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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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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).

Reference	Study Name	Location	Study Design	Study period ¹	Sample size ²	Exposure Window)	Age at outcome (yrs)	Exposure Assessment	Pollutant(s)	Neuropsychological test(s)	Cognitive Domain(s)
Basagaña 2016	BREATHE	Barcelona, Spain	Cohort	2012– 2013	2,618	Average in year of assessment	Mean 8.5	Traffic-specific source apportionment	PM _{2.5} road dust, PM _{2.5} traffic	Attentional Network Task, n-back test	Attention (1-year change), Working memory (1-year change)
Chiu 2013	MISSEB	Boston, Massachusetts, United States	Cohort	1986 – 1998	174	Birth to assessment	9 to 11	LUR	BC	Conners Continuous Performance Test	Attention, response inhibition
Clark 2012	RANCH UK	London, United Kingdom	Cross- sectional	2002	719	Annual average at assessment	9 to 10	LUR	NO ₂	Suffolk Reading Scale 2, Child Memory Scale, The Search and Memory Task	Reading comprehension, working memory, memory
Cowell 2015	ACCESS	Boston, Massachusetts, United States	Cohort	2002– 2015	258	Entire pregnancy	6	LUR	BC	Wide Range Assessment of Memory and Learning	Memory
Forns 2017	BREATHE	Barcelona, Spain	Cohort	2012– 2015	1,439	8.5	8.5 and 11.4	Surface monitoring	PM _{2.5} traffic, EC, NO ₂ , PNC 10–700 nm	<i>n</i> -back test	Working memory (3.5-year change)
Freire 2010	INMA Granada	Granada, Spain	Cross- sectional	2000– 2006	210	Average in year of assessment	4	LUR	NO ₂	McCarthy Scales of Children's Abilities	General, verbal, perceptual- performance, and quantitative cognition; memory
Fuertes 2016	GINIplus, LISAplus	Multiple cities, Germany	Cohort	1995 – 2013	4,745	Annual average at birth, 10 and 15	10 and 15	LUR	PM _{2.5} abs, NO ₂ , PM ₁₀ mass, PM _{2.5} mass	Parent and self-reported questionnaire	Dyslexia condition or symptoms
Gonzalez- Casanova 2018	POSGRAD	Mexico City, Mexico	Cohort	2005 2014	718	Entire pregnancy	1, 1.5, 5, and 7	LUR	Benzene, NO ₂ , NO _X	Composite of Bayley Scales of Infant Development II, McCarthy Scales of Children's Abilities, Wechsler Abbreviated Scale of Intelligence	General cognitive development (over 6 years)
Guxens 2012	INMA	Multiple cities, Spain	Cohort	2002 – 2010	1,854	Entire pregnancy	14 months	LUR	Benzene, NO ₂	Bayley Scales of Infant Development	Infant cognition
Guxens 2014	ESCAPE	Multiple cities, multiple countries	Cohort	2000 – 2011	9,482	Entire pregnancy	1 to 6	Distance or density, LUR	PM _{2.5} abs, NO ₂ , NO _x , PM ₁₀ mass, PM _{2.5} mass, PM _{coarse} mass, traffic density	Composite of Bayley Scales of Infant Development I, II & III, McArthur Communicative Development Inventory, Denver Developmental Screening Test II, McCarthy Scales of Children's Abilities	General cognition, verbal cognition

Reference	Study Name	Location	Study Design	Study period ¹	Sample size ²	Exposure Window)	Age at outcome (yrs)	Exposure Assessment	Pollutant(s)	Neuropsychological test(s)	Cognitive Domain(s)
Guxens 2018	Generation R	Rotterdam, The Netherlands	Cohort	2002 2012	783	Entire pregnancy	6 to 10	LUR	PM _{2.5} abs, PM _{2.5} mass, PM _{coarse} mass	Developmental Neuropsychological Assessment	Attention, response inhibition, memory
Ha 2019	Upstate KIDS	Multiple cities, United States	Cohort	2008 – 2013	5,825	Entire pregnancy, Birth to 3	8 months, 1, 1.5, 2, 2.5, and 3	Distance or density	Traffic distance	Ages and Stages Questionnaire	Communication, personal- social functioning, and problem-solving ability
Harris 2015	Project Viva	Boston, Massachusetts, United States	Cohort	1999 – 20120	1,109	Third trimester, birth to 6, year before assessment	8	Distance or density, LUR	EC, PM _{2.5,} traffic density, traffic distance,	Kaufman Brief Intelligence Test, Wide Range Assessment of Memory and Learning	Verbal cognition, nonverbal cognition, memory
Harris 2016	Project Viva	Boston, Massachusetts, United States	Cohort	1999 – 2010	1,212	Third trimester, birth to 3, birth to 6, year before assessment	6.6 to 10.9, median 7.7	Distance or density, LUR	BC, PM _{2.5} mass, traffic density, traffic distance,	Behavior Rating Inventory of Executive Function, Strengths and Difficulties Questionnaire (parent and teacher report)	Executive function, behavior problems
Khan 2019	Quito Child Health	Quito, Ecuador	Cross- sectional	2016	174	Annual average at assessment	8 to 14	Distance or density	Traffic distance	Behavioral Assessment and Research System	Attention, working memory, memory
Kicinski 2015	Flemish Environmental Health Cohort	Flanders, Belgium	Cross- sectional	2008 – 2011	606	Average at assessment	15	Distance or density	Traffic density	Neurobehavioral Evaluation System -3	Attention, memory
Lertxundi 2015	INMA Gipuzkoa	Gipuzkoa, Spain	Cohort	2006 – 2010	438	Entire pregnancy	15 months	LUR	Benzene, NO ₂	Bayley Scales of Infant Development	Infant cognition
Lertxundi 2019	INMA	Multiple cities, Spain	Cohort	2004 – 2014	1,119	Entire pregnancy	4 to 6	LUR	NO2, PM2.5 mass	McCarthy Scales of Children's Abilities	General, verbal, perceptual- performance, and quantitative cognition, memory
Loftus 2019	CANDLE	Shelby County, Tennessee, United States	Cohort	2006– 2017	905	Entire pregnancy	4 to 6	Distance or density, LUR	NO ₂ , PM ₁₀ mass, traffic distance	Stanford Binet Intelligence Scales, edition 5	General, verbal and quantitative cognition
Lubczyńska 2017	ESCAPE	Multiple cities, multiple countries	Cohort	2000— 2011	7,426	Annual average at birth	1 to 9	LUR, traffic- specific source apportionment	PM _{2.5} Cu, PM _{2.5} Fe, PM _{2.5} Zn, traffic PCA component	Composite of multiple tests ³	General, verbal and non- verbal cognition
Mortamais 2017	BREATHE	Barcelona, Spain	Cohort	2012– 2014	242	Average in year before assessment	8 to 12 (mean 9)	Surface monitoring	Benzo[a]pyren e	Attentional Network Test	Attention (1-year change)
Porta 2016	GASPII	Rome, Italy	Cohort	2003– 2011	474	Annual average at birth	7	Distance or density, LUR	NO2. traffic density	Wechsler Intelligence Scale for Children-III	General, verbal, and perceptual-performance cognition

Reference	Study Name	Location	Study	Study	Sample	Exposure	Age at outcome	Exposure	Pollutant(s)	Neuropsychological test(s)	Cognitive Domain(s)
			Design	period ¹	size ²	Window)	(yrs)	Assessment			
Pujol 2016	BREATHE	Barcelona, Spain	Cohort	2012– 2013	2,827	Annual average at assessment	8 to 12 (mean 9)	Surface monitoring	PM _{2.5} Cu	Attentional Network Test	Attention (1-year change)
Rivas 2019	BREATHE	Barcelona, Spain	Cohort	2012 – 2013	2,221	Entire pregnancy, birth to 1, entire pregnancy to 7	7 to 10 (mean 8.5)	LUR	PM _{2.5} mass	Attentional Network Test, n-back test	Attention, working memory (1-year change)
Saenen 2016	COGNAC	Flanders, Belgium	Cohort	2011– 2014	310	Year before assessment	10	Distance or density, LUR	BC, PM ₁₀ mass, PM _{2.5} mass, traffic density	Stroop Test, Neurobehavioral Evaluation System: Continuous Performance Test, Digit Span Forward and Backward Tests, Digit-Symbol Test, and Pattern Comparison Test	Executive function, attention, working memory, memory
Sentís 2017	INMA	Multiple cities, Spain	Cohort	2003– 2013	1,298	Entire pregnancy, birth to assessment	4 to 5	LUR	NO ₂	Kiddie-Conners Continuous Performance Test	Attention, response inhibition
Suglia 2008	MISSEB	Boston, Massachusetts, United States	Cohort	1986– 2001	218	Birth to assessment	8 to 11, mean 9.7	LUR	BC	Kaufman Brief Intelligence Test, Wide Range Assessment of Memory and Learning	General, verbal and nonverbal cognition, memory
Sunyer 2015	BREATHE	Barcelona, Spain	Cohort	2012– 2013	2,715	Annual average at assessment	9	Distance or density, surface monitoring	EC, NO ₂ , PNC 10-700 nm, traffic density	Attentional Network Test, n-back test	Attention (1-year change), working memory (1-year change)
van Kempen 2012	RANCH Netherlands	Amsterdam, The Netherlands	Cross- sectional	2002	485	Annual average at assessment	10	LUR	NO ₂	Neurobehavioral Evaluation System: Simple Reaction Time Test, Switching Attention Test, Symbol Digit Substitution Test, Digit Memory Span Test	Attention, working memory, memory
Wang 2017	RFAB	Los Angeles, California, United States	Cohort	1990– 2015	1,042	Average in year before assessment	9 to 11, 18 to 20	Dispersion / CTM	NOx	Wechsler Abbreviated Scale of Intelligence	General, verbal, and perceptual-performance cognition

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.

³Composite 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.

Reference	e Study Name ¹	Location	Study period	Sample size	Mean or median exposure ²	Cognitive Domain(s)	Neuropsychologic al test(s)	Exposure Window	Age at outcome (years)	Outcome (direction ³)	Effect measure	Effect Estimate (95% Cl)⁴	Increment
Fuertes 2016	GINIplus, LISAplus	Multiple cities, Germany	1995– 2013	4,745	13.3 South, 17.2 North	Dyslexia	Parent questionnaire	Annual average at birth	10 and 15	Dyslexia (+)	Odds ratio	1.01 (0.82 to 1.25)	1.2 μg/m³ South, 0.9 μg/m³ North
								10				1.08 (0.95 to 1.23)	
								15				1.03 (0.90 to 1.17)	
Guxens 2014	ESCAPE	Multiple cities, multiple countries	2000– 2011	9,482	13.4 to 22.3	General cognition	Composite ⁵	Entire pregnancy	1 to 6	General cognition (–)	Mean difference	0.09(–2.95 to 3.12)	5 μg/m³
						Verbal cognition				Language development (–)		–0.64 (–1/64 to 0.36)	
Guxens 2018	Generation R	Rotterdam, The Netherlands	2002– 2012	783	20.2	Attention	Developmental Neuropsychologic al Assessment	Entire pregnancy	6 to 10	Auditory attention: correct responses (–)	Incidence rate ratio	1.00 (0.99 to 1.01)	5 μg/m³
										Auditory attention:		0.98 (0.92 to 1.03)	
										omission errors Response set: correct responses		1.01 (1.00 to 1.02)	
						Posponso				Response set: omission errors		0.97 (0.94 to 1.00)	
						inhibition				inhibition errors		1.10 (0.63 to 1.93)	
										commission errors		1.00 (0.89 to 1.16)	
										Response set: inhibition errors		1.07 (1.01 to 1.14)	
										commission errors		1.00 (0.96 to 1.04)]

Table 12A-2. Associations of $PM_{2.5}$ mass with cognitive function.

Harris	Project Viva	Boston,	1999–	960	12.3	Verbal	Kaufman Brief	Third trimester	6 to 10 (mean	Verbal IQ (–)	Mean	-0.1 (-1.3 to 1.2)	3.8 μg/m ³
2015		Massachuset	: 2010			cognition	Intelligence Test		8.0)		difference		
		ts, United											
		States											
						Non-verbal				Non-verbal IQ (–)		–0.2 (–1.8 to 1.5)	
						cognition							
						Verbal		Birth to 6 vears		Verbal IQ (–)		0.7 (-0.4 to 1.7)	2.1 µg/m ³
						cognition		,				- (,	1.0
						Nonverbal				Non-verbal IQ (–)		1.1 (–0.2 to 2.5)	
						cognition							
						Verbal		Year before		Verbal IQ (–)		1.1 (0.0 to 2.2)	2.5 µg/m ³
						cognition		assessment				(,	
						Nonverbal				Non-verbal IQ (–)		0.7 (–0.8 to 2.1)	
						cognition							
						Memory	Wide Range	Third trimester		Design Memory (-)		-0.1 (-0.3 to 0.2)	
							Assessment of						1.01
							Memory and						
							Learning						
										Picture Memory (–)		0.1 (–0.2 to 0.4)	
								Birth to 6 years		Design Memory ()		$-0.2(-0.4 \pm 0.01)$	2 1 µg/m ³
										Design Memory ()		0.2 (0.4 (0 0.1)	2.1 μg/
										Picture Memory (–)		0.1 (–0.1 to 0.4)	
								Year before		Design Memory ()		-0.1(-0.4 to 0.1)	2 5 µg/m ³
								assessment				0.1 (0.1 (0 0.1)	2.5 µ6/11
										Picture Memory (–)		0.0 (–0.2 to 0.3)	
Harris	Proiect Viva	Boston.	1999–	1.212	9.4	Executive	Behavior Rating	Third trimester	7.7	Global Executive	Mean	-0.1 (-1.2 to 0.9)	3.8 µg/m ³
2016		Massachuse	2010	-)		function	Inventory of			Function (+)	difference		010 48/111
		ts, United					Executive Function						
		States					(Teacher rated)						
										Behavioral		0.2 (–0.8 to 1.3)	
										Regulation Index (+)			
										Metacognition Index		–0.3 (–1.4 to 0.8)	
										(+)			
								Birth to 3		Global Executive		$0.3(-0.6 \pm 0.1.2)$	2 2 µg/m ³
										Function (+)		0.5 (0.0 (0 1.2)	2.2 μg/11
		1											

						Behavioral Regulation Index (+)	0.4 (–0.5 to 1.3)	
						Metacognition Index (+)	0.2 (–0.7 to 1.1)	
					Birth to 6	Global Executive Function (+)	0.5 (–0.5 to 1.4)	2.1 μg/m³
						Behavioral Regulation Index (+)	0.7 (–0.2 to 1.6)	
						Metacognition Index (+)	0.3 (–0.7 to 1.3)	
					Average in year before	Global Executive Function (+)	0.2 (–0.8 to 1.1)	2.5 μg/m³
					assessment	Behavioral Regulation Index (+)	0.1 (–0.9 to 1.1)	
						Metacognition Index (+)	0.1 (–0.8 to 1.1)	
			Behavior problems	Strengths and Difficulties Questionnaire (teacher report)	Third trimester	Total difficulties (+)	0.3 (–0.3 to 0.9)	3.8 μg/m³
					Birth to 3		0.1 (–0.4 to 0.6)	2.2 μg/m³
					Birth to 6		0.1 (–0.4 to 0.6)	2.1 μg/m³
					Average in year before assessment		0.1 (–0.5 to 0.6)	2.5 μg/m³
				Strengths and Difficulties Questionnaire	Third trimester	Total difficulties (+)	-0.3 (-0.7 to 0.1)	 3.8 μg/m³
				(parent report)	Birth to 3		0.0 (–0.4 to 0.3)	 2.2 μg/m³
					Birth to 6		-0.1 (-0.5 to 0.3)	2.1 μg/m³

								Average in year before assessment				-0.1 (-0.5 to 0.3)	2.1 μg/m³
Lertxundi 2019	INMA	Multiple cities, Spain	2004– 2014	1,119	17.7	General cognition	McCarthy Scales of Children's	Entire pregnancy	4 to 6	General cognition (–)	Mean difference	–0.38 (–0.83 to 0.07)	1 μg/m³
						Verbal cognition	Admities			Verbal (–)		–0.30 (–0.78 to 0.17)	
						Perceptual- performance				Perceptive- Manipulative (–)		–0.35 (–0.80 to 0.11)	
						Quantitative cognition				Numeric (–)		0.03 (–0.45 to 0.50)	
						Memory				Memory (–)		–0.38 (–0.87 to 0.09)	
Rivas 2019	BREATHE	Barcelona, Spain	2012 - 2013	2,221	17	Attention	Attentional Network Test	Entire pregnancy	7 to 10 mean 8.5)	Hit reaction time standard error (+)	Mean difference	–3.93 (–7.58 to – 0.28)	3.44 μg/m³
								Birth to 1				–3.48 (–6.91 to – 0.05)	3.15 μg/m³
								Pregnancy to 7				—2.63 (–6.09 to 0.84	3.11 μg/m³
								Entire pregnancy		Conflict network (+)		1.49 (0.01 to 2.98)	
								Birth to 1				0.84 (–0.56 to 2.23)	
								Pregnancy to 7				2.06 (0.67 to 3.45)	
						Working memory	n-back test	Entire pregnancy		3-back detectability (–)		–3.17 (–6.56 to 0.22)	
								Birth to 1				–2.89 (–6.06 to 0.29)	
								Pregnancy to 7				–2.73 (–5.92 to 0.46)	
Saenen 2016	COGNAC	Flanders, Belgium	2011– 2014	310	15.7	Executive function	Stroop Test	Average in year before assessment	10	Selective attention (+)	Mean difference	59.9 (8.1 to 111.6)	1.16 μg/m³
						Attention	NES 3 ⁶ : Continuous Performance Test			Reaction time (+)		9.45 (2.59 to 16.3)	

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Working	NES3: Digit Span	Digit span backward	0.06 (-0.07 to 0.18)
memory	Test	(+)	
	NES3: Pattern	Pattern comparison	0.05 (–0.09 to 0.19)
	Comparison Test	latency (+)	
	NES3: Digit	Digit symbol latency	2.1 (-0.65 to 4.91)
	Symbol Test	(+)	
Memory	NES3: Digit Span	Digit span forward	–0.03 (–0.15 to
	Test	(+)	0.10)

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; a positive direction (+) means that a higher 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; a positive direction (+) means that a higher 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; a positive direction (+) means that a higher 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; a positive direction (+) means that a higher 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; a positive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive direction (+) means that a higher score indicates poorer cognitive direction or greater cognitive direction (+) means that a higher score indicates poorer cognitive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive direction (+) means that a higher score indicates poorer cognitive direction (+) means that a higher score direction (+) means that a hig

^aDark 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; 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.

Reference	Study Name ¹	Location	Study period	Sample size	Pollutant	Mean or median exposure ²	Cognitive Domain(s)	Neuropsychological test(s)	Exposure Window	Age at outcome (yrs)	Outcome (direction ³)	Effect measure	Effect Estimate (95% CI) ^₄	Increment
Fuertes 2016	GINIplus, LISAplus	Multiple cities, Germany	1995– 2013	4,745	PM ₁₀ mass	20.4 South, 25.2 North	Dyslexia	Parent questionnaire	Annual average at birth	10 and 15	Dyslexia (+)	Odds ratio	1.12 (0.98 to 1.27)	3.0 μg/m³ South, 1.5 μg/m³ North
									10				1.05 (0.92 to 1.20)	
									15				0.98 (0.86 to 1.12)	
Guxens 2014	ESCAPE	Multiple cities, multiple	2000– 2011	9,482	PM ₁₀ mass	33 to 42	General cognition	Composite ⁵	Entire pregnancy	1 to 6	General cognition (–)	Mean differenc e	0.75 (–1.72 to 3.21)	10 μg/m³
		countries					Verbal cognition				Language development (–)		–0.08 (–0.99 to 0.82)	
					PM _{coarse} mass	7 to 20	General cognition				General cognition (–)		0.59 (–0.99 to 2.17)	5 μg/m³
							Verbal cognition				Language development (–)		0.23 (–0.49 to 0.94)	
Guxens 2018	Generation R	Rotterdam, The Netherlands	2002– 2012	783	PM _{coarse} mass	11.8	Attention	Developmental Neuropsychological Assessment	Entire pregnancy	6 to 10	Auditory attention task: omission errors (+)	Incidenc e rate ratio	0.98 (0.92 to 1.05)	5 μg/m³
							Response				Response set task: omission errors (+) Auditory attention		0.98 (0.94 to 1.02) 0.98 (0.55 to 1.76)	
							inition				(+) Auditory attention task: commission		0.99 (0.87 to 1.13)	
											Response set task: inhibition errors (+)		1.04 (0.97 to 1.12)	
											Response set task: commission errors (+)		0.97 (0.92 to 1.02)	

Table 12A-3. Associations of PM_{10} mass and PM_{coarse} mass with cognitive function.

Reference	Study	Location	Study	Sample	Pollutant	Mean or	Cognitive	Neuropsychological	Exposure	Age at	Outcome (direction ³)	Effect	Effect Estimate	Increment
	Name ¹		period	size		median exposure ²	Domain(s)	test(s)	Window	outcome (yrs)		measure	(95% CI)⁴	
Loftus 2019	CANDLE	Shelby County, Tennessee, United States	2006– 2017	905	PM ₁₀ mass	20.88	General cognition	Stanford Binet Intelligence Scales, edition 5	Entire pregnancy	4 to 6	Full Scale IQ (–)	Mean differenc e	-2.44 (-4.80 to - 0.09)	5 μg/m³
							Verbal cognition				Verbal IQ (–)		–2.67 (–5.01 to – 0.34)	
							Nonverbal cognition				Nonverbal IQ (–)		–1.86 (–4.25 to 0.53)	
Saenen 2016	COGNAC	Flanders, Belgium	2011– 2014	310	PM ₁₀ mass	21.3	Executive function	Stroop Test	Average in year before assessment	10	Selective attention (+)	Mean differenc e	76.5 (29.3 to 123.6)	1.61 μg/m³
							Attention	NES3 ⁶ : Continuous Performance Test			Reaction time (+)		8.66 (2.50 to 14.8)	
							Working memory	NES3: Digit Span Test			Digit span backward (+)		0.06 (–0.06 to 0.18)	
								NES3: Pattern Comparison Test			Pattern comparison latency (+)		0.02 (–0.10 to 0.15)	
								NES3: Digit Symbol Test			Digit symbol latency (+)		2.09 (–0.39 to 4.57)	
							Memory	NES3: Digit Span Test			Digit span forward (+)		-0.06 (-0.18 to 0.06)	

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.

⁵ Composite 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.

Reference	Study Name ¹	Location	Study period	Sample size	Pollutant	Mean or median exposure ²	Cognitive Domain(s)	Neuropsychological test(s)	Exposure Window	Age at outcome (years)	Outcome (direction ³)	Effect measure	Effect Estimate (95% Cl) ^₄	Increment
Basagaña 2016	BREAT HE	Barcelona, Spain	2012– 2013	2,618	PM _{2.5} road dust	1.1	Attention	Attentional Network Task			Hit rate standard error (1-year change) (+	Mean difference	2.0 (–0.6 to 4.6)	1.2 μg/m³
							Working memory	<i>n</i> -back test	Annual average at	8.5	2-back detectability (1-		–0.5 (–4.3 to 3.2)	
								n-back test	assessment		3-back detectability (1- year change) (–)		0.4 (–2.5 to 3.4)	
					PM _{2.5} traffic	5.2	Attention	Attentional Network Task			Hit reaction standard error (1- year change) (+)		3.5 (0.9 to 6.1)	2.7 μg/m³
							Working memory	n-back test			2-back detectability (1- year change) (–)		–2.2 (–5.9 to 1.5)	
								n-back test			3-back detectability (1- year change) (–)		–3.6 (–6.5 to –0.6)	
Forns 2017	BREAT HE	Barcelona, Spain	2012– 2015	1,439	PM _{2.5} traffic		Working memory	n-back test	Annual average at first assessment	8.5 and 11.4	3-back detectability (3.5 year change) (–)	Mean difference	–2.30 (–3.65 to 0.96)	2.7 μg/m³
Lubczyńska 2017	ESCAPE	Multiple cities, multiple countries	2000– 2011	7,426	PM _{2.5} Cu	4.95– 12.85	General cognition	Multiple tests ⁵	Annual average at birth	1 to 9	General cognitive function (–)	Mean difference	–1.68 (–5.08 to 1.72)	5 ng/m³
							Verbal cognition				Verbal intelligence (–)		-0.27 (-1.58 to 1.04)	
							cognition				intelligence (–)		0.30)	
					PM _{2.5} Fe	127–251	General cognition Verbal cognition				General cognitive function (–) Verbal intelligence (–)		–1.26 (–3.21 to 0.70) –0.28 (–1.47 to 0.91)	100 ng/m³
							Nonverbal cognition				Non-verbal intelligence (–)		–1.09 (–2.28 to 0.11)	
					PM _{2.5} Zn	19.42– 37.53	General cognition Verbal				General cognitive function (–) Verbal intelligence		–0.66 (–1.87 to 0.55) –0.05 (–0.92 to	10 ng/m³
							cognition Nonverbal cognition				(–) Non-verbal intelligence (–)		0.81) 0.09 (–0.74 to 0.92)	

Table 12A-4.	Associations	of PM co	mponents	with co	ognitive f	function.

Reference	Study	Location	Study	Sample	Pollutant	Mean or	Cognitive	Neuropsychological	Exposure	Age at	Outcome	Effect	Effect Estimate	Increment
	Name ¹		period	size		median	Domain(s)	test(s)	Window	outcome	(direction ³)	measure	(95% CI)⁴	
						exposure ²				(years)				
					PCA traffic	-0.59-	General				General cognitive		–0.26 (–0.65 to	1 unit
					component	5.19	cognition				function (–)		0.14)	
							Verbal				verbal intelligence		–0.16 (–0.51 to	
							cognition				()		0.19)	
							Nonverbal				Non-verbal		–0.20 (–0.55 to	
							cognition				intelligence (–)		0.15)	
Pujol 2016	BREAT	Barcelona,	2012-	2,827	PM _{2.5} Cu	8.7	Attention	Attentional	Annual	8 to 12	Hit reaction time	Mean	4.7 (1.8 to 7.5)	1 ng/m ³
	HE	Spain	2013					Network Test	average at	(mean 9)	(1- year change)	difference		
									assessment		(+)			
											Hit reaction time		3.4 (1.4 to 5.5)	
											standard error (1-			
											vear change) (+)			

¹Study design is cohort for all studies

²Unit 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)

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.

^sComposite 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.

Reference	Study	Location	Study	Sample	Mean or	Cognitive	Neuropsychological	Exposure	Age at	Outcome (direction ³)	Effect	Effect	Increment
	Name ¹		period	size	median	Domain(s)	test(s)	Window	outcome		measure	Estimate	
					exposure ²				(yrs)			(95% CI)⁴	
Forns	BREATHE	Barcelona,	2012-	1,439	21,935	Working memory	<i>n</i> -back test	Annual	8.5 and	3-back detectability	Mean	-3.75 (-5.68	12,770 particles/cm ³
2017		Spain	2015					average in	11.4	(3.5-year change) (–)	difference	to –1.83)	
								year of first					
								assessment					
								(8.5)					
Sunyer	BREATHE	Barcelona,	2012–	2,715	14,407	Attention	Attentional Network	Annual	9	Hit reaction time	Mean	3.9 (0.31 to	6,110 particles/cm ³
2015		Spain	2013				Task	average in		standard error (1-year	difference	7.6)	
								year of		change) (+)			
								assessment					
						Working memory	n-back test			2-back detectability (1-		-4.9 (-10,	
										year change) (–)		0.22)	
										3-back detectability (1-		–5 (–9.1 to –	
										year change) (–)		0.96)	
¹ Study desi	an is cohe	rt for all stu	idioc	•						•			

Table 12A-5. Associations of UFP measured as PNC 10-700 nm with cognitive function.

Study 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.

Reference	Study Name ¹	Location	Study period	Sample size	Mean or median exposure ²	Cognitive Domain(s)	Neuropsychological test(s)	Exposure Window	Age at outcome (yrs)	Outcome (direction ³)	Effect measure	Effect Estimate (95% CI)⁴	Increment
Gonzalez- Casanova 2018	POSGRAD	Mexico City, Mexico	2005– 2014	718	2.3	General cognition	Composite ⁵	Entire pregnancy	1, 1.5, 5, and 7	Low vs. positive cognitive development (–)	Odds ratio	1.00 (0.96 to 1.04)	2.6 µg/m³
										Average vs. positive cognitive development (–)		1.00 (0.96 to 1.03)	2.6 μg/m³
Guxens 2012	INMA	Multiple cities, Spain	2002– 2010	1,854	1.5	Infant cognition	Bayley Scales of Infant Development	Entire pregnancy	14 months	Infant cognition (–)	Mean difference	–1.57 (– 3.69 to 0.56)	doubling
Lertxundi 2015	INMA Gipuzkoa	Gipuzkoa, Spain	2006– 2010	438	0.86	Infant cognition	Bayley Scales of Infant Development	Entire pregnancy	13 to 18 months (mean 15 months)	Infant cognition (–)	Mean difference	–2.35 (90% CI: –8.46 to 3.75)	1 μg/m³

Table 12A-6. Associations of benzene with cognitive function.

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.

⁵ Composite 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 penzolalpyrene) with cognitive t
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Reference	Study	Location	Study	Sample	Mean or	Cognitive	Neuropsychological	Exposure	Age at	Outcome	Effect	Effect	Increment
	Name ¹		period	size	median	Domain(s)	test(s)	Window	outcome (yrs)	(direction ³)	measure	Estimate	
					exposure ²							(95% CI)⁴	
Mortamais	BREATHE	Barcelona,	2012-	242	99	Attention	Attentional Network Test	Year before	8 to 12 (mean	Hit reaction	Mean	3.9 (–5.9	67 pg/m ³
2017		Spain	2014					assessment	9)	time standard	difference	to 13.7)	
										error (1-year			
										change) (+)			

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.

Reference	Study Name ¹	Location	Study	Sample	Traffic	Cognitive	Neuropsychological	Exposure	Age at	Outcome (direction ²)	Effect	Effect Estimate (95% CI) ³	Increment
			period	size	measure	Domain(s)	test(s)	window	outcome (years)		measure		
Guxens 2014	ESCAPE	Multiple cities, multiple countries	2000– 2011	9,482	Density	Verbal cognition	Composite ⁴	Entire pregnancy	1 to 6	Language development (–)	Mean difference	-0.04 (-0.62 to 0.54)	4,000 vehicle- km/day on major roads <100m
Ha 2019	Upstate KIDS	Multiple cities, United States	2008– 2013	5,825	Distance	General cognition	Ages and Stages Questionnaire	Birth to 3	8 months, 1, 1.5, 2, 2.5, and 3	Failure to meet developmental milestones by age 3y (>2 SD below mean) (+)	Relative risk	1.18 (0.75 to 1.86), 1.20 (0.77 to 1.86)	<50 vs. >1,000 m, 50-100 vs. >1,000 m to major road
						Personal-social functioning,				Failure to meet personal-social developmental milestones by age 3y (>2 SD below mean) (+)		2.05 (0.96 to 4.37), 1.87 (0.88 to 3.98)	
						Problem- solving ability				Failure to meet problem-solving developmental milestones by age 3y (>2 SD below mean) (+)		1.32 (0.61 to 2.86), 1.41 (0.69 to 2.89)	
						Communication				Failure to meet communications developmental milestones by age 3y (>2 SD below mean) (+)		1.74 (0.80 to 3.77), 2.12 (1.00 to 4.52)	
Harris 2015	Project Viva	Boston, Massachu setts, United States	1999– 2010	1,101	Density	Verbal cognition	Kaufman Brief Intelligence Test	At birth	6 to 10 (mean 8.0)	Verbal IQ (–)	Mean difference	0.3 (-0.3 to 0.8)	1.6 ln(vehicle- km/day) on roads <100m
						Nonverbal cognition				Non-verbal IQ (–)		0.8 (0.1 to 1.6)	

Table 12A-8. Associations of indirect traffic measures (density, distance) with cognitive function.

Reference	Study Name ¹	Location	Study	Sample	Traffic	Cognitive	Neuropsychological	Exposure	Age at	Outcome (direction ²)	Effect	Effect Estimate (95% CI) ³	Increment
			period	size	measure	Domain(s)	test(s)	Window	outcome (years)		measure		
						Memory	Wide Range Assessment of Memory and Learning			Design Memory (–)		0.1 (0.0 to 0.2)	
										Picture Memory (–)		0.1 (–0.1 to 0.2)	
						Verbal cognitiion	Kaufman Brief Intelligence Test	At midchildho od		Verbal IQ (–)		1.1 (0.0 to 2.2)	1.8 ln(vehicle- km/day) on roads <100 m
						Nonverbal				Non-verbal IQ (–)		1.1 (–0.4 to 2.5)	
						Memory	Wide Range			Design Memory (–)		0.1 (–0.1 to 0.4)	
							Memory and Learning			Picture Memory (–)		0.0 (–0.3 to 0.3)	
					Distance	Verbal cognition	Kaufman Brief	At birth		Verbal IQ (–)		–3.6 (-8.0 to 0.8)	<50 vs. >200 m to major road
						Nonverbal cognition	intelligence rest			Non-verbal IQ (–)		–7.3 (–12.9 to –1.7)	
						Memory	Wide Range			Design Memory (–)		-0.1 (-1.1 to 0.9)	
							Memory and Learning			Picture Memory (–)		–0.4 (–1.5 to 0.6)	
						Verbal cognition	Kaufman Brief Intelligence Test	At ,idchildhoo d		Verbal IQ (–)		1.0 (–4.0 to 6.0)	
						Nonverbal cognition		ŭ		Non-verbal IQ (–)		–5.6 (–11.9 to 0.8)	
						Memory	Wide Range Assessment of Memory and Learning			Design Memory (–)		0.2 (-0.9 to 1. 3)	
										Picture Memory (–)		0.2 (–1.0 to 1.4)	
Harris 2016	Project Viva	Boston, Massachu setts, United States	1999– 2010	1,212	Density	Executive function	Behavior Rating Inventory of Executive Function (Teacher rated)	At birth	7.7	Global Executive Function (+)	Mean difference	-0.1 (-0.6 to 0.4)	1425 vehicle- km/day on roads <100 m
										Behavioral Regulation Index (+) Metacognition Index (+)		0.1 (0.4 to 0.6) 0.2 (0.7 to 0.3)	

Reference	Study Name ¹	Location	Study	Sample	Traffic	Cognitive	Neuropsychological	Exposure	Age at	Outcome (direction ²)	Effect	Effect Estimate (95% CI) ³	Increment
			period	size	measure	Domain(s)	test(s)	Window	outcome		measure		
									(years)				
								At		Global Executive		0.2 (-0.3 to 0.8)	
								midchildho		Function (+)			
								od					
										Behavioral Regulation		0.6 (0.1 to 1.1)	
										Index (+)			
										Metacognition Index		–0.0 (–0.5 to 0.5)	
										(+)			
					Distance			At birth		Global Executive		2.7 (–1.6 to 7.1)	<50 vs. >200 m to
										Function (+)			major road
										Behavioral Regulation		3.5 (–0.7 to 7.8)	
										Index (+)			
										Metacognition Index		1.8 (–2.6 to 6.3)	
										(+)			
								At		Global Executive		1.2 (–3.1 to 5.5)	
								midchildho		Function (+)			
								od				20/22/202	
												2.0 (-2.2 to 6.3)	
										Motocognition Index			
												0.5 (-3.9 (0 5.0)	
					Donsity	Behavior	Strengths and	At hirth		(+) Total difficulties (+)		$0.0(-0.3 \pm 0.03)$	1 425 vehicle-
					Density	nrohlems	Difficulties	AUDIT				0.0 (-0.5 10 0.5)	km/day on roads
						problems	Questionnaire						<100 m
							(teacher report)						100 111
							()	At				0.1 (-0.2 to 0.3)	1.241 vehicle-
								midchildho					km/day on roads
								od					<100 m
					Distance			At birth				1.5 (–1.0 to 3.9)	<50 vs. >200 m to
													major road
								At				0.1 (–2.4 to 2.5)	
								midchildho					
								od					
					Density		Strengths and	At birth		Total difficulties (+)		0.1 (–0.1 to 0.3)	1,425 vehicle-
							Difficulties						km/day on roads
							Questionnaire						<100 m
							(parent report)						
								At				0.1 (–0.1 to 0.3)	1,241 vehicle-
								midchildho					km/day on roads
								od					<100 m
					Distance			At birth				0.9 (–0.6 to 2.5)	<50 vs. >200 m to
								۸ <i>+</i>				02/21+015	major road
								AL				-0.3 (-2.1 to 1.5)	
			1					ad					
			1					ua			1		

Reference	Study Name ¹	Location	Study	Sample	Traffic	Cognitive	Neuropsychological	Exposure	Age at	Outcome (direction ²)	Effect	Effect Estimate (95% CI) ³	Increment
	-		period	size	measure	Domain(s)	test(s)	Window	outcome		measure		
									(years)				
Khan 2019	Quito Child Health	Quito, Ecuador	2016	174	Distance	Attention	Behavioral Assessment and Research System	Annual average at assessment	8 to 14	Continuous performance fraction correct (–)	Mean difference	-0.03 (-0.10 to 0.04)	<100 vs. >200 m to major road >10,000 vehicles/day
						Attention Working memory	Child Behavioral Checklist Behavioral Assessment and Research System			Attention Problems (+) Digit span backward (–)		0.64 (–0.80 to 2.02) 0.48 (–0.15 to 1.13)	
						Memory				Match to sample correct count (–)		–0.16 (–1.11 to 0.78)	
										Digit span forward (–)		0.25 (–0.21 to 0.72)	
Kicinski 2015	Flemish Environmental Health Cohort	Flanders, Belgium	2008– 2011	606	Density	Attention	Neurobehavioral Evaluation System - 3	Average at assessment	15	Sustained attention (–)	Mean difference	-0.02 (-0.12 to 0.08)	doubling
						Memory				Short term memory (– –)		0.07 (–0.01 to 0.16)	
Loftus 2019	CANDLE	Shelby County, Tennesse e, United	2006– 2017	905	Distance	General cognition	Stanford Binet Intelligence Scales, edition 5	Annual average at birth	4 to 6	Full Scale IQ (–)	Mean difference	-0.49 (-2.27 to 1.30)	<150 vs. >150 m to major road
		States				Verbal cognition				Verbal IQ (–)		–0.54 (–2.36 to 1.29)	
						Nonverbal cognition				Nonverbal IQ (–)		-0.63 (-2.47 to 1.21)	
Porta 2016	GASPII	Rome, Italy	2003– 2011	474	Density	General cognition	Wechsler Intelligence Scale for Children-III	At birth	7	Full scale IQ (–)	Mean difference	-1.1 (-2.3 to 0.10)	4,000 vehicle- km/day on roads <100 m
						Verbal cognition				Verbal IQ (–)		–1.8 (–3.5 to –0.80)	
						Perceptual- performance				Performance IQ (–)		-1.7 (-3.6 to 0.20)	

Reference	Study Name ¹	Location	Study	Sample	Traffic	Cognitive	Neuropsychological	Exposure	Age at	Outcome (direction ²)	Effect	Effect Estimate (95% CI) ³	Increment
			period	size	measure	Domain(s)	test(s)	Window	outcome (years)		measure		
Saenen 2016	COGNAC	Flanders, Belgium	2011– 2014	310	Distance	Executive function	Stroop Test	Average in year before assessment	10	Selective attention (+)	Mean difference	0.90 (–20.6 to 22.4)	living twice as close to major road
						Attention	NES3⁵: Continuous Performance Test			Reaction time (+)		1.92 (–1.0 to 4.85)	
						Working memory				Digit span backward (+)		-0.04 (-0.1 to 0.01)	
							NES3: Pattern Comparison Test			Pattern comparison latency (+)		0.00 (–0.06 to 0.06)	
							NES3: Digit Symbol Test			Digit symbol latency (+)		0.39 (–0.79 to 1.58)	
						Memory	NES3: Digit Span Test			Digit span forward (+)		–0.05 (–0.10 to 0.01)	
Sunyer 2015	BREATHE	Barcelona , Spain	2012– 2013	2,715	Density	Attention	Attentional Network Task	Annual average in year of assessment	9	Hit reaction time standard error (1-year change) (+)	Mean difference	5.2 (0.68 to 9.7)	high vs. low traffic
						Working memory	n-back test			2-back detectability (1-year change) (–)		–9.9 (–16 to –3.5)	
										3-back detectability (1-year change) (–)		–5.8 (–11.0 to –0.74)	

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.

Exposure 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	characteristic	cs of stu	dies includ	ed in th	ne literatur	e review for	ADHD and rel	ated behaviors in chil	dren – pollutants	and
indirect traft	fic measure	es (N=8).									

Reference	Study Name	Location	Study Design	Study period ¹	Sample size ²	Exposure Window	Age at outcome (yrs)	Exposure Assessment	Pollutant(s)	Neuropsychological test(s)
Forns 2016	BREATHE	Barcelona, Spain	Cross- sectional	2012–2013	2,714	At assessment	7 to 11	Surface monitoring	EC, NO ₂	Strengths and Difficulties Questionnaire (parent report), ADHD-DSM-IV list criteria (teacher report)
Forns 2018	ESCAPE	Multiple cities, multiple countries	Cohort	1992 – 2012	29,127	Entire pregnancy	3 to 10	Distance or density, LUR	Traffic density, PM _{2.5} abs, NO ₂ , NO _X , PM ₁₀ mass, PM _{2.5} mass, PM _{coarse} mass	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)
Fuertes 2016	GINIplus, LISAplus	Multiple cities, Germany	Cohort	1995–2013	4,745	Annual average at birth, 10, 15	10 and 15	LUR	PM _{2.5} abs, NO ₂ , PM ₁₀ mass, PM _{2.5} mass	Strengths and Difficulties Questionnaire (parent and self-report)
Gong 2014	CATSS	Stockholm, Sweden	Cohort	1992–2012	3,426	Entire pregnancy, 1, year before assessment	9 or 12	Dispersion / CTM	NO _x , PM ₁₀ mass	Autism-Tics, ADHD, and other Comorbidities inventory (parent report)
Mortamais 2017	BREATHE	Barcelona, Spain	Cohort	2012–2014	242	Year before assessment	8 to 12	Surface monitoring	Benzo[a]pyrene	ADHD-DSM-IV list criteria (teacher report)
Newman 2013	CCAAPS	Cincinnati, Ohio, United States	Cohort	2001–2010	576	First year of life	7	LUR	EC	ADHD symptoms on the Behavioral Assessment System for Children, 2nd Edition (parent report)
Roberts 2019	E-Risk Longitudinal Twin Study	London, United Kingdom	Cohort	1994–2013	284	12	12 and 18	Dispersion / CTM	NO ₂ , PM _{2.5} mass	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)
Saez 2018	IAS Girona Spain	Girona, Spain	Case- control	1998–2012	5,193	In first year of follow-up, up to 8	Up to 15	Distance or density	Traffic distance	Diagnosis of ADHD by health service primary care physician on WHO criteria (ICD-10: F90.0, F98.8)

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.

Reference	Study Name ¹	Location	Study period	Sample size	Exposure Window	Age at outcome (years)	Exposure Assessment	Mean or median exposure ²	Neuropsychological test(s)	Outcome (direction ³)	Effect measure	Effect Estimate (95% CI) ^₄	Increment
Forns 2018	ESCAPE	Multiple cities, multiple countries	1992– 2012	29,127	Entire pregnancy	3–10	LUR	9 - 23	Multiple tests⁵	ADHD traits within borderline or clinical range (+)	Odds ratio	0.98 (0.80 to 1.19)	5 μg/m³
Fuertes 2016	GINIplus, LISAplus	Multiple cities, Germany	1995– 2013	4,745	Annual average at birth 10 15	10 and 15	LUR	13.3 South, 17.2 North	Strengths and Difficulties Questionnaire (parent report at 10 years, self- report at 15 years)	Hyperactivity/inattentio n problems: borderline/abnormal vs. normal (+)	Odds ratio	1.06 (0.96 to 1.17) 1.12 (1.01 to 1.23) 1.11 (1.01 to 1.22)	1.2 μg/m³ South, 0.9 μg/m³ North
Roberts 2019	E-Risk Longitudinal Twin Study	London, United Kingdom	1994– 2013	284	12	12	Dispersion / CTM	14.09	DSM-IV criteria and the Rutter Child Scales (parent and teacher reported)	ADHD traits - inattention, hyperactivity-impulsivity (+)	Mean difference	0.05 (-0.11 to 0.20)	1 μg/m³
									(parent and co-informant reported)	ADHD traits - (+)		0.04 (-0.14 to	
									Diagnostic Interview Schedule using DSM-IV, DSM-V criteria	ADHD psychiatric diagnosis (+)	Odds ratio	1.16 (0.64 to 2.10)	

-1 (36/10) -1 Z (3 Z (3 10) (3 1	Table 12B-2, Association	s of PM₂₅ m	ass with ADHD a	and related behaviors.
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¹Study design is cohort except for Forns 2016 which is cross-sectional.

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.

⁵Autism-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.

Reference	Study Name ¹	Location	Study period	Sample size	Exposure Assessment	Pollutant	Mean or median exposure ²	Neuropsychological test(s)	Exposure Window	Age at outcome (years)	Outcome (direction ³)	Effect measure	Effect Estimate (95% CI) ⁴	Increment
Forns 2018	ESCAPE	Multiple cities, multiple countries	1992– 2012	29,127	LUR	PM ₁₀ mass	18 - 42	Multiple tests ⁵	Entire pregnancy	3 to 10	ADHD traits within borderline or clinical range (+)	Odds ratio	0.97 (0.79 to 1.19)	10 μg/m³
						PM _{coarse} mass	8 - 21						0.98 (0.84 to 1.13)	5 μg/m³
Fuertes 2016	GINIplus, LISAplus	Multiple cities, Germany	1995– 2013	4,745	LUR	PM ₁₀ mass	20.4 South, 25.2 North	Strengths and Difficulties Questionnaire (parent report at 10y and self- report at 15y)	Annual average at birth 10 15	10 and 15	Hyperactivity/inat tention problems: borderline/abnor mal vs. normal (+)	Odds ratio	1.07 (0.96 to 1.18) 1.05 (0.95 to 1.17) 1.04 (0.94 to 1.15)	3.0 μg/m ³ South, 1.5 μg/m ³ North
Gong 2014	CATSS	Stockholm, Sweden	1992– 2012	3,426	Dispersion / CTM	PM ₁₀ mass	3.5	Autism-Tics, ADHD, and other Comorbidities inventory (parent report)	Entire pregnancy First year Year before	9 or 12	Probable ADHD diagnosis based on DSM-IV criteria (+)	Odds ratio	0.85 (0.48 to 1.50) 0.95 (0.56 to 1.61) 1.33 (0.73 to 2.41)	95th to 5th percentile difference

Table 12B-3. Associations of PM₁₀ mass and PM_{coarse} mass with ADHD and related behaviors.

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; a positive direction (+) means that a higher 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; a positive direction (+) means that a higher score indicates poorer cognitive function or greater cognitive difficulty; a positive 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; Light blue=suggestive evidence; Light blue=suggestive; Light blue=suggestive;

^sAutism-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)

Reference	Study Name ¹	Location	Study period	Sample size	Exposure Assessment	Mean or median exposure ²	Neuropsychological test(s)	Exposure Window	Age at outcome (years)	Outcome (direction ³)	Effect measure	Effect Estimate (95% CI) ^₄	Increment
Mortamais	BREATHE	Barcelona,	2012-	242	Surface	99	ADHD-DSM-IV	Annual	8 to 12,	Total ADHD score (+)	Relative	1.18 (0.96 to	67 pg/m ³
2017		Spain	2014		monitoring		criteria (teacher)	average in	mean 9		risk	1.45)	
								year before		Inattention (+)		1.20 (0.98 to	
								assessment				1.46)	
										Hyperactivity (+)		1.17 (0.92 to	
												1 47)	

Table 12B-4. Associations of PAH measured as benzo[a]pyrene with ADHD and related behaviors.

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.

Reference	Study Name ¹	Location	Study period	Sample size	Traffic measure	Neuropsychological test(s)	Exposure Window	Age at outcome (years)	Outcome (direction ²)	Effect measure	Effect Estimate (95% CI) ³	Increment
Forns 2018	ESCAPE	Multiple cities, multiple countries	1992– 2012	29,127	Density	Multiple tests ⁴	Entire pregnancy	3 to 10	ADHD traits within borderline or clinical range (+)	Odds ratio	1.04 (0.96–1.13)	4,000 vehicle- km/day
Saez 2018	IAS Girona Spain	Girona, Spain	1998– 2012	5,193	Distance	Diagnosis of ADHD by primary physician	At assessment	Up to 8 at start, up to 15 at end	Diagnosis of ADHD by primary physician (ICD- 10: F90.0, F98.8) (+)	Odds ratio	1.88 (0.14–14.30) 1.16 (0.19–5.25) 1.08 (0.25–3.67) 1.22 (0.29–4.10)	<50 vs. >300 m to nearest road 50–100 vs. >300 m to nearest road 101–200 vs. >300 m to nearest road 201–300 vs. >300 m to nearest road

Table 12B-5. Associations of indirect traffic measures (density, distance) with ADHD and related behaviors.

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).

Reference	Study Name	Location	Study Design	Study period ¹	Sample size ²	Exposure Window)	Age at outcome (yrs)	Exposure Assessment	Pollutant(s)	Neuropsychological Test(s)/ Diagnostic Tool(s)
Becerra 2013	Los Angeles County DDS	Los Angeles County, California, United States	Case-control	1998 – 2009	58,423	Entire pregnancy	3 to 5	LUR	NO, NO2	Autistic disorder (AD) diagnosis identified using California DDS database
Chen 2018	Shanghai Early Life	Shanghai, China	Case-control	2014	1,364	First 3 years	3 to 12	LUR	PM ₁₀ mass, PM _{2.5} mass	Population-based screening using the Social Communication Questionnaire (parent and teacher report) followed by confirmatory ASD diagnosis by pediatrician based on DSM-V
Gong 2014	CATSS	Stockholm, Sweden	Cohort	1992– 2012	3,426	Entire pregnancy, first year, year before assessment	9 or 12	Dispersion / CTM	NOx, PM10 mass	Autistic traits on Autism-Tics, ADHD, and other Comorbidities inventory (parent report)
Gong 2017	Stockholm Youth Cohort	Stockholm, Sweden	Case-control	2001– 2011	23,373	Entire pregnancy, first year	Up to 13	Dispersion / CTM	NO _x , PM ₁₀ mass	ASD diagnosis from national registries, based on ICD 9/10 and DSM-IV criteria, with and without intellectual disability (ID)
Goodrich 2018	CHARGE	California, United States	Case-control	2002 – 2011	606	Entire pregnancy and each trimester	2 to 5	Dispersion / CTM	NOx	ASD diagnosis using California Department of Developmental Services criteria (uses Autism Diagnostic Observation Schedule-Generic (ADOS) Autism Diagnostic Interview-Revised (ADI-R)
Guxens 2016	ESCAPE	Multiple cities, multiple countries	Cohort	1992– 2012	8,079	Entire pregnancy	4 to 10	Distance or density, LUR	Traffic density, PM _{2.5} abs, NO ₂ , NO _x PM ₁₀ mass, PM _{2.5} mass, PM _{coarse} mass	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
Pagalan 2019	Vancouveı 2004 - 2009 birth	Vancouver, British Columbia, Canada	Cohort	2004– 2014	129,436	Entire pregnancy	Up to 5	LUR	NO, NO2	ASD diagnosis by physician on standardized health service criteria, using Autism Diagnostic Observation Schedule (ADOS) and Autism Diagnostic Interview Revised (ADI-R)
Raz 2018	NII Israel	Multiple cities, Israel	Case-control	2005– 2014	56,290	Entire pregnancy, first 9 months	4 to 9	Dispersion / CTM	NO ₂	ASD disability determined by physician-led team on DSM-IV criteria, from national insurance database

Reference	Study	Location	Study Design	Study	Sample size ²	Exposure	Age at outcome	Exposure	Pollutant(s)	Neuropsychological Test(s)/ Diagnostic Tool(s)
	Name			period		Window)	(yrs)	Assessment		
Ritz 2018	Danish ASD	Denmark	Case-control	1995- 2016	83,526	Entire pregnancy,	not reported	Dispersion / CTM	NO ₂ , PM _{2.5} mass, PM ₁₀	ASD as reported in Danish National Patient Register, based on admissions and
						first 9 months			mass	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
Talbott 2015a	SW PA children	Pittsburgh, Pennsylvania, United States	Case-control	2011– 2013	430	Entire pregnancy, first year, second year	Not reported	LUR	PM _{2.5} mass	ASD diagnosis by psychiatrist psychologist and high score on Autism Diagnostic Observation Schedule (ADOS) or other test, and high score on Social Communications Questionnaire
Talbott 2015b	SW PA children	Pittsburgh, Pennsylvania, United States	Case-control	2011– 2013	441	Entire pregnancy	Not reported	Dispersion / CTM	Diesel PM ₁₀	ASD diagnosis by psychiatrist psychologist with Autism Diagnostic Observation Schedule (ADOS) or other test, and high score on Social Communications Questionnaire
Volk 2011	CHARGE	California, United States	Case-control	2003– 2009	563	Entire pregnancy	2 to 5	Distance or density	Traffic distance	ASD diagnosis identified using California Department of Developmental Services (uses Autism Diagnostic Observation Schedule- Generic (ADOS) Autism Diagnostic Interview- Revised (ADI-R))
Volk 2013	CHARGE	California, United States	Case-control	2003– 2009	524	Entire pregnancy, each trimester, first year	2 to 5	Dispersion / CTM	NOx	ASD diagnosis identified using California Department of Developmental Services (uses Autism Diagnostic Observation Schedule- Generic (ADOS) Autism Diagnostic Interview- Revised (ADI-R))
von Ehrenstein 2014	Los Angeles County DDS	Los Angeles County, California, United States	Cohort	1998– 2009	126,402	Entire pregnancy	3 to 6	Surface monitoring	Benzene, PAH, PM2.5 Cu	Autistic disorder primary diagnosis from Client Evaluation Report of the California Department of Developmental Services records

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.

							Mean or		Age at			
	Study		Study	Study	Sample	Exposure	median	Exposure	outcome			
Reference	Name	Location	Design	period	size	Assessment	exposure ¹	Window	(years)	ASD diagnosis or neuropsychological test(s)	Odds Ratio (95% CI) ²	Increment
Becerra	Los	Los Angeles	Case-	1998–	58,423	LUR	28.7	Entire	3 to 5	Autistic disorder (AD) diagnosis identified	1.02 (0.96–1.08)	18.46 ppb
2013	Angeles	County,	control	2009				pregnancy		using California DDS database (DSM-IV-R		
	County	California,								299.00)		
	DDS	United States										
Pagalan	Vancouver	Vancouver,	Cohort	2004–	129,436	LUR	18.3	Entire	6 to 11	ASD diagnosis by physician on standardized	1.07 (1.01–1.13)	10.7 ppb
2019	2004 -	British		2014				pregnancy		health service criteria, using Autism		
	2009 birth	Columbia,								Diagnostic Observation Schedule (ADOS) and		
		Canada								Autism Diagnostic Interview Revised (ADI-R)		
¹ Unit in th	e increment	column.										
2Odds ratio	>10 indic	ata highar rick f	or ASD									

Table 12C-2. Associations of NO with ASD and related behaviors.

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.

							Mean or		Age at			
	Study		Study	Study	Sample	Exposure	median	Exposure	outcome			
Reference	Name	Location	Design	period	size	Assessment	exposure ¹	Window	(yrs)	ASD diagnosis or neuropsychological test(s)	Odds Ratio (95% CI) ²	Increment
Chen	Shanghai	Shanghai,	Case-	2005–	1,364	LUR	66.2	First year	7	Population-based screening using the Social	1.07 (0.80–1.43)	3.4 μg/m³
2018	Early Life	China	control	2014						Communication Questionnaire followed by		
								Second year		confirmatory ASD diagnosis by pediatrician	1.50 (1.01–2.22)	
								Third year		based on DSM-V	1.78 (1.05–3.02)	
								First 3 years			1.78 (1.14–2.76)	
Guxens 2016	ESCAPE	Multiple cities, multiple countries	Cohort	1992– 2012	8,079	LUR	8.4-22.4	Entire pregnancy	4 to 10	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 Clinical range for ASD using validated	0.71 (0.37–1.37) 1.01 (0.63–1.63)	5 μg/m³
										cuttoffs as described above		
Ritz 2018	Danish ASD	Denmark	Case-	1995-	83,526	Dispersion /	14.39	Entire	Below 5 to	ASD as reported in Danish National Patient	0.96 (0.91–1.02)	3.61 μg/m³
			control	2016		СТМ		pregnancy	not	Register, based on admissions and		
									reported	outpatient/emergency room consultations,		
								First 9		and the Danish Psychiatric Central Register	1.06 (1.01–1.11)	
								months		(PCR) based on psychiatric admissions to		
										hospitals and outpatient clinics		
Talbott	SW PA	Pittsburgh,	Case-	2011–	430	LUR	14.8	Entire	Not	ASD diagnosis by psychiatrist or psychologist	1.20 (0.88–1.63)	2.84 μg/m³
2015a	children	Pennsylvania,	control	2013				pregnancy	reported	including Autism Diagnostic Observation		
		United States						First year		Schedule (ADOS) or other test, and high	1.37 (0.95–1.97)	
								Second year		score on Social Communications Questionnaire	1.45 (1.01–2.08)	

Table 12C-3. Associations of PM_{2.5} mass with ASD and related behaviors.

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.

								Mean or		Age at			
	Study		Study	Study	Sample	Exposure		median	Exposure	outcome	ASD diagnosis or	Odds Ratio (95%	
Reference	Name	Location	Design	period	size	Assessment	Pollutant	exposure1	Window	(yrs)	neuropsychological test(s)	CI) ²	Increment
Chen 2018	Shanghai Early Life	Shanghai, China	Case- control	2014	1,364	LUR	PM ₁₀ mass	95.4	First year	Mean 7	Population-based screening using the Social Communication Questionnaire followed by 2	1.16 (0.91–1.49)	4.9 μg/m³
									Second year		independent ASD diagnoses by pediatricians according to DSM-V	1.73 (1.11–2.68)	
									Third year		criteria	1.58 (0.98–2.56)	
									First 3 years			1.68 (1.09–2.59)	
Gong	CATSS	Stockholm,	Cohort	1992–	3,426	Dispersion /	PM ₁₀ mass	3.5	Entire	9 or 12	Autism-Tics, ADHD, and other	0.78 (0.39–1.56)	95th to 5th
2014		Sweden		2012		СТМ			pregnancy		Comorbidities inventory, used a cut- off consistent with ASD diagnosis		percentile difference
									First year		based on DSM-IV criteria	0.92 (0.47–1.79)	
									Vear before	-		1 97 (0 58-6 76)	-
									assessment			1.57 (0.58 0.70)	
Gong	Stockholm	Stockholm,	Case-	2001-	23,373	Dispersion /	PM ₁₀ mass	4.2	Entire	Up to 13	ASD diagnosis from national	1.00 (0.86–1.15)	20 µg/m³
2017	Cohort	Sweden	control	2011					First year		DSM-IV criteria, with and without intellectual disability (ID)	1.03 (0.87–1.21)	
Guxens 2016	ESCAPE	Multiple cities, multiple countries	Cohort	1992– 2012	8,079	LUR	PM ₁₀ mass	18-42	Entire pregnancy	4 to 10	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	0.90 (0.68–1.19)	10 μg/m³
											Clinical range for ASD using validate cutoffs as described above	0.92 (0.55–1.54)	
							PM _{coarse} mass	9-19			Borderline/clinical range for ASD using validated cutoffs as described above	0.96 (0.72–1.28)	5 μg/m³
											Clinical range for ASD using validated cutoffs as described above	0.87 (0.55–1.38)	

Table 12C-4. Associations of PM₁₀ mass and PM_{coarse} mass with ASD and related behaviors.

Reference	Study Name	Location	Study Design	Study period	Sample size	Exposure Assessment	Pollutant	Mean or median exposure ¹	Exposure Window	Age at outcome (yrs)	ASD diagnosis or neuropsychological test(s)	Odds Ratio (95% CI) ²	Increment
Ritz 2018	Danish ASD	Denmark	Case-	1995–	83,526	Dispersion /	PM ₁₀ mass	17.13	Entire	Below 5 to	ASD as reported in Danish National	0.95 (0.91–1.00)	3.80 µg/m³
			control	2016		СТМ			pregnancy	not	Patient Register, based on		
										reported	admissions and		
									9 months		outpatient/emergency room	1.04 (1.00-1.09)	
											consultations, and the Danish		
											Psychiatric Central Register (PCR)		
											based on psychiatric admissions to		
											hospitals and outpatient clinics		

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.

Reference	Study	Location	Study	Study	Sample	Exposure	Pollutant	Mean or	Exposure	Age at	ASD diagnosis or	Odds Ratio (95%	Increment
	Name		Design	period	size	Assessment		median	Window	outcome	neuropsychological test(s)	CI) ²	
Talbott	SW PA	Pittsburgh,	Case-	2011–	441	Dispersion /	Diesel PM ₁₀	399.98	Entire	Not	ASD diagnosis by psychiatrist	1.04 (0.59–1.84)	>589 vs.
2015b	children	Pennsylvania, United States	control	2013		СТМ			pregnancy	reported	or psychologist with Autism Diagnostic Observation Schedule (ADOS) or other test, and high score on Social Communications Questionnaire	1.00 (0.57–1.77)	<255 ng/m ³ 400-589 vs. <255 ng/m ³
												1.15 (0.66–2.00)	255-400 vs. <255 ng/m ³
von Ehrenstein 2014	Los Angeles County DDS	Los Angeles County, California, United States	Cohort	1998– 2009	78,721	Surface monitoring	PM _{2.5} Cu	59.12	Entire pregnancy	3 to 6	Autistic disorder primary diagnosis recorded by California Department of Developmental Services	1.09 (1.02–1.16)	22.81 ng/m ³
¹ Unit in the i ² Odds ratio >	Unit in the increment column.												

Table 12C-5. Associations of PM components with ASD and related behaviors.

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.

Reference	Study Name	Location	Study Design	Study period	Sample size	Exposure Assessment	Mean or median exposure ¹	Exposure Window	Age at outcome (yrs)	ASD diagnosis or neuropsychological test(s)	Odds Ratio (95% Cl) ²	Increment
von	Los	Los Angeles	Cohort	1998–	109,062	Surface	1.14	Entire	3 to 6	Autistic disorder primary	1.03 (0.84–1.26)	0.79 ppb
Ehrenstein	Angeles	County,		2009		monitoring		pregnancy		diagnosis recorded by		
2014	County	California,								California Department of		
	DDS	United								Developmental Services		
		States										

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.

							Mean or		Age at			
			Study	Study	Sample	Exposure	median	Exposure	outcome	ASD diagnosis or	Odds Ratio (95%	
Reference	Study Name	Location	Design	period	size	Assessment	exposure ¹	Window	(yrs)	neuropsychological test(s)	CI) ²	Increment
von Ehrenstein	Los Angeles	Los Angeles	Cohort	1998–	126,402	Surface	1.16	Entire	3 to 6	Autistic disorder primary	1.46 (1.12–1.89)	0.78 ppb
2014	County DDS	County, California,		2009		monitoring		pregnancy		diagnosis recorded by California		
		United States								Department of Developmental		
										Services		
¹ Unit in the incr	¹ Unit in the increment column.											
² Odds ratio >1.0 indicate higher risk for ASD.												
³ Dark orange=e	³ 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 orange=suggestive evidence of association with ASD or more ASD traits; Dark blue=evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits; Light orange=suggestive evidence of association with ASD or more ASD traits;											
traits; Light blue	e=suggestive e	vidence of associati	on with	ASD or n	nore ASD tr	aits.						

Reference	Study Name	Location	Study Design	Study period	Sample size	Traffic measure	Exposure Window	Age at outcome (yrs)	ASD diagnosis or neuropsychological test(s)	Odds Ratio (95% CI) ¹	Increment						
Guxens 2016	ESCAPE	Multiple cities, Italy, multiple countries	Cohort	1992– 2012	8,079	Density	At birth	4 to 10	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	1.02 (0.89–1.16)	4,000 vehicle-km/day on major roads <100 m						
									Clinical range for ASD using validated cutoffs as described above	0.90 (0.70–1.16)							
Volk 2011	CHARGE	California, United States	California, United States	Case- control	2003– 2009	563	Distance to nearest freeway	Entire pregnancy	2 to 5	ASD diagnosis identified using California Department of Developmental Services criteria (uses Autism Diagnostic Observation Schedule-Generic (ADOS) Autism	1.86 (1.03–3.45)	<309m (closest 10%) to nearest freeway vs. >1,419m (furthest 50%)					
									Diagnostic Interview-Revised (ADI-R))	0.96 (0.58–1.56)	309-647m (closest 10- 25%ile) to nearest freeway vs. >1,419m (furthest 50%)						
										1.11 (0.73–1.67)	647-1,419m (closest 25- 50%ile) to nearest freeway vs. >1,419m (furthest 50%)						
												Distance to major road		0.71 (0.	0.71 (0.39–1.26)	≤42m (closest 10%) to major road vs. >209m (furthest 50%)	
																	1.29 (0.77–2.18)
															0.83 (0.55–1.26)	96-209m (closest 25- 50%ile) to major road vs. >209m (furthest 50%)	

Table 12C-8. Associations of indirect traffic measures with ASD and related behaviors.

¹Odds ratio >1.0 indicate higher risk for ASD.

²Dark 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).

Neighborhood socioeconomic status

Appendix 12D References for studies included in the literature review of neurodevelopmental outcomes

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