index (+)</td>
<td>1.8 (-2.6 to 6.3)</td>
<td>1.8 (-2.6 to 6.3)</td>
<td>0.9 (-0.6 to 2.5)</td>
<td>1,241 vehicle-km/day on roads &lt;100 m</td>
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<tr>
<td></td>
<td></td>
<td>Density</td>
<td>Strengths and Difficulties Questionnaire (parent report)</td>
<td>At birth</td>
<td>Total difficulties (+)</td>
<td>0.0 (-0.3 to 0.3)</td>
<td>0.0 (-0.3 to 0.3)</td>
<td>0.0 (-0.3 to 0.3)</td>
<td>0.0 (-0.3 to 0.3)</td>
<td>0.0 (-0.3 to 0.3)</td>
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<td></td>
<td>At midchildhood</td>
<td>Global Executive Function (+)</td>
<td>0.2 (-0.3 to 0.8)</td>
<td>0.2 (-0.3 to 0.8)</td>
<td>0.2 (-0.3 to 0.8)</td>
<td>0.2 (-0.3 to 0.8)</td>
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<td>At birth</td>
<td>Behavioral Regulation Index (+)</td>
<td>-0.0 (-0.5 to 0.5)</td>
<td>-0.0 (-0.5 to 0.5)</td>
<td>-0.0 (-0.5 to 0.5)</td>
<td>-0.0 (-0.5 to 0.5)</td>
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<td>At midchildhood</td>
<td>Metacognition Index (+)</td>
<td>2.7 (-1.6 to 7.1)</td>
<td>2.7 (-1.6 to 7.1)</td>
<td>2.7 (-1.6 to 7.1)</td>
<td>2.7 (-1.6 to 7.1)</td>
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<td>At birth</td>
<td>Global Executive Function (+)</td>
<td>0.6 (0.1 to 1.1)</td>
<td>0.6 (0.1 to 1.1)</td>
<td>0.6 (0.1 to 1.1)</td>
<td>0.6 (0.1 to 1.1)</td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>Study Name</td>
<td>Location</td>
<td>Study period</td>
<td>Sample size</td>
<td>Traffic measure</td>
<td>Cognitive Domain(s)</td>
<td>Neuropsychological test(s)</td>
<td>Exposure Window</td>
<td>Age at outcome (years)</td>
<td>Outcome (direction)</td>
<td>Effect measure</td>
<td>Effect Estimate (95% CI)</td>
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</tr>
<tr>
<td>Khan 2019</td>
<td>Quito Child Health</td>
<td>Quito, Ecuador</td>
<td>2016</td>
<td>174</td>
<td>Distance</td>
<td>Attention</td>
<td>Behavioral Assessment and Research System</td>
<td>Annual average at assessment</td>
<td>8 to 14</td>
<td>Continuous performance fraction correct (−)</td>
<td>Mean difference</td>
<td>−0.03 (−0.10 to 0.04)</td>
</tr>
<tr>
<td>Kicinski 2015</td>
<td>Flemish Environmental Health Cohort</td>
<td>Flanders, Belgium</td>
<td>2008–2011</td>
<td>606</td>
<td>Density</td>
<td>Attention</td>
<td>Neurobehavioral Evaluation System - 3</td>
<td>Average at assessment</td>
<td>15</td>
<td>Sustained attention (−)</td>
<td>Mean difference</td>
<td>−0.02 (−0.12 to 0.08)</td>
</tr>
<tr>
<td>Loftus 2019</td>
<td>CANDLE</td>
<td>Shelby County, Tennessee, United States</td>
<td>2006–2017</td>
<td>905</td>
<td>Distance</td>
<td>General cognition</td>
<td>Stanford Binet Intelligence Scales, edition 5</td>
<td>Annual average at birth</td>
<td>4 to 6</td>
<td>Full Scale IQ (−)</td>
<td>Mean difference</td>
<td>−0.49 (−2.27 to 1.30)</td>
</tr>
<tr>
<td>Porta 2016</td>
<td>GASPII</td>
<td>Rome, Italy</td>
<td>2003–2011</td>
<td>474</td>
<td>Density</td>
<td>General cognition</td>
<td>Wechsler Intelligence Scale for Children-III</td>
<td>At birth</td>
<td>7</td>
<td>Full scale IQ (−)</td>
<td>Mean difference</td>
<td>−1.1 (−2.3 to 0.10)</td>
</tr>
<tr>
<td>Reference</td>
<td>Study Name</td>
<td>Location</td>
<td>Study period</td>
<td>Sample size</td>
<td>Traffic measure</td>
<td>Cognitive Domain(s)</td>
<td>Neuropsychological test(s)</td>
<td>Exposure Window</td>
<td>Age at outcome (years)</td>
<td>Outcome (direction)</td>
<td>Effect measure</td>
<td>Effect Estimate (95% CI)</td>
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<td>----------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Saenen 2016</td>
<td>COGNAC</td>
<td>Flanders, Belgium</td>
<td>2011–2014</td>
<td>310</td>
<td>Distance</td>
<td>Executive function</td>
<td>Stroop Test</td>
<td>Average in year before assessment</td>
<td>10</td>
<td>Selective attention (+)</td>
<td>Mean difference</td>
<td>0.90 (–20.6 to 22.4)</td>
</tr>
<tr>
<td>Sunyer 2015</td>
<td>BREATHE</td>
<td>Barcelona, Spain</td>
<td>2012–2013</td>
<td>2,715</td>
<td>Density</td>
<td>Attention</td>
<td>Attentional Network Task</td>
<td>Annual average in year of assessment</td>
<td>9</td>
<td>Hit reaction time standard error (1-year change) (+)</td>
<td>Mean difference</td>
<td>5.2 (0.68 to 9.7)</td>
</tr>
</tbody>
</table>

1Study design is cohort for all studies except Khan 2019 and Kicinski 2015.

2A negative direction (-) means that a lower score indicates poorer cognitive function or greater cognitive difficulty; a positive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive difficulty. Ratio measures (RRs, ORs, IRRs) >1.0 indicate higher risk for the outcome.

3Dark orange = evidence of association with poorer cognition; light orange = suggestive evidence of association with poorer cognition; dark blue = evidence of association with better cognition; light blue = suggestive evidence of association with better cognition.

4Composite of Bayley Scales of Infant Development I, II & III, McArthur Communicative Development Inventory, Denver Developmental Screening Test II, McCarthy Scales of Children’s Abilities.

5NES3 is Neurobehavioral Evaluation System – 3.

6Exposure assessment for all studies is traffic distance or traffic density.
Appendix 12B Attention deficit hyperactivity disorder diagnosis and related behaviors

Table 12B-1. Key study characteristics of studies included in the literature review for ADHD and related behaviors in children – pollutants and indirect traffic measures (N=8).

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name</th>
<th>Location</th>
<th>Study Design</th>
<th>Study period</th>
<th>Sample size</th>
<th>Exposure Window</th>
<th>Age at outcome (yrs)</th>
<th>Exposure Assessment</th>
<th>Pollutant(s)</th>
<th>Neuropsychological test(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forns 2016</td>
<td>BREATHE</td>
<td>Barcelona, Spain</td>
<td>Cross-sectional</td>
<td>2012–2013</td>
<td>2,714</td>
<td>At assessment</td>
<td>7 to 11</td>
<td>Surface monitoring</td>
<td>EC, NO₂</td>
<td>Strengths and Difficulties Questionnaire (parent report), ADHD-DSM-IV list criteria (teacher report)</td>
</tr>
<tr>
<td>Forns 2018</td>
<td>ESCAPE</td>
<td>Multiple cities, multiple countries</td>
<td>Cohort</td>
<td>1992–2012</td>
<td>29,127</td>
<td>Entire pregnancy</td>
<td>3 to 10</td>
<td>Distance or density, LUR</td>
<td>Traffic density, PM₂.₅₅₃₃ abs, NOₓ, NO₂, PM₁₀, mass, PM₂.₅₅₃₃ mass</td>
<td>Autism-tics, Attention Deficit and Hyperactivity (parent report); Child Behavior Checklist for Toddlers (parent report); Strengths and Difficulties Questionnaire (parent report); ADHD-DSM-IV list criteria (teacher-report)</td>
</tr>
<tr>
<td>Fuertes 2016</td>
<td>GINIplus, LISAplus</td>
<td>Multiple cities, Germany</td>
<td>Cohort</td>
<td>1995–2013</td>
<td>4,745</td>
<td>Annual average at birth, 10, 15</td>
<td>10 and 15</td>
<td>LUR</td>
<td>PM₂.₅₅₃₃ abs, NO₂, PM₁₀, mass, PM₂.₅₅₃₃ mass</td>
<td>Strengths and Difficulties Questionnaire (parent and self-report)</td>
</tr>
<tr>
<td>Gong 2014</td>
<td>CATSS</td>
<td>Stockholm, Sweden</td>
<td>Cohort</td>
<td>1992–2012</td>
<td>3,426</td>
<td>Entire pregnancy, 1, year before assessment</td>
<td>9 or 12</td>
<td>Dispersion / CTM</td>
<td>NOₓ, PM₁₀ mass</td>
<td>Autism-Tics, ADHD, and other Comorbidities inventory (parent report)</td>
</tr>
<tr>
<td>Mortamais 2017</td>
<td>BREATHE</td>
<td>Barcelona, Spain</td>
<td>Cohort</td>
<td>2012–2014</td>
<td>242</td>
<td>Year before assessment</td>
<td>8 to 12</td>
<td>Surface monitoring</td>
<td>Benzo[a]pyrene</td>
<td>ADHD-DSM-IV list criteria (teacher report)</td>
</tr>
<tr>
<td>Roberts 2019</td>
<td>E-Risk Longitudinal Twin Study</td>
<td>London, United Kingdom</td>
<td>Cohort</td>
<td>1994–2013</td>
<td>284</td>
<td>12</td>
<td>12 and 18</td>
<td>Dispersion / CTM</td>
<td>NOₓ, PM₂.₅₅₃₃ mass</td>
<td>ADHD traits on DSM-IV criteria and the Rutter Child Scales at 12 years (parent and teacher report); ADHD traits on Diagnostic Interview Schedule (DSM-IV, DSM-V) at 18 years (mother and co-twin report)</td>
</tr>
<tr>
<td>Saez 2018</td>
<td>IAS Girona Spain</td>
<td>Girona, Spain</td>
<td>Case-control</td>
<td>1998–2012</td>
<td>5,193</td>
<td>In first year of follow-up, up to 8</td>
<td>Up to 15</td>
<td>Distance or density</td>
<td>Traffic distance</td>
<td>Diagnosis of ADHD by health service primary care physician on WHO criteria (ICD-10: F90.0, F98.8)</td>
</tr>
</tbody>
</table>

1 For studies using a cohort recruited at prenatal/birth, where prenatal/early covariates were included in analysis, study period starts at prenatal/birth recruitment and ends at last year of child’s assessment. For cohort studies of school-age children (e.g. BREATHE), period starts at recruitment and ends when cognitive assessment ends. For case control studies, period is period of case identification, even if perinatal/early life covariates are included. For cross-sectional studies, period is period of recruitment and assessment.

2 Sex was both in all studies.
Table 12B-2. Associations of PM$_{2.5}$ mass with ADHD and related behaviors.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name$^1$</th>
<th>Location</th>
<th>Study period</th>
<th>Sample size</th>
<th>Exposure Window</th>
<th>Age at outcome (years)</th>
<th>Exposure Assessment</th>
<th>Mean or median exposure$^2$</th>
<th>Neuropsychological test(s)</th>
<th>Outcome (direction$^3$)</th>
<th>Effect measure</th>
<th>Effect Estimate (95% CI)$^4$</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forns 2018</td>
<td>ESCAPE</td>
<td>Multiple cities, multiple countries</td>
<td>1992–2012</td>
<td>29,127</td>
<td>Entire pregnancy</td>
<td>3–10</td>
<td>LUR</td>
<td>9 - 23</td>
<td>Multiple tests$^5$</td>
<td>ADHD traits within borderline or clinical range (+)</td>
<td>Odds ratio</td>
<td>0.98 (0.80 to 1.19)</td>
<td>5 µg/m$^3$</td>
</tr>
<tr>
<td>Fuertes 2016</td>
<td>GINIplus, LISAplus</td>
<td>Multiple cities, Germany</td>
<td>1995–2013</td>
<td>4,745</td>
<td>Annual average at birth 10 and 15</td>
<td>10.3 South, 17.2 North</td>
<td>LUR</td>
<td>Strengths and Difficulties Questionnaire (parent report at 10 years, self-report at 15 years)</td>
<td>Hyperactivity/inattention problems: borderline/abnormal vs. normal (+)</td>
<td>Odds ratio</td>
<td>1.06 (0.96 to 1.17)</td>
<td>1.2 µg/m$^3$ South, 0.9 µg/m$^3$ North</td>
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<td></td>
<td></td>
<td>1.12 (1.01 to 1.23)</td>
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<td></td>
<td></td>
<td></td>
<td>1.11 (1.01 to 1.22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roberts 2019</td>
<td>E-Risk Longitudinal Twin Study</td>
<td>London, United Kingdom</td>
<td>1994–2013</td>
<td>284</td>
<td>12</td>
<td>12</td>
<td>Dispersion / CTM</td>
<td>14.09</td>
<td>DSM-IV criteria and the Rutter Child Scales (parent and teacher reported)</td>
<td>ADHD traits - inattention, hyperactivity-impulsivity (+)</td>
<td>Mean difference</td>
<td>0.05 (–0.11 to 0.20)</td>
<td>1 µg/m$^3$</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>DSM-IV, DSM-V criteria (parent and co-informant reported)</td>
<td>ADHD traits (-)</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>Diagnostic Interview Schedule using DSM-IV, DSM-V criteria</td>
<td>ADHD psychiatric diagnosis (+)</td>
<td>Odds ratio</td>
<td>1.16 (0.64 to 2.10)</td>
<td></td>
</tr>
</tbody>
</table>

$^1$Study design is cohort except for Forns 2016 which is cross-sectional.

$^2$Unit is in Increment.

$^3$A negative direction (-) means that a lower score indicates poorer cognitive function or greater cognitive difficulty; a positive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive difficulty. Ratio measures (RRs, ORs, IRRs) >1.0 indicate higher risk for the outcome.

$^4$Dark orange = evidence of association with poorer cognition; Light orange = suggestive evidence of association with poorer cognition; Dark blue = evidence of association with better cognition; Light blue = suggestive evidence of association with better cognition.

$^5$Autism-tics, Attention Deficit and Hyperactivity and Other Co-Morbidities. Child Behavior Checklist for Toddlers, attention deficit/hyperactivity problems; Strengths and Difficulties Questionnaire hyperactivity/inattention; ADHD-DSM-IV list criteria.
Table 12B-3. Associations of PM$_{10}$ mass and PM$_{coarse}$ mass with ADHD and related behaviors.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name$^1$</th>
<th>Location</th>
<th>Study period</th>
<th>Sample size</th>
<th>Exposure Assessment</th>
<th>Pollutant</th>
<th>Mean or median exposure$^2$</th>
<th>Neuropsychological test(s)</th>
<th>Exposure Window</th>
<th>Age at outcome (years)</th>
<th>Outcome (direction$^3$)</th>
<th>Effect measure</th>
<th>Effect Estimate (95% CI)$^4$</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forns 2018</td>
<td>ESCAPE</td>
<td>Multiple cities, multiple countries</td>
<td>1992–2012</td>
<td>29,127</td>
<td>LUR</td>
<td>PM$_{10}$ mass</td>
<td>18 - 42</td>
<td>Multiple tests$^5$</td>
<td>Entire pregnancy</td>
<td>3 to 10</td>
<td>ADHD traits within borderline or clinical range (+)</td>
<td>Odds ratio</td>
<td>0.97 (0.79 to 1.19)</td>
<td>10 µg/m$^3$</td>
</tr>
<tr>
<td>Fueres 2016</td>
<td>GINIplus, LISAplus</td>
<td>Multiple cities, Germany</td>
<td>1995–2013</td>
<td>4,745</td>
<td>LUR</td>
<td>PM$_{10}$ mass</td>
<td>8 - 21</td>
<td>Strengths and Difficulties Questionnaire (parent report at 10y and self-report at 15y)</td>
<td>Annual average at birth</td>
<td>10</td>
<td>Hyperactivity/inattention problems: borderline/abnormal vs. normal (+)</td>
<td>Odds ratio</td>
<td>0.98 (0.84 to 1.13)</td>
<td>5 µg/m$^3$</td>
</tr>
<tr>
<td>Gong 2014</td>
<td>CATSS</td>
<td>Stockholm, Sweden</td>
<td>1992–2012</td>
<td>3,426</td>
<td>Dispersion / CTM</td>
<td>PM$_{10}$ mass</td>
<td>3.5</td>
<td>Autism-Tics, ADHD, and other Comorbidities inventory (parent report)</td>
<td>Entire pregnancy</td>
<td>9 or 12</td>
<td>Probable ADHD diagnosis based on DSM-IV criteria (+)</td>
<td>Odds ratio</td>
<td>1.07 (0.96 to 1.18)</td>
<td>South, 3.0 µg/m$^3$; North, 1.5 µg/m$^3$</td>
</tr>
</tbody>
</table>

$^1$Study design is cohort.

$^2$Unit is in Increment.

$^3$A negative direction (-) means that a lower score indicates poorer cognitive function or greater cognitive difficulty; a positive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive difficulty. Ratio measures (RRs, ORs, IRRs) >1.0 indicate higher risk for the outcome.

$^4$Dark orange=evidence of association with poorer cognition; Light orange=suggestive evidence of association with poorer cognition; Dark blue=evidence of association with better cognition; Light blue=suggestive evidence of association with better cognition

$^5$Autism-tics, Attention Deficit and Hyperactivity and Other Co-Morbidities (parent report); Child Behavior Checklist for Toddlers, attention deficit/hyperactivity problems (parent report); Strengths and Difficulties Questionnaire, hyperactivity/inattention (parent report); ADHD-DSM-IV list criteria (teacher-report)
Table 12B-4. Associations of PAH measured as benzo[a]pyrene with ADHD and related behaviors.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name¹</th>
<th>Location</th>
<th>Study period</th>
<th>Sample size</th>
<th>Exposure Assessment</th>
<th>Mean or median exposure²</th>
<th>Neuropsychological test(s)</th>
<th>Exposure Window</th>
<th>Age at outcome (years)</th>
<th>Outcome (direction³)</th>
<th>Effect measure</th>
<th>Effect Estimate (95% CI)⁴</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortamais 2017</td>
<td>BREATHE Barcelona, Spain 2012–2014 242</td>
<td>Surface monitoring 99</td>
<td>ADHD-DSM-IV criteria (teacher)</td>
<td>Annual average in year before assessment 8 to 12, mean 9</td>
<td>Total ADHD score (+)</td>
<td>Relative risk 1.18 (0.96 to 1.45)</td>
<td>67 pg/m³</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Inattention (+)</td>
<td>Relative risk 1.20 (0.98 to 1.46)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hyperactivity (+)</td>
<td>Relative risk 1.17 (0.92 to 1.47)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹Study design is cohort.
²Unit is in Increment.
³A negative direction (-) means that a lower score indicates poorer cognitive function or greater cognitive difficulty; a positive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive difficulty. Ratio measures (RRs, ORs, IRRs) >1.0 indicate higher risk for the outcome.
⁴Dark orange=evidence of association with poorer cognition; Light orange=suggestive evidence of association with poorer cognition; Dark blue=evidence of association with better cognition; Light blue=suggestive evidence of association with better cognition.
Table 12B-5. Associations of indirect traffic measures (density, distance) with ADHD and related behaviors.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name</th>
<th>Location</th>
<th>Study period</th>
<th>Sample size</th>
<th>Traffic measure</th>
<th>Neuropsychological test(s)</th>
<th>Exposure Window</th>
<th>Age at outcome (years)</th>
<th>Outcome (direction)</th>
<th>Effect measure</th>
<th>Effect Estimate (95% CI)</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forns 2018</td>
<td>ESCAPE</td>
<td>Multiple cities, multiple countries</td>
<td>1992–2012</td>
<td>29,127</td>
<td>Density</td>
<td>Multiple tests</td>
<td>Entire pregnancy</td>
<td>3 to 10</td>
<td>ADHD traits within borderline or clinical range (+)</td>
<td>Odds ratio</td>
<td>1.04 (0.96–1.13)</td>
<td>4,000 vehicle-km/day</td>
</tr>
<tr>
<td>Saez 2018</td>
<td>IAS Girona, Spain</td>
<td>Girona, Spain</td>
<td>1998–2012</td>
<td>5,193</td>
<td>Distance</td>
<td>Diagnosis of ADHD by primary physician</td>
<td>At assessment</td>
<td>Up to 8 at start, up to 15 at end</td>
<td>Diagnosis of ADHD by primary physician (ICD-10: F90.0, F98.8) (+)</td>
<td>Odds ratio</td>
<td>1.88 (0.14–14.30)</td>
<td>&lt;50 vs. &gt;300 m to nearest road</td>
</tr>
</tbody>
</table>

1Study design for Forns 2018 is cohort and for Saez, 2018 is case-control.
2A negative direction (-) means that a lower score indicates poorer cognitive function or greater cognitive difficulty; a positive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive difficulty. Ratio measures (RRs, ORs, IRRs) >1.0 indicate higher risk for the outcome.
3Dark orange=evidence of association with poorer cognition; Light orange=suggestive evidence of association with poorer cognition. Dark blue=evidence of association with better cognition; Light blue=suggestive evidence of association with better cognition.
4Autism-tics, Attention Deficit and Hyperactivity and Other Co-Morbidities (parent report); Child Behavior Checklist for Toddlers, attention deficit/hyperactivity problems (parent report); Strengths and Difficulties Questionnaire, hyperactivity/inattention (parent report); ADHD-DSM-IV list criteria (teacher-report).
# Appendix 12C. Autism spectrum disorder (ASD) diagnosis and related behaviors

Table 12C-1. Key study characteristics of studies included in the literature review for ASD and related behaviors in children – pollutants and indirect traffic measures (N=14).

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name</th>
<th>Location</th>
<th>Study Design</th>
<th>Study period</th>
<th>Sample size</th>
<th>Exposure Window</th>
<th>Age at outcome (yrs)</th>
<th>Exposure Assessment</th>
<th>Pollutant(s)</th>
<th>Neuropsychological Test(s)/ Diagnostic Tool(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Becerra 2013</td>
<td>Los Angeles County DDS</td>
<td>Los Angeles County, California, United States</td>
<td>Case-control</td>
<td>1998–2009</td>
<td>58,423</td>
<td>Entire pregnancy</td>
<td>3 to 5</td>
<td>LUR</td>
<td>NO, NO₂</td>
<td>Autistic disorder (AD) diagnosis identified using California DDS database</td>
</tr>
<tr>
<td>Chen 2018</td>
<td>Shanghai Early Life</td>
<td>Shanghai, China</td>
<td>Case-control</td>
<td>2014</td>
<td>1,364</td>
<td>First 3 years</td>
<td>3 to 12</td>
<td>LUR</td>
<td>PM₁₀ mass, PM₂₅ mass</td>
<td>Population-based screening using the Social Communication Questionnaire (parent and teacher report) followed by confirmatory ASD diagnosis by pediatrician based on DSM-V</td>
</tr>
<tr>
<td>Gong 2014</td>
<td>CATSS</td>
<td>Stockholm, Sweden</td>
<td>Cohort</td>
<td>1992–2012</td>
<td>3,426</td>
<td>Entire pregnancy, first year, year before assessment</td>
<td>9 or 12</td>
<td>Dispersion / CTM</td>
<td>NOₓ, PM₁₀ mass</td>
<td>Autistic traits on Autism-Tics, ADHD, and other Comorbidities inventory (parent report)</td>
</tr>
<tr>
<td>Gong 2017</td>
<td>Stockholm Youth Cohort</td>
<td>Stockholm, Sweden</td>
<td>Case-control</td>
<td>2001–2011</td>
<td>23,373</td>
<td>Entire pregnancy, first year</td>
<td>Up to 13</td>
<td>Dispersion / CTM</td>
<td>NOₓ, PM₁₀ mass</td>
<td>ASD diagnosis from national registries, based on ICD 9/10 and DSM-IV criteria, with and without intellectual disability (ID)</td>
</tr>
<tr>
<td>Goodrich 2018</td>
<td>CHARGE</td>
<td>California, United States</td>
<td>Case-control</td>
<td>2002–2011</td>
<td>606</td>
<td>Entire pregnancy and each trimester</td>
<td>2 to 5</td>
<td>Dispersion / CTM</td>
<td>NOₓ</td>
<td>ASD diagnosis using California Department of Developmental Services criteria (uses Autism Diagnostic Observation Schedule-Generic (ADOS) Autism Diagnostic Interview-Revised (ADI-R))</td>
</tr>
<tr>
<td>Guxens 2016</td>
<td>ESCAPE</td>
<td>Multiple cities, multiple countries</td>
<td>Cohort</td>
<td>1992–2012</td>
<td>8,079</td>
<td>Entire pregnancy</td>
<td>4 to 10</td>
<td>Distance or density, LUR</td>
<td>Traffic density, PM₁₀ abs, NOₓ, NO₂, PM₂₅ mass, PM₁₀ mass, PM₁₀ coarse mass</td>
<td>Autistic traits on Autism-Tics, ADHD, and other Comorbidities inventory, Pervasive Developmental Problems of the Child Behavior Checklist for Toddlers, Social Responsiveness Scale, Childhood Autism Spectrum Test</td>
</tr>
<tr>
<td>Pagalan 2019</td>
<td>Vancouver 2004 - 2009 birth</td>
<td>Vancouver, British Columbia, Canada</td>
<td>Cohort</td>
<td>2004–2014</td>
<td>129,436</td>
<td>Entire pregnancy</td>
<td>Up to 5</td>
<td>LUR</td>
<td>NO, NO₂</td>
<td>ASD diagnosis by physician on standardized health service criteria, using Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview Revised (ADI-R)</td>
</tr>
<tr>
<td>Raz 2018</td>
<td>NII Israel</td>
<td>Multiple cities, Israel</td>
<td>Case-control</td>
<td>2005–2014</td>
<td>56,290</td>
<td>Entire pregnancy, first 9 months</td>
<td>4 to 9</td>
<td>Dispersion / CTM</td>
<td>NO₂</td>
<td>ASD disability determined by physician-led team on DSM-IV criteria, from national insurance database</td>
</tr>
<tr>
<td>Reference</td>
<td>Study Name</td>
<td>Location</td>
<td>Study Design</td>
<td>Study period</td>
<td>Sample size</td>
<td>Exposure Window</td>
<td>Age at outcome (yrs)</td>
<td>Exposure Assessment</td>
<td>Pollutant(s)</td>
<td>Neuropsychological Test(s)/ Diagnostic Tool(s)</td>
</tr>
<tr>
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</tr>
<tr>
<td>Ritz 2018</td>
<td>Danish ASD</td>
<td>Denmark</td>
<td>Case-control</td>
<td>1995-2016</td>
<td>83,526</td>
<td>Entire pregnancy, first 9 months</td>
<td>not reported</td>
<td>Dispersion / CTM</td>
<td>NO\textsubscript{2}, PM\textsubscript{2.5} mass, PM\textsubscript{10} mass</td>
<td>ASD as reported in Danish National Patient Register, based on admissions and outpatient/emergency room consultations, and the Danish Psychiatric Central Register (PCR) based on psychiatric admissions to hospitals and outpatient clinics. On ICD-10 codes of F84.0, F84.1, F84.5, F84.8 or F84.9</td>
</tr>
<tr>
<td>Talbott 2015a</td>
<td>SW PA children</td>
<td>Pittsburgh, Pennsylvania, United States</td>
<td>Case-control</td>
<td>2011–2013</td>
<td>430</td>
<td>Entire pregnancy, first year, second year</td>
<td>Not reported</td>
<td>LUR</td>
<td>PM\textsubscript{2.5} mass</td>
<td>ASD diagnosis by psychiatrist psychologist and high score on Autism Diagnostic Observation Schedule (ADOS) or other test, and high score on Social Communications Questionnaire</td>
</tr>
<tr>
<td>Talbott 2015b</td>
<td>SW PA children</td>
<td>Pittsburgh, Pennsylvania, United States</td>
<td>Case-control</td>
<td>2011–2013</td>
<td>441</td>
<td>Entire pregnancy</td>
<td>Not reported</td>
<td>Dispersion / CTM</td>
<td>Diesel PM\textsubscript{10}</td>
<td>ASD diagnosis by psychiatrist psychologist with Autism Diagnostic Observation Schedule (ADOS) or other test, and high score on Social Communications Questionnaire</td>
</tr>
<tr>
<td>Volk 2011</td>
<td>CHARGE</td>
<td>California, United States</td>
<td>Case-control</td>
<td>2003–2009</td>
<td>563</td>
<td>Entire pregnancy</td>
<td>2 to 5</td>
<td>Distance or density</td>
<td>Traffic distance</td>
<td>ASD diagnosis identified using California Department of Developmental Services (uses Autism Diagnostic Observation Schedule-Generic (ADOS) Autism Diagnostic Interview-Revised (ADI-R))</td>
</tr>
<tr>
<td>Volk 2013</td>
<td>CHARGE</td>
<td>California, United States</td>
<td>Case-control</td>
<td>2003–2009</td>
<td>524</td>
<td>Entire pregnancy, each trimester, first year</td>
<td>2 to 5</td>
<td>Dispersion / CTM</td>
<td>NO\textsubscript{x}</td>
<td>ASD diagnosis identified using California Department of Developmental Services (uses Autism Diagnostic Observation Schedule-Generic (ADOS) Autism Diagnostic Interview-Revised (ADI-R))</td>
</tr>
<tr>
<td>von Ehrenstein 2014</td>
<td>Los Angeles County DDS</td>
<td>Los Angeles County, California, United States</td>
<td>Cohort</td>
<td>1998–2009</td>
<td>126,402</td>
<td>Entire pregnancy</td>
<td>3 to 6</td>
<td>Surface monitoring</td>
<td>Benzene, PAH, PM\textsubscript{2.5}, Cu</td>
<td>Autistic disorder primary diagnosis from Client Evaluation Report of the California Department of Developmental Services records</td>
</tr>
</tbody>
</table>

1For studies using a cohort recruited at prenatal/birth, where prenatal/early covariates were included in analysis, study period starts at prenatal/birth recruitment and ends at last year of child’s assessment. For cohort studies of school-age children (e.g. BREATHE), period starts at recruitment and ends when cognitive assessment ends. For case control studies, period is period of case identification, even if perinatal/early life covariates are included. For cross-sectional studies, period is period of recruitment and assessment.

2Sex was both in all studies.
### Table 12C-2. Associations of NO with ASD and related behaviors.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name</th>
<th>Location</th>
<th>Study Design</th>
<th>Study period</th>
<th>Sample size</th>
<th>Exposure Median or Mean</th>
<th>Exposure Window</th>
<th>Age at outcome (years)</th>
<th>ASD diagnosis or neuropsychological test(s)</th>
<th>Odds Ratio (95% CI)&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Becerra 2013</td>
<td>Los Angeles County DDS</td>
<td>Los Angeles County, California, United States</td>
<td>Case-control</td>
<td>1998–2009</td>
<td>58,423</td>
<td>LUR 28.7</td>
<td>Entire pregnancy</td>
<td>3 to 5</td>
<td>Autistic disorder (AD) diagnosis identified using California DDS database (DSM-IV-R 299.00)</td>
<td>1.02 (0.96–1.08)</td>
<td>18.46 ppb</td>
</tr>
<tr>
<td>Pagalan 2019</td>
<td>Vancouver 2004 - 2009 birth</td>
<td>Vancouver, British Columbia, Canada</td>
<td>Cohort</td>
<td>2004–2014</td>
<td>129,436</td>
<td>LUR 18.3</td>
<td>Entire pregnancy</td>
<td>6 to 11</td>
<td>ASD diagnosis by physician on standardized health service criteria, using Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview Revised (ADI-R)</td>
<td>1.07 (1.01–1.13)</td>
<td>10.7 ppb</td>
</tr>
</tbody>
</table>

<sup>1</sup>Unit in the increment column.

<sup>2</sup>Odds ratio >1.0 indicate higher risk for ASD.

**Dark orange** = evidence of association with ASD or more ASD traits; **Light orange** = suggestive evidence of association with ASD or more ASD traits; **Dark blue** = evidence of association with ASD or more ASD traits; **Light blue** = suggestive evidence of association with ASD or more ASD traits.
Table 12C-3. Associations of PM$_{2.5}$ mass with ASD and related behaviors.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name</th>
<th>Location</th>
<th>Study Design</th>
<th>Study period</th>
<th>Sample size</th>
<th>Exposure Assessment</th>
<th>Mean or median exposure$^1$</th>
<th>Exposure Window</th>
<th>Age at outcome (yrs)</th>
<th>ASD diagnosis or neuropsychological test(s)</th>
<th>Odds Ratio (95% CI)$^2$</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen 2018</td>
<td>Shanghai Early Life</td>
<td>Shanghai, China</td>
<td>Case-control</td>
<td>2005–2014</td>
<td>1,364</td>
<td>LUR</td>
<td>66.2</td>
<td>First year</td>
<td>7</td>
<td>Population-based screening using the Social Communication Questionnaire followed by confirmatory ASD diagnosis by pediatrician based on DSM-V</td>
<td>1.07 (0.80–1.43)</td>
<td>3.4 µg/m$^3$</td>
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<td>1.50 (1.01–2.22)</td>
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<td>1.78 (1.05–3.02)</td>
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<td>1.78 (1.14–2.76)</td>
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<tr>
<td>Guxens 2016</td>
<td>ESCAPE</td>
<td>Multiple cities, multiple countries</td>
<td>Cohort</td>
<td>1992–2012</td>
<td>8,079</td>
<td>LUR</td>
<td>8.4-22.4</td>
<td>Entire pregnancy</td>
<td>4 to 10</td>
<td>Borderline/clinical range for ASD using validated cut-offs for 4 tests (depending on cohort): Autism-Tics, ADHD, and other Comorbidities inventory, Pervasive Developmental Problems of the Child Behavior Checklist for Toddlers, Social Responsiveness Scale, Childhood Autism Spectrum Test</td>
<td>0.71 (0.37–1.37)</td>
<td>5 µg/m$^3$</td>
</tr>
<tr>
<td>Ritz 2018</td>
<td>Danish ASD</td>
<td>Denmark</td>
<td>Case-control</td>
<td>1995–2016</td>
<td>83,526</td>
<td>Dispersion / CTM</td>
<td>14.39</td>
<td>Entire pregnancy</td>
<td>Below 5 to not reported</td>
<td>ASD as reported in Danish National Patient Register, based on admissions and outpatient/emergency room consultations, and the Danish Psychiatric Central Register (PCR) based on psychiatric admissions to hospitals and outpatient clinics</td>
<td>0.96 (0.91–1.02)</td>
<td>3.61 µg/m$^3$</td>
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<td>1.06 (1.01–1.11)</td>
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<tr>
<td>Talbot 2015a</td>
<td>SW PA children</td>
<td>Pittsburgh, Pennsylvania, United States</td>
<td>Case-control</td>
<td>2011–2013</td>
<td>430</td>
<td>LUR</td>
<td>14.8</td>
<td>Entire pregnancy</td>
<td>Not reported</td>
<td>ASD diagnosis by psychiatrist or psychologist including Autism Diagnostic Observation Schedule (ADOS) or other test, and high score on Social Communications Questionnaire</td>
<td>1.20 (0.88–1.63)</td>
<td>2.84 µg/m$^3$</td>
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<td>1.37 (0.95–1.97)</td>
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<td>1.45 (1.01–2.08)</td>
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</tbody>
</table>

$^1$Unit in the increment column.

$^2$Odds ratio >1.0 indicate higher risk for ASD.

*Darker orange* = evidence of association with ASD or more ASD traits; *Light orange* = suggestive evidence of association with ASD or more ASD traits; *Dark blue* = evidence of association with ASD or more ASD traits; *Light blue* = suggestive evidence of association with ASD or more ASD traits.
Table 12C-4. Associations of PM$_{10}$ mass and PM$_{coarse}$ mass with ASD and related behaviors.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name</th>
<th>Location</th>
<th>Study Design</th>
<th>Study period</th>
<th>Sample size</th>
<th>Exposure Assessment</th>
<th>Pollutant</th>
<th>Mean or median exposure$^1$</th>
<th>Exposure Window</th>
<th>Age at outcome (yrs)</th>
<th>ASD diagnosis or neuropsychological test(s)</th>
<th>Odds Ratio (95% CI)$^2$</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen 2018</td>
<td>Shanghai Early Life</td>
<td>Shanghai, China</td>
<td>Case-control</td>
<td>2014</td>
<td>1,364</td>
<td>LUR</td>
<td>PM$_{10}$ mass</td>
<td>95.4</td>
<td>First year</td>
<td>Mean 7</td>
<td>Population-based screening using the Social Communication Questionnaire followed by 2 independent ASD diagnoses by pediatricians according to DSM-V criteria</td>
<td>1.16 (0.91–1.49)</td>
<td>4.9 µg/m$^3$</td>
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<td>Second year</td>
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<td>Third year</td>
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<td>First 3 years</td>
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<tr>
<td>Gong 2014</td>
<td>CATSS</td>
<td>Stockholm, Sweden</td>
<td>Cohort</td>
<td>1992–2012</td>
<td>3,426</td>
<td>Dispersion / CTM</td>
<td>PM$_{10}$ mass</td>
<td>3.5</td>
<td>Entire pregnancy</td>
<td>9 or 12</td>
<td>Autism-Tics, ADHD, and other Comorbidities inventory, used a cut-off consistent with ASD diagnosis based on DSM-IV criteria</td>
<td>0.78 (0.39–1.56)</td>
<td>95th to 5th percentile difference</td>
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<td>First year</td>
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<td>Year before assessment</td>
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<tr>
<td>Gong 2017</td>
<td>Stockholm Youth Cohort</td>
<td>Stockholm, Sweden</td>
<td>Case-control</td>
<td>2001–2011</td>
<td>23,373</td>
<td>Dispersion / CTM</td>
<td>PM$_{10}$ mass</td>
<td>4.2</td>
<td>Entire pregnancy</td>
<td>Up to 13</td>
<td>ASD diagnosis from national registries, based on ICD 9/10 and DSM-IV criteria, with and without intellectual disability (ID)</td>
<td>1.00 (0.86–1.15)</td>
<td>20 µg/m$^3$</td>
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<td>First year</td>
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<td>Year before assessment</td>
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<tr>
<td>Guxens 2016</td>
<td>ESCAPE</td>
<td>Multiple cities, multiple countries</td>
<td>Cohort</td>
<td>1992–2012</td>
<td>8,079</td>
<td>LUR</td>
<td>PM$_{10}$ mass</td>
<td>18-42</td>
<td>Entire pregnancy</td>
<td>4 to 10</td>
<td>Borderline/clinical range for ASD using validated cut-offs for 4 tests (depending on cohort): Autism-Tics, ADHD, and other Comorbidities inventory, Pervasive Developmental Problems of the Child Behavior Checklist for Toddlers, Social Responsiveness Scale, Childhood Autism Spectrum Test</td>
<td>0.90 (0.68–1.19)</td>
<td>10 µg/m$^3$</td>
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<td></td>
<td>Borderline/clinical range for ASD using validated cutoffs as described above</td>
<td>0.92 (0.55–1.54)</td>
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<td></td>
<td>Borderline/clinical range for ASD using validated cutoffs as described above</td>
<td>0.96 (0.72–1.28)</td>
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<td>Clinical range for ASD using validated cutoffs as described above</td>
<td>0.87 (0.55–1.38)</td>
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<tr>
<td>Reference</td>
<td>Study Name</td>
<td>Location</td>
<td>Study Design</td>
<td>Study period</td>
<td>Sample size</td>
<td>Exposure Assessment</td>
<td>Pollutant</td>
<td>Mean or median exposure&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Exposure Window</td>
<td>Age at outcome (yrs)</td>
<td>ASD diagnosis or neuropsychological test(s)</td>
<td>Odds Ratio (95% CI)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Increment</td>
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</tr>
<tr>
<td>Ritz 2018</td>
<td>Danish ASD</td>
<td>Denmark</td>
<td>Case-control</td>
<td>1995–2016</td>
<td>83,526</td>
<td>Dispersion / CTM</td>
<td>PM&lt;sub&gt;10&lt;/sub&gt; mass</td>
<td>17.13</td>
<td>Entire pregnancy</td>
<td>Below 5 to not reported</td>
<td>ASD as reported in Danish National Patient Register, based on admissions and outpatient/emergency room consultations, and the Danish Psychiatric Central Register (PCR) based on psychiatric admissions to hospitals and outpatient clinics</td>
<td>0.95 (0.91–1.00)</td>
<td>3.80 µg/m&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>1</sup>Unit in the increment column.

<sup>2</sup>Odds ratio >1.0 indicate higher risk for ASD.

<sup>3</sup>Dark orange=evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Dark blue=evidence of association with ASD or more ASD traits; Light blue=suggestive evidence of association with ASD or more ASD traits.
Table 12C-5. Associations of PM components with ASD and related behaviors.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name</th>
<th>Location</th>
<th>Study Design</th>
<th>Study period</th>
<th>Sample size</th>
<th>Exposure Assessment</th>
<th>Pollutant</th>
<th>Mean or median exposure</th>
<th>Exposure Window</th>
<th>Age at outcome (yrs)</th>
<th>ASD diagnosis or neuropsychological test(s)</th>
<th>Odds Ratio (95% CI)</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Talbott 2015b</td>
<td>SW PA children</td>
<td>Pittsburgh, Pennsylvania, United States</td>
<td>Case-control</td>
<td>2011–2013</td>
<td>441</td>
<td>Dispersion / CTM</td>
<td>Diesel PM₁₀</td>
<td>399.98</td>
<td>Entire pregnancy</td>
<td>Not reported</td>
<td>ASD diagnosis by psychiatrist or psychologist with Autism Diagnostic Observation Schedule (ADOS) or other test, and high score on Social Communications Questionnaire</td>
<td>1.04 (0.59–1.84)</td>
<td>&gt;589 vs. &lt;255 ng/m³</td>
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<td></td>
<td>1.00 (0.57–1.77)</td>
<td>400-589 vs. &lt;255 ng/m³</td>
<td>1.15 (0.66–2.00)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Los Angeles County DDS</td>
<td>Los Angeles County, California, United States</td>
<td>Cohort</td>
<td>1998–2009</td>
<td>78,721</td>
<td>Surface monitoring</td>
<td>PM₂.₅ Cu</td>
<td>59.12</td>
<td>Entire pregnancy</td>
<td>3 to 6</td>
<td>Autistic disorder primary diagnosis recorded by California Department of Developmental Services</td>
<td>1.09 (1.02–1.16)</td>
</tr>
</tbody>
</table>

1Unit in the increment column.
2Odds ratio >1.0 indicate higher risk for ASD.
3Dark orange=evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Dark blue=evidence of association with ASD or more ASD traits; Light blue=suggestive evidence of association with ASD or more ASD traits.

Table 12C-6. Associations of PAH with ASD and related behaviors.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name</th>
<th>Location</th>
<th>Study Design</th>
<th>Study period</th>
<th>Sample size</th>
<th>Exposure Assessment</th>
<th>Mean or median exposure</th>
<th>Exposure Window</th>
<th>Age at outcome (yrs)</th>
<th>ASD diagnosis or neuropsychological test(s)</th>
<th>Odds Ratio (95% CI)</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>von Ehrenstein 2014</td>
<td>Los Angeles County DDS</td>
<td>Los Angeles County, California, United States</td>
<td>Cohort</td>
<td>1998–2009</td>
<td>109,062</td>
<td>Surface monitoring</td>
<td>1.14</td>
<td>Entire pregnancy</td>
<td>3 to 6</td>
<td>Autistic disorder primary diagnosis recorded by California Department of Developmental Services</td>
<td>1.03 (0.84–1.26)</td>
<td>0.79 ppb</td>
</tr>
</tbody>
</table>

1Unit in the increment column.
2Odds ratio >1.0 indicate higher risk for ASD.
3Dark orange=evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Dark blue=evidence of association with ASD or more ASD traits; Light blue=suggestive evidence of association with ASD or more ASD traits.
Table 12C-7. Associations of Benzene with ASD and related behaviors.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name</th>
<th>Location</th>
<th>Study Design</th>
<th>Study period</th>
<th>Sample size</th>
<th>Exposure Assessment</th>
<th>Mean or median exposure&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Exposure Window</th>
<th>Age at outcome (yrs)</th>
<th>ASD diagnosis or neuropsychological test(s)</th>
<th>Odds Ratio (95% CI)&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>von Ehrenstein 2014</td>
<td>Los Angeles County DDS</td>
<td>Los Angeles County, California, United States</td>
<td>Cohort</td>
<td>1998–2009</td>
<td>126,402</td>
<td>Surface monitoring</td>
<td>1.16</td>
<td>Entire pregnancy</td>
<td>3 to 6</td>
<td>Autistic disorder primary diagnosis recorded by California Department of Developmental Services</td>
<td>1.46 (1.12–1.89)</td>
<td>0.78 ppb</td>
</tr>
</tbody>
</table>

<sup>1</sup>Unit in the increment column.
<sup>2</sup>Odds ratio >1.0 indicate higher risk for ASD.

*Dark orange = evidence of association with ASD or more ASD traits; Light orange = suggestive evidence of association with ASD or more ASD traits; Dark blue = evidence of association with ASD or more ASD traits; Light blue = suggestive evidence of association with ASD or more ASD traits.*
Table 12C-8. Associations of indirect traffic measures with ASD and related behaviors.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Name</th>
<th>Location</th>
<th>Study Design</th>
<th>Study period</th>
<th>Sample size</th>
<th>Traffic measure</th>
<th>Exposure Window</th>
<th>Age at outcome (yrs)</th>
<th>ASD diagnosis or neuropsychological test(s)</th>
<th>Odds Ratio (95% CI)*</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guxens 2016</td>
<td>ESCAPE</td>
<td>Multiple cities, Italy, multiple countries</td>
<td>Cohort</td>
<td>1992–2012</td>
<td>8,079</td>
<td>Density</td>
<td>At birth</td>
<td>4 to 10</td>
<td>Borderline/clinical range for ASD using validated cut-offs for 4 tests (depending on cohort): Autism-Tics, ADHD, and other Comorbidities inventory, Pervasive Developmental Problems of the Child Behavior Checklist for Toddlers, Social Responsiveness Scale, Childhood Autism Spectrum Test</td>
<td>1.02 (0.89–1.16)</td>
<td>4,000 vehicle-km/day on major roads &lt;100 m</td>
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<tr>
<td>Volk 2011</td>
<td>CHARGE</td>
<td>California, United States</td>
<td>Case-control</td>
<td>2003–2009</td>
<td>563</td>
<td>Distance to nearest freeway</td>
<td>Entire pregnancy</td>
<td>2 to 5</td>
<td>ASD diagnosis identified using California Department of Developmental Services criteria (uses Autism Diagnostic Observation Schedule-Generic (ADOS) Autism Diagnostic Interview-Revised (ADI-R))</td>
<td>1.86 (1.03–3.45)</td>
<td>&lt;309m (closest 10%) to nearest freeway vs. &gt;1,419m (furthest 50%)</td>
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<td><strong>Clinical range for ASD using validated cutoffs as described above</strong></td>
<td>0.96 (0.58–1.56)</td>
<td>309-647m (closest 10-25%ile) to nearest freeway vs. &gt;1,419m (furthest 50%)</td>
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<td></td>
<td>1.11 (0.73–1.67)</td>
<td>647-1,419m (closest 25-50%ile) to nearest freeway vs. &gt;1,419m (furthest 50%)</td>
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<td></td>
<td>0.71 (0.39–1.26)</td>
<td>647-1,419m (closest 25-50%ile) to nearest freeway vs. &gt;1,419m (furthest 50%)</td>
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<td>1.29 (0.77–2.18)</td>
<td>1,419m (closest 50%ile) to major road vs. &gt;209m (furthest 50%)</td>
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<td>0.83 (0.55–1.26)</td>
<td>96-209m (closest 25-50%ile) to major road vs. &gt;209m (furthest 50%)</td>
</tr>
</tbody>
</table>

*Odds ratio >1.0 indicate higher risk for ASD.

**Dark orange** = evidence of association with ASD or more ASD traits; **Light orange** = suggestive evidence of association with ASD or more ASD traits; **Dark blue** = evidence of association with ASD or more ASD traits; **Light blue** = suggestive evidence of association with ASD or more ASD traits.
Figure 12C-1. Directed acyclic graph (DAG) of TRAP and neurodevelopment (inclusive of all outcomes: cognitive function, ADHD, and ASD).
Appendix 12D References for studies included in the literature review of neurodevelopmental outcomes


