

Additional file 1

Environmental Pollutants as Risk Factors for Autism Spectrum Disorders: A Systematic Review and Meta-Analysis of Cohort Studies

Tatiana Duque-Cartagena^{1,8}, Marcello Dala Bernardina Dalla^{2,3,4}, Eduardo Mundstock^{5,6}, Felipe Kalil Neto⁷, Sergio Angelo Rojas Espinoza⁸, Sara Kvitko de Moura⁹, Gabriele Zanirati^{1,10}, Alexandre Vontobel Padoin¹, Juan Gabriel Piñeros Jimenez¹¹, Airton Tetelbom Stein^{12,13}, Wilson Cañon-Montañez¹⁴, Rita Mattiello⁸.

¹Pontifical Catholic University of Rio Grande do Sul (PUCRS), School of Medicine, Post-Graduate Program in Medicine and Health Sciences, Porto Alegre, RS, Brazil.

²Cassiano Antônio de Moraes University Hospital, Universidade Federal do Espírito Santo (HUCAM/UFES), Vitória, ES, Brazil.

³Capixaba Institute for Teaching Research and Innovation of the State Health Department of Espírito Santo (ICEPI-SESA), Vitória, ES, Brazil.

⁴Espirito Santense College – FAESA, Cariacica, ES, Brazil.

⁵Universidade Leonardo da Vinci, Polo Canela, RS, Brazil.

⁶Secretaria da Educação Esporte e Lazer de Canela-Escola Zeferino José Lopes, Canela, RS, Brazil.

⁷ Pontifical Catholic University of Rio Grande do Sul (PUCRS), School of Medicine, Porto Alegre, RS, Brazil.

⁸Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil.

⁹Presidente Vargas Maternal and Child Hospital, Porto Alegre, RS, Brazil.

¹⁰Brain Institute of Rio Grande do Sul (BraIns), Porto Alegre, RS, Brazil.

¹¹National Faculty of Public Health, Universidad de Antioquia, Medellín, Colombia.

¹²Departamento de Saúde Pública, Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, RS, Brazil.

¹³Hospital Conceição, Porto Alegre, RS, Brazil.

¹⁴Faculty of Nursing, Universidad de Antioquia, Medellín, Colombia.

Corresponding Author: Rita Mattiello, rita.mattiello@ufrgs.br, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil.

Supplementary Chart 1. Databases search strategy

	PUBMED
1	(((((("Pregnancy") OR ("Fetus")) OR ("Newborn")) OR ("Infant")) OR ("Preschool Child")) OR ("Children")) OR ("Adolescent"))
2	((((((((((("Environmental Pollution") OR ("Air Pollution")) OR ("Particulate Matter")) OR ("Carbon Compounds, Inorganic")) OR ("Lead")) OR ("Sulfur Oxides")) OR ("Nitrogen Oxides")) OR ("Soot")) OR ("Inorganic Chemicals")) OR ("Pesticides")) OR ("Hydrocarbons")) OR ("Volatile Organic Compounds")) OR ("Polychlorinated Biphenyls")) OR ("Endocrine Disruptors")) OR ("Plasticizers")) OR ("Plastics"))
3	((("Autism Spectrum Disorder"[Title/Abstract]) OR ("Autism Spectrum Disorders"[Title/Abstract])) OR ("Autistic Spectrum Disorder"[Title/Abstract])) OR ("Disorder, Autistic Spectrum"[Title/Abstract]))
4	#1AND#2AND#3 (((((((("Pregnancy") OR ("Fetus")) OR ("Newborn")) OR ("Infant")) OR ("Preschool Child")) OR ("Children")) OR ("Adolescent")) AND (((((((((((("Environmental Pollution") OR ("Air Pollution")) OR ("Particulate Matter")) OR ("Carbon Compounds, Inorganic")) OR ("Lead")) OR ("Sulfur Oxides")) OR ("Nitrogen Oxides")) OR ("Soot")) OR ("Inorganic Chemicals")) OR ("Pesticides")) OR ("Hydrocarbons")) OR ("Volatile Organic Compounds")) OR ("Polychlorinated Biphenyls")) OR ("Endocrine Disruptors")) OR ("Plasticizers")) OR ("Plastics")) AND (((("Autism Spectrum Disorder"[Title/Abstract]) OR ("Autism Spectrum Disorders"[Title/Abstract])) OR ("Autistic Spectrum Disorder"[Title/Abstract])) OR ("Disorder, Autistic Spectrum"[Title/Abstract]))
	EMBASE
1	'pregnancy':ti,ab OR 'fetus':ti,ab OR 'newborn':ti,ab OR 'infant':ti,ab OR 'preschool child':ti,ab OR 'child':ti,ab OR 'adolescent':ti,ab
2	'pollution':ti,ab OR 'air pollution':ti,ab OR 'particulate matter':ti,ab OR 'carbon compounds':ti,ab OR 'lead':ti,ab OR 'sulfur oxide':ti,ab OR 'nitrogen oxide':ti,ab OR 'soot':ti,ab OR 'inorganic compound':ti,ab OR 'pesticide':ti,ab OR 'hydrocarbon':ti,ab OR 'volatile organic compound':ti,ab OR 'polychlorinated biphenyl':ti,ab OR 'endocrine disruptor':ti,ab OR 'plasticizer':ti,ab OR 'plastic':ti,ab
3	'autism':ti,ab OR 'autism spectrum disorders':ti,ab
4	#1AND#2AND#3 ('pregnancy':ti,ab OR 'fetus':ti,ab OR 'newborn':ti,ab OR 'infant':ti,ab OR 'preschool child':ti,ab OR 'child':ti,ab OR 'adolescent':ti,ab) AND ('pollution':ti,ab OR 'air pollution':ti,ab OR 'particulate matter':ti,ab OR 'carbon compounds':ti,ab OR 'lead':ti,ab OR 'sulfur oxide':ti,ab OR 'nitrogen oxide':ti,ab OR 'soot':ti,ab OR 'inorganic compound':ti,ab OR 'pesticide':ti,ab OR 'hydrocarbon':ti,ab OR 'volatile organic compound':ti,ab OR 'polychlorinated biphenyl':ti,ab OR 'endocrine disruptor':ti,ab OR 'plasticizer':ti,ab OR 'plastic':ti,ab) AND ('autism':ti,ab OR 'autism spectrum disorders':ti,ab)

	SCOPUS
1	TITLE-ABS-KEY((((("Pregnancy") OR ("Fetus")) OR ("Newborn")) OR ("Infant")) OR ("Preschool Child")) OR ("Children")) OR ("Adolescent")
2	TITLE-ABS-KEY((((((((((((("Environmental Pollution") OR ("Air Pollution")) OR ("Particulate Matter")) OR ("Carbon Compounds, Inorganic")) OR ("Lead")) OR ("Sulfur Oxides")) OR ("Nitrogen Oxides")) OR ("Soot")) OR ("Inorganic Chemicals")) OR ("Pesticides")) OR ("Hydrocarbons")) OR ("Volatile Organic Compounds")) OR ("Polychlorinated Biphenyls")) OR ("Endocrine Disruptors")) OR ("Plasticizers")) OR ("Plastics")
3	TITLE-ABS-KEY(("Autism Spectrum Disorder") OR ("Autism Spectrum Disorders")) OR ("Autistic Spectrum Disorder") OR ("Disorder, Autistic Spectrum")
4	#1 AND #2 AND #3
	Web of Science, CINAHL
1	((((("Pregnancy") OR ("Fetus")) OR ("Newborn")) OR ("Infant")) OR ("Preschool Child")) OR ("Children")) OR ("Adolescent")
2	((((((((((((("Environmental Pollution") OR ("Air Pollution")) OR ("Particulate Matter")) OR ("Carbon Compounds, Inorganic")) OR ("Lead")) OR ("Sulfur Oxides")) OR ("Nitrogen Oxides")) OR ("Soot")) OR ("Inorganic Chemicals")) OR ("Pesticides")) OR ("Hydrocarbons")) OR ("Volatile Organic Compounds")) OR ("Polychlorinated Biphenyls")) OR ("Endocrine Disruptors")) OR ("Plasticizers")) OR ("Plastics")
3	AB=(("Autism Spectrum Disorder") OR ("Autism Spectrum Disorders")) OR ("Autistic Spectrum Disorder") OR ("Disorder, Autistic Spectrum")
4	#1 AND #2 AND #3
	LILACS
1	((((("Pregnancy") OR ("Fetus")) OR ("Newborn")) OR ("Infant")) OR ("Preschool Child")) OR ("Children")) OR ("Adolescent") [Palavras] and ((((((((((((("Environmental Pollution") OR ("Air Pollution")) OR ("Particulate Matter")) OR ("Carbon Compounds, Inorganic")) OR ("Lead")) OR ("Sulfur Oxides")) OR ("Nitrogen Oxides")) OR ("Soot")) OR ("Inorganic Chemicals")) OR ("Pesticides")) OR ("Hydrocarbons")) OR ("Volatile Organic Compounds")) OR ("Polychlorinated Biphenyls")) OR ("Endocrine Disruptors")) OR ("Plasticizers")) OR ("Plastics") [Palavras] and (("Autism Spectrum Disorder") OR ("Autism Spectrum Disorders")) OR ("Autistic Spectrum Disorder") OR ("Disorder, Autistic Spectrum") [Palavras]
	COCHRANE
1	((((("Pregnancy") OR ("Fetus")) OR ("Newborn")) OR ("Infant")) OR ("Preschool Child")) OR ("Children")) OR ("Adolescent") in All Text AND ((((((((((((("Environmental Pollution") OR ("Air Pollution")) OR ("Particulate Matter")) OR ("Carbon Compounds, Inorganic")) OR ("Lead")) OR ("Sulfur Oxides")) OR ("Nitrogen Oxides")) OR ("Soot")) OR ("Inorganic Chemicals")) OR ("Pesticides")) OR ("Hydrocarbons")) OR ("Volatile Organic Compounds")) OR ("Polychlorinated Biphenyls")) OR ("Endocrine Disruptors")) OR ("Plasticizers")) OR ("Plastics") in All Text AND (("Autism Spectrum Disorder") OR ("Autism Spectrum Disorders")) OR ("Autistic Spectrum Disorder") OR ("Disorder, Autistic Spectrum") in Title Abstract Keyword - (Word variations have been searched)

	PsycInfo
1	All Fields: "Pregnancy" OR "Fetus" OR "Newborn" OR "Infant" OR "Preschool Child" OR "Children" OR "Adolescent"
2	All Fields: "Environmental Pollution" OR "Air Pollution" OR "Particulate Matter" OR "Carbon Compounds, Inorganic" OR "Lead" OR "Sulfur Oxides" OR "Nitrogen Oxides" OR "Soot" OR "Inorganic Chemicals" OR "Pesticides" OR "Hydrocarbons" OR "Volatile Organic Compounds" OR "Polychlorinated Biphenyls" OR "Endocrine Disruptors" OR "Plasticizers" OR "Plastic"
3	Abstract: "Autism Spectrum Disorder" OR "Autism Spectrum Disorders" OR "Autistic Spectrum Disorder" OR "Disorder, Autistic Spectrum"
4	#1 AND #2 AND #3

Table S1. Quality of Studies by the National Heart, Lung, and Blood Institute Tool.

First Author, Publication year	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Quality Rating
Alampi JD (2021)	Y	Y	Y	Y	NR	Y	Y	Y	Y	N	Y	NR	Y	Y	Good
Barkoski JM (2021)	Y	Y	Y	Y	NR	Y	Y	Y	Y	Y	Y	NR	Y	Y	Good
Bernardo BA (2019)	Y	Y	Y	Y	NR	Y	Y	Y	Y	N	Y	NR	Y	Y	Good
Braun JM (2014)	Y	Y	Y	Y	NR	Y	Y	Y	Y	N	Y	NR	N	Y	Fair
Carter SA (2022)	Y	Y	CD	Y	NR	Y	Y	Y	Y	Y	Y	NR	CD	Y	Good
Gong T (2014)	Y	Y	Y	Y	NR	Y	Y	Y	Y	Y	Y	NR	Y	Y	Good
Granillo L (2019)	Y	Y	CD	Y	NR	Y	Y	Y	Y	Y	Y	NR	CD	Y	Good
Guxens M (2016)	Y	Y	CD	Y	NR	NR	Y	Y	Y	Y	Y	NR	CD	Y	Good
Haggerty DK (2021)	Y	Y	CD	Y	N	Y	Y	Y	Y	N	Y	NR	CD	Y	Fair
Hansen JB (2021)	Y	Y	N	Y	NR	Y	Y	Y	Y	N	Y	NR	Y	Y	Good
Jo H (2019)	Y	Y	Y	Y	NR	Y	Y	Y	Y	N	Y	NR	Y	Y	Good
Joyce E (2022)	Y	Y	Y	Y	NR	Y	Y	CD	Y	CD	Y	NR	CD	Y	Fair
Jung CR (2013)	Y	Y	Y	Y	NR	Y	Y	Y	Y	Y	Y	NR	Y	Y	Good
Kim JI (2021)	Y	Y	Y	Y	NR	Y	Y	Y	Y	Y	Y	NR	Y	Y	Good
Lizé M (2022)	Y	Y	N	Y	NR	Y	Y	Y	Y	N	Y	NR	N	Y	Fair

Nowack N (2015)	Y	Y	Y	Y	NR	Y	Y	Y	Y	N	Y	NR	Y	Y	Good
Oudin A (2019)	Y	Y	Y	Y	NR	Y	Y	Y	Y	N	Y	NR	Y	Y	Good
Oulhote Y (2020)	Y	Y	Y	Y	NR	Y	Y	Y	Y	N	Y	NR	Y	Y	Good
Pagalan L (2019)	Y	Y	Y	Y	NR	Y	Y	Y	Y	N	Y	NR	Y	Y	Good
Pham C (2022)	Y	Y	Y	Y	NR	Y	Y	Y	Y	Y	Y	NR	Y	Y	Good
Philippat C (2018)	Y	Y	Y	Y	NR	Y	Y	Y	Y	N	Y	NR	Y	Y	Good
Rahman MM (2022)	Y	Y	Y	Y	NR	Y	Y	Y	Y	N	Y	NR	Y	Y	Good
Rahman MM (2023)	Y	Y	Y	Y	NR	Y	Y	Y	Y	N	Y	NR	Y	Y	Good
Sagiv SK (2018)	Y	Y	Y	Y	NR	Y	Y	Y	Y	Y	Y	NR	N	Y	Fair
Van den Dries MA (2019)	Y	Y	Y	Y	NR	Y	Y	Y	Y	Y	Y	NR	Y	Y	Good
Von Ehrenstein OS (2014)	Y	Y	Y	Y	NR	Y	Y	Y	Y	Y	Y	NR	Y	Y	Good
Wang SY (2021)	Y	Y	Y	Y	NR	Y	Y	Y	Y	Y	Y	NR	Y	Y	Good

Y= Yes; N = No; CD = cannot determine; NA = not applicable; NR = not reported; 1. Was the research question or objective in this paper clearly stated? 2. Was the study population clearly specified and defined? 3. Was the participation rate of eligible persons at least 50%? 4. Were all the subjects selected or recruited from the same or similar populations (including the same time period) Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants? 5. Was a sample size justification, power description, or variance and effect estimates provided? 6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured? 7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed? 8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)? 9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? 10. Was the exposure(s) assessed more than once over time? 11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? 12. Were the outcome assessors blinded to the exposure status of participants? 13. Was loss to follow-up after baseline 20% or less? 14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s).

Table S2. Results reported in each included study.

<i>Study (Year)</i>	<i>Type of pollutant</i>	<i>Outcome</i>
Alampi JD (2021)	Arsenic	Beta coefficient (CI 95%) Arsenic: 0.00 (-0.50 to 0.50)
	Cadmium	Cadmium: 0.50 (0.00 to 1.00)
	Lead	Lead: 0.05 (-0.90 to 1.25)
	Manganese	Manganese: -1.00 (-2.25 to 0.00)
	Mercury	Mercury: 0.00 (-0.30 to 0.30)
	β-hexachlorocyclohexane (β-HCH)	β-hexachlorocyclohexane (β-HCH): 0.05 (-0.25 to 0.50)
	p,p-dichlorodiphenyldichloroethylene (DDE)	p,p-dichlorodiphenyldichloroethylene (DDE): 0.40 (-1.00 to 0.02)
	Oxychlorane	Oxychlorane: 0.00 (-0.90 to 0.75)
	trans-Nonachlor.	trans-Nonachlor: -0.25 (-1.00 to 0.50)
	diethylphosphate (DEP)	diethylphosphate (DEP): -0.25 (-0.60 to 0.30)
	dimethylphosphate (DMP)	dimethylphosphate (DMP): -0.90 (-0.30 to 0.30)
	dimethylthiophosphate (DMTP)	dimethylthiophosphate (DMTP): -0.90 (-0.30 to 0.20)
	bisphenol-A (BPA)	bisphenol-A (BPA): 0.30 (0.00 to 0.60)
	monobutyl phthalate (MBP)	monobutyl phthalate (MBP): 0.30 (0.00 to 0.80)
	mono-benzyl phthalate (MBzP)	mono-benzyl phthalate (MBzP): 0.10 (-0.29 to 0.50)
	mono-3-carboxypropyl phthalate (MCP)	mono-3-carboxypropyl phthalate (MCP): 0.40 (0.00 to 0.70)
	mono-(2-ethyl-5-hydroxy-hexyl) phthalate (MEHHP)	Sum of mono-(2-ethyl-5-hydroxy-hexyl) phthalate (MEHHP); mono-(2-ethylhexyl) phthalate (MEHP); mono-(2-ethyl-5-oxo-hexyl) and phthalate (MEOHP): 0.01 (-0.40 to 0.40)
	mono-(2-ethylhexyl) phthalate (MEHP)	mono-ethyl phthalate (MEP): -0.25 (-0.50 to 0.00)
	mono-(2-ethyl-5-oxo-hexyl) phthalate (MEOHP)	polychlorinated biphenyl 118 (PCB118): 0.01 (-0.50 to 0.75)
	mono-ethyl phthalate (MEP)	polychlorinated biphenyl 138 (PCB138): 0.39 (-0.10 to 1.00)
	polychlorinated biphenyl 118 (PCB118)	polychlorinated biphenyl 153 (PCB153): 0.30 (-0.25 to 0.90)
	polychlorinated biphenyl 138 (PCB138)	polychlorinated biphenyl 180 (PCB180) : 0.30 (-0.10 to 0.80)
	polychlorinated biphenyl 153 (PCB153)	Triclosan: 0.35 (-0.25 to 0.90)
	polychlorinated biphenyl 180 (PCB180)	
	Triclosan	
	Barkoski JM (2021)	3-phenoxybenzoic acid (3-PBA)
Bernardo BA (2019)	polychlorinated biphenyl 118 (PCB118)	Bayesian Predictive Odds Ratios (BPORs) polychlorinated biphenyl 118 (PCB118): 1.20 (0.72 to 1.89)
	polychlorinated biphenyl 138 (PCB138)	polychlorinated biphenyl 138 (PCB138): 1.76 (0.99 to 2.92)
	polychlorinated biphenyl 153 (PCB153)	polychlorinated biphenyl 153 (PCB153): 1.82 (1.02 to 3.02)
	polychlorinated biphenyl 170 (PCB170)	polychlorinated biphenyl 180 (PCB170): 1.39 (0.80 to 2.24)
	polychlorinated biphenyl 180 (PCB180)	polychlorinated biphenyl 180 (PCB180): 1.20 (0.67 to 1.98)
	polychlorinated biphenyl 187 (PCB187)	polychlorinated biphenyl 180 (PCB187): 1.46 (0.89 to 2.24)

Braun JM (2014)		Beta coefficient (CI 95%)
	Mono-n-butyl phthalate (MBP)	Mono-n-butyl phthalate (MBP): 0.8 (-1.7 to 3.3)
	Mono-i-butyl phthalate (MiBP)	Mono-i-butyl phthalate (MiBP): 1.3 (-0.9 to 3.4)
	Mono-ethyl phthalate (MEP)	Mono-ethyl phthalate (MEP): 1.3 (-1.1 to 3.6)
	Mono-benzyl phthalate (MBzP)	Mono-benzyl phthalate (MBzP): 2.4 (-0.2 to 5.0)
	Mono-3-carboxypropyl phthalate (MCP)	Mono-3-carboxypropyl phthalate (MCP): -0.4 (-3.0 to 2.1)
	Mono-2-ethyl-hexyl phthalate (MEHP)	Mono-2-ethyl-hexyl phthalate (MEHP): -0.7 (-3.5 to 2.2)
	Mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP)	Mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP): -0.5 (-3.4 to 2.4)
	Mono-2-ethyl-5-carboxypentyl phthalate (MECPP)	Mono-2-ethyl-5-carboxypentyl phthalate (MECPP): -0.3 (-3.0 to 2.4)
	Bisphenol A (BPA)	Bisphenol A (BPA): 1.6 (-0.7 to 3.8)
	Polychlorinated biphenyl 28 (PCB 28)	Polychlorinated biphenyl 28 (PCB 28): -0.4 (-2.5 to 1.8)
	Polychlorinated biphenyl 66 (PCB 66)	Polychlorinated biphenyl 66 (PCB 66): 0.3 (-2.4 to 2.9)
	Polychlorinated biphenyl 74 (PCB 74)	Polychlorinated biphenyl 74 (PCB 74): -3.3 (-5.8 to -0.8)
	Polychlorinated biphenyl 99 (PCB 99)	Polychlorinated biphenyl 99 (PCB 99): -0.7 (-2.9 to 1.5)
	Polychlorinated biphenyl 101 (PCB 101)	Polychlorinated biphenyl 101 (PCB 101): 1.2 (-1.9 to 4.4)
	Polychlorinated biphenyl 105 (PCB 105)	Polychlorinated biphenyl 105 (PCB 105): 0.7 (-1.5 to 2.9)
	Polychlorinated biphenyl 118 (PCB 118)	Polychlorinated biphenyl 118 (PCB 118): -1.1 (-2.9 to 0.8)
	Polychlorinated biphenyl 138/158 (PCB 138/158)	Polychlorinated biphenyl 138/158 (PCB 138/158): -2.5 (-5.1 to 0.1)
	Polychlorinated biphenyl 146 (PCB 146)	Polychlorinated biphenyl 146 (PCB 146): -3.5 (-5.7 to -1.2)
	Polychlorinated biphenyl 153 (PCB 153)	Polychlorinated biphenyl 153 (PCB 153): -4.8 (-7.1 to -2.6)
	Polychlorinated biphenyl 156 (PCB 156)	Polychlorinated biphenyl 156 (PCB 156): -5.2 (-7.9 to -2.5)
	Polychlorinated biphenyl 157 (PCB 157)	Polychlorinated biphenyl 157 (PCB 157): -3.7 (-6.2 to -1.2)
	Polychlorinated biphenyl 167 (PCB 167)	Polychlorinated biphenyl 167 (PCB 167): -2.6 (-5.3 to 0.1)
	Polychlorinated biphenyl 170 (PCB 170)	Polychlorinated biphenyl 170 (PCB 170): -5.3 (-8.5 to -2.1)
	Polychlorinated biphenyl 172 (PCB 172)	Polychlorinated biphenyl 172 (PCB 172): -5.3 (-7.5 to -3.0)
	Polychlorinated biphenyl 177 (PCB 177)	Polychlorinated biphenyl 177 (PCB 177): -3.3 (-6.0 to -0.6)
	Polychlorinated biphenyl 178 (PCB 178)	Polychlorinated biphenyl 178 (PCB 178): -5.5 (-8.0 to -3.0)
	Polychlorinated biphenyl 183 (PCB 183)	Polychlorinated biphenyl 183 (PCB 183): -3.1 (-5.3 to -1.0)
	Polychlorinated biphenyl 187 (PCB 187)	Polychlorinated biphenyl 187 (PCB 187): -4.1 (-6.5 to -1.7)
	Polychlorinated biphenyl 194 (PCB 194)	Polychlorinated biphenyl 194 (PCB 194): -6.8 (-9.5 to -4.1)
	Polychlorinated biphenyl 195 (PCB 195)	Polychlorinated biphenyl 195 (PCB 195): -3.8 (-6.2 to -1.4)
	Polychlorinated biphenyl 196/203 (PCB 196/203)	Polychlorinated biphenyl 196/203 (PCB 196/203): -4.3 (-7.0 to -1.6)
	Polychlorinated biphenyl 206 (PCB 206)	
	Polychlorinated biphenyl 209 (PCB 209)	
	β-Hexachlorocyclohexane (β-HCH)	Polychlorinated biphenyl 199 (PCB 199): -5.3 (-

	Hexachlorobenzene (HCB)	8.2 to -2.5)
	p#p#-Dichlorodiphenyltrichloroethane (PP DDT)	Polychlorinated biphenyl 206 (PCB 206): -3.0 (-6.1 to 0.1)
	p#p#-Dichlorodiphenyldichloroethylene (PP DDE)	Polychlorinated biphenyl 209 (PCB 209): -4.3 (-6.6 to -2.0)
	Oxychlorodane	β-Hexachlorocyclohexane (β-HCH): -3.2 (-5.6 to -0.8)
	trans-Nonachlor	Hexachlorobenzene (HCB): 1.3 (-0.8 to 3.3)
	Brominated biphenyl 153 (BB 153)	p#p#-Dichlorodiphenyltrichloroethane (PP DDT): 2.2 (-0.4 to 4.7)
	Polybrominated diphenyl ether 28 (PBDE 28)	p#p#-Dichlorodiphenyldichloroethylene (PP DDE): -1.4 (-3.5 to 0.6)
	Polybrominated diphenyl ether 47 (PBDE 47)	Oxychlorodane: -1.2 (-3.4 to 0.9)
	Polybrominated diphenyl ether 85 (PBDE 85)	trans-Nonachlor: -0.6 (-2.9 to 1.8)
	Polybrominated diphenyl ether 99 (PBDE 99)	Brominated biphenyl 153 (BB 153): -4.1 (-7.0 to -1.2)
	Polybrominated diphenyl ether 100 (PBDE 100)	Polybrominated diphenyl ether 28 (PBDE 28): 4.5 (1.9 to 7.0)
	Polybrominated diphenyl ether 153 (PBDE 153)	Polybrominated diphenyl ether 47 (PBDE 47): 5.5 (2.6 to 8.4)
	Polybrominated diphenyl ether 154 (PBDE 154)	Polybrominated diphenyl ether 85 (PBDE 85): 2.1 (-0.4 to 4.7)
	Polybrominated diphenyl ether 183 (PBDE 183)	Polybrominated diphenyl ether 99 (PBDE 99): 5.6 (2.7 to 8.5)
	Perfluorooctanoate (PFOA)	Polybrominated diphenyl ether 100 (PBDE 100): 4.0 (1.3 to 6.7)
	Perfluorooctane sulfate (PFOS)	Polybrominated diphenyl ether 153 (PBDE 153): 0.8 (-1.5 to 3.1)
	Perfluorononanoate (PFNA)	Polybrominated diphenyl ether 154 (PBDE 154): 3.1 (0.4 to 5.9)
	Perfluorohexane sulfonate (PFHxS)	Polybrominated diphenyl ether 183 (PBDE 183): Not described
		Perfluorooctanoate (PFOA): -0.8 (-3.0 to 1.5)
		Perfluorooctane sulfate (PFOS): 0.1 (-2.3 to 2.6)
		Perfluorononanoate (PFNA): -0.1 (-2.6 to 2.4)
		Perfluorohexane sulfonate (PFHxS): -1.2 (-3.8 to 1.4)
Carter SA (2022)	Particular matter 2.5 (PM 2.5)	Hazard ratios - HR (CI 95%) Particular matter 2.5: 1.03 (1.00 to 1.05)
Gong T (2014)	Nitrogen oxides (NOx) Particular matter 10 (PM 10)	Odds ratios-ORs (CI 95%) Nitrogen oxides (NOx): 1.11 (0.33 to 3.73) Particular matter 10 (PM 10): 1.73 (0.49 to 6.17)
Granillo L (2019)	Polychlorinated biphenyl 11 (PCB 11) Polychlorinated biphenyl 52 (PCB 52) Polychlorinated biphenyl 77 (PCB 77) Polychlorinated biphenyl 84 (PCB 84) Polychlorinated biphenyl 91 (PCB 91) Polychlorinated biphenyl 95 (PCB 95) Polychlorinated biphenyl 101 (PCB 101) Polychlorinated biphenyl 118 (PCB 118) Polychlorinated biphenyl 132 (PCB 132) Polychlorinated biphenyl 136 (PCB 136) Polychlorinated biphenyl 138 (PCB 138) Polychlorinated biphenyl 153 (PCB	Odds ratios-ORs (CI 95%) Polychlorinated biphenyl 11 (PCB 11): 1.86 (0.67 to 5.13) Polychlorinated biphenyl 52 (PCB 52): 2.44 (0.86 to 6.92) Polychlorinated biphenyl 77 (PCB 77): 0.80 (0.29 to 2.15) Polychlorinated biphenyl 84 (PCB 84): 2.14 (0.76 to 6.04) Polychlorinated biphenyl 91 (PCB 91): 0.47 (0.17 to 1.30) Polychlorinated biphenyl 95 (PCB 95): 1.74 (0.63 to 4.80) Polychlorinated biphenyl 101 (PCB 101): 3.91 (1.27 to 12.05) Polychlorinated biphenyl 118 (PCB 118): 2.86 (0.98 to 8.36)

	153) Polychlorinated biphenyl 174 (PCB 174) Polychlorinated biphenyl 175 (PCB 175) Polychlorinated biphenyl 176 (PCB 176) Polychlorinated biphenyl 180 (PCB 180) Polychlorinated biphenyl 196 (PCB 196)	Polychlorinated biphenyl 132 (PCB 132): 0.96 (0.36 to 2.60) Polychlorinated biphenyl 136 (PCB 136): 0.27 (0.09 to 0.78) Polychlorinated biphenyl 138 (PCB 138): 2.14 (0.76 to 6.04) Polychlorinated biphenyl 153 (PCB 153): 0.80 (0.29 to 2.15) Polychlorinated biphenyl 174 (PCB 174): 0.36 (0.16 to 1.01) Polychlorinated biphenyl 175 (PCB 175): 0.31 (0.10 to 0.90) Polychlorinated biphenyl 176 (PCB 176): 0.15 (0.04 to 0.49) Polychlorinated biphenyl 180 (PCB 180): 0.47 (0.17 to 1.32) Polychlorinated biphenyl 196 (PCB 196): 1.99 (0.72 to 5.49)
Guxens M (2016)	Nitrogen dioxide (NO ₂) Nitrogen oxides (NO _X) Particulate matter 10 (PM 10) Particulate matter 2.5 (PM 2.5) PM coarse PM _{2.5} absorbance	Odds ratios-ORs (CI 95%) Nitrogen dioxide (NO ₂): 1.02 (0.87 to 1.19) Nitrogen oxides (NO _X): 1.04 (0.90 to 1.19) Particulate matter 10 (PM 10): 0.90 (0.67 to 1.20) Particulate matter 2.5 (PM 2.5): 0.79 (0.48 to 1.31) PM coarse: 0.95 (0.73 to 1.23) PM _{2.5} absorbance: 0.86 (0.62 to 1.21)
Haggerty DK (2021)	di-(2-ethylhexyl) phthalate (DEHP) monobutyl phthalate (mBP) monoethyl phthalate (mEP) mono-isobutyl phthalate (miBP)	Beta coefficient (CI 90%) di-(2-ethylhexyl) phthalate (DEHP): 0.4 (-1.2 to 2.1) monobutyl phthalate (mBP): -0.1 (-2.6 to 2.4) monoethyl phthalate (mEP): -0.3 (-2.2 to 1.6) mono-isobutyl phthalate (miBP): 1.0 (-0.2 to 2.1)
Hansen JB (2021)	Bisphenol A (BPA)	Odds ratios-ORs (CI 95%) Bisphenol A (BPA): 1.89 (0.99 to 3.58)
Jo H (2019)	Ozone (O ₃) Particulate matter 2.5 (PM 2.5) Particulate matter 10 (PM 10) Nitrogen dioxide (NO ₂)	Adjusted hazard ratios - HRs (CI 95%) Ozone (O ₃): 1.00 (0.87 to 1.16) Particulate matter 2.5 (PM 2.5): 1.22 (1.07 to 1.39) Particulate matter 10 (PM 10): 1.06 (0.94 to 1.21) Nitrogen dioxide (NO ₂): 1.15 (1.00 to 1.31)
Joyce EE (2022)	Pesticides by previously developed pesticide residue burden score (PRBS): Organochlorine (OC-PRBS) Organophosphate (OP-PRBS)	Beta coefficient (CI 90%) Organochlorine (OC-PRBS): 3.31 (-6.0 to 12.7) Organophosphate (OP-PRBS): 1.30 (-8.1 to 10.7)
Jung CR (2013)	Carbon monoxide (CO) Nitrogen dioxide (NO ₂) Sulfur dioxide (SO ₂) Ozone (O ₃) Particulate matter 10 (PM 10)	Hazard ratios - HR (CI 95%) Carbon monoxide (CO): 1.12 (1.01 to 1.23) Nitrogen dioxide (NO ₂): 1.36 (1.30 to 1.43) Sulfur dioxide (SO ₂): 2.70 (2.13 to 3.42) Ozone (O ₃): 0.83 (0.75 to 0.93) Particulate matter 10 (PM 10): 0.94 (0.86 to 1.02)
Kim JI (2021)	Mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) Mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP) Mono-n-butyl phthalate (MnBP)	% change (95% CI) Mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP): 0.2 (-0.1 to 0.5) Mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP): 0.3 (0.0 to 0.6)

		Mono-n-butyl phthalate (MnBP): 0.1 (-0.1 to 0.4)
Lizé M (2022)	Dialkylphosphates Dimethylphosphates Diethylphosphates Diazinon Terbufos Chlorpyrifos-oxon 3,5,6-trichloro-2-pyridinol	Incidence Rate Ratio (CI 95%) Dialkylphosphates: 0.93 (0.75 to 1.15) Dimethylphosphates: 0.91 (0.74 to 1.12) Diethylphosphates: 0.93 (0.75 to 1.14) Diazinon: 1.25 (0.99 to 1.57) Terbufos: 1.03 (0.84 to 1.25) Chlorpyrifos-oxon: 1.29 (1.07 to 1.57) 3.5.6-trichloro-2-pyridinol: 1.00 (0.74 to 1.35)
Nowack N (2015)	Polychlorinated dibenzo-p-dioxins and dibenzofurans Polychlorinated biphenyls	Beta coefficient (CI 95%) Polychlorinated dibenzo-p-dioxins and dibenzofurans: -6.66 (-11.88 to -1.44) Polychlorinated biphenyls: -3.99 (-8.61 to 0.64)
Oudin A (2019)	Nitrogen oxides	Odds Ratio (CI 95%) Nitrogen oxides: 1.55 (1.18 to 2.04)
Oulhote Y (2020)	Mono-n-butyl phthalate (MBP) Mono-benzyl phthalate (MBzP) Mono-ethyl phthalate (MEP) Mono-3-carboxypropyl phthalate (MCP) Three metabolites of di-(2-ethylhexyl) phthalate (DEHP)	Beta coefficient (CI 95%) Mono-n-butyl phthalate (MBP): 0.6 (0.1 to 1.0) Mono-benzyl phthalate (MBzP): 0.2 (-0.2 to 0.6) Mono-ethyl phthalate (MEP): -0.1 (-0.4 to 0.1) Mono-3-carboxypropyl phthalate (MCP): 0.5 (0.1 to 0.8) Three metabolites of di-(2-ethylhexyl) phthalate (DEHP): 0.1 (-0.4 to 0.6)
Pagalan L (2019)	Particulate matter 2.5 Nitrogen Dioxide Nitric oxide	Odds Ratio (CI 95%) Particulate matter 2.5: 1.08 (1.03 to 1.14) Nitrogen Dioxide: 1.11 (1.05 to 1.17) Nitric oxide: 1.09 (1.03 to 1.14)
Pham C (2022)	Particulate matter 2.5 Nitrogen Dioxide	Beta coefficient (CI 95%) Particulate matter 2.5: 0.17 (0.02 to 0.32) Nitrogen Dioxide: 0.06 (-0.02 to 0.13)
Philippat C (2018)	3,5,6-trichloro-2-pyridinol Dimethylthiophosphate Diethylphosphate	Odds Ratio (CI 95%) 3.5.6-trichloro-2-pyridinol: 0.80 (0.57 to 1.12) Dimethylthiophosphate: 0.99 (0.79 to 1.25) Diethylphosphate: 0.94 (0.74 to 1.20)
Rahman MM (2022)	Particulate matter 2.5 Nitrogen Dioxide Ozone	Cumulative hazard ratio (CI 95%) Particulate matter 2.5: 1.17 (1.08 to 1.27) Nitrogen Dioxide: 0.99 (0.90 to 1.09) Ozone: 0.97 (0.85 to 1.10)
Rahman MM (2023)	Elemental carbon Organic carbon Copper Iron Manganese	Cumulative hazard ratio (CI 95%) Elemental carbon: 1.11 (1.06 to 1.16) Organic carbon: 1.09 (1.04 to 1.15) Copper: 1.08 (1.00 to 1.15) Iron: 1.14 (1.09 to 1.20) Manganese: 1.17 (1.12 to 1.22)
Sagiv SK (2018)	Dialkyl phosphates Diethyl phosphates Dimethyl phosphates Chlorpyrifos Diazinon Malathion Oxydemeton-methyl	Beta coefficient (CI 95%) Dialkyl phosphates: 2.7 (0.9 to 4.5) Diethyl phosphates: 1.0 (-0.8 to 2.7) Dimethyl phosphates: 2.4 (0.8 to 4.0) Chlorpyrifos: -0.6 (-1.8 to 0.7) Diazinon: -0.4 (-2.0 to 1.1) Malathion: 0.5 (-0.7 to 1.8) Oxydemeton-methyl: -0.3 (-1.7 to 1.0)
Van den Dries MA (2019)	Dialkyl phosphates Diethyl alkyl phosphates Dimethyl alkyl phosphates	Beta coefficient (CI 95%) Dialkyl phosphates: -0.07 (-0.43 to 0.30)

Diethyl alkyl phosphates: -0.29 (-0.56 to -0.02)
Dimethyl alkyl phosphates: 0.03 (-0.32 to 0.39)

Von Ehrenstein OS (2014)	Benzene	Odds Ratio (CI 95%)
	Perchloroethylene	Benzene: 1.69 (1.12 to 1.89)
	1,3-Butadiene	Perchloroethylene: 1.77 (1.09 to 1.80)
	Toluene	1,3-Butadiene: 1.75 (1.18 to 2.15)
	Ortho-Xylene	Toluene: 1.62 (1.12 to 1.67)
	Meta/para-Xylen	Ortho-Xylene: 1.61 (1.19 to 1.70)
	Ethyl Benzene	Meta/para-Xylen: 1.70 (1.26 to 1.82)
	Methylene Chloride	Ethyl Benzene: 1.60 (1.25 to 1.75)
	Polycyclic aromatic hydrocarbon	Methylene Chloride: 1.17 (0.93 to 1.26)
	Lead	Polycyclic aromatic hydrocarbon: 1.15 (0.84 to 1.26)
	Vanadium	Lead: 1.35 (1.23 to 1.81)
	Chromium	Vanadium: 0.69 (0.54 to 0.83)
	Manganese	Chromium: 1.02 (0.97 to 1.06)
	Nickel	Manganese: 1.03 (0.98 to 1.07)
	Selenium	Nickel: 0.97 (0.89 to 1.05)
	Acetaldehyde	Selenium: 1.04 (0.95 to 1.16)
	Formaldehyde	Acetaldehyde: 1.33 (1.07 to 1.34)
	Ortho-dichlorobenz	Formaldehyde: 1.37 (1.17 to 1.52)
	Paradichlorobenzene	Ortho-dichlorobenz: 1.07 (0.96 to 1.14)
	Chloroform	Paradichlorobenzene: 0.94 (0.91 to 1.01)
Trichloroethylene	Chloroform: 1.19 (0.95 to 1.17)	
Copper	Trichloroethylene: 1.06 (1.03 to 1.27)	
Hexavalentchromium	Copper: 1.08 (1.02 to 1.16)	
Molybdenum	Hexavalentchromium: 1.05 (0.86 to 1.09)	
	Molybdenum: 0.97 (0.69 to 1.19)	
Wang SY (2021)	Particular matter 10	Hazard ratio (CI 95%)
	Carbon monoxide	Particular matter 10: 0.90 (0.86 to 0.94)
	Nitrogen Dioxide	Carbon monoxide: 1.57 (1.25 to 1.97)
	Sulfur dioxide	Nitrogen dioxide: 1.17 (1.04 to 1.33)
	Ozone	Sulfur dioxide: 0.99 (0.96 to 1.01)
	Ozone: 0.86 (0.70 to 1.05)	

Dimethyl alkyl phosphates					0
dimethylphosphate (DMP)	0		0		+
dimethylthiophosphate (DMTP)	0				
Elemental carbon					+
Ethyl Benzene					+
Formaldehyde					+
Hexachlorobenzene (HCB)	0				
Hexavalent chromium					0
Iron					+
Lead	0				+
Malathion					0
Manganese	0				+
Mercury	0				
Meta/para-Xylen					+
Methylene Chloride					0
Molybdenum					0
Mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP)	0		0		
Mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP)			0		
Mono-2-ethyl-5-carboxypentyl phthalate (MECPP)	0				
Mono-2-ethyl-hexyl phthalate (MEHP)	0	0			
Mono-3-carboxypropyl phthalate (MCPP)	+	0			+
Mono-benzyl phthalate (MBzP)	0	0			0
Mono-ethyl phthalate (MEP)	0	0	0		0

Perfluorooctane sulfate (PFOS)	0			
Perfluorooctanoate (PFOA)	0			
Polybrominated diphenyl ether 100 (PBDE 100)	+			
Polybrominated diphenyl ether 153 (PBDE 153)	0			
Polybrominated diphenyl ether 154 (PBDE 154)	+			
Polybrominated diphenyl ether 183 (PBDE 183)	NR			
Polybrominated diphenyl ether 28 (PBDE 28)	+			
Polybrominated diphenyl ether 47 (PBDE 47)	+			
Polybrominated diphenyl ether 85 (PBDE 85)	0			
Polybrominated diphenyl ether 99 (PBDE 99)	+			
Polychlorinated biphenyl 172 (PCB 172)	-			
Polychlorinated biphenyl 101 (PCB 101)	0	+		
Polychlorinated biphenyl 105 (PCB 105)	0			
Polychlorinated biphenyl 11 (PCB 11)			0	
Polychlorinated biphenyl 118 (PCB 118)	0	0	0	0
Polychlorinated biphenyl 132 (PCB 132)				0
Polychlorinated biphenyl 136 (PCB 136)				-
Polychlorinated biphenyl 138 (PCB 138)	0	+		0
Polychlorinated biphenyl 138/158 (PCB 138/158)			0	

Polychlorinated biphenyl 146 (PCB 146)			-	
Polychlorinated biphenyl 153 (PCB 153)	0	0	-	0
Polychlorinated biphenyl 156 (PCB 156)			-	
Polychlorinated biphenyl 157 (PCB 157)			-	
Polychlorinated biphenyl 167 (PCB 167)			0	
Polychlorinated biphenyl 170 (PCB 170)			-	
Polychlorinated biphenyl 174 (PCB 174)				0
Polychlorinated biphenyl 175 (PCB 175)				-
Polychlorinated biphenyl 176 (PCB 176)				-
Polychlorinated biphenyl 177 (PCB 177)				-
Polychlorinated biphenyl 178 (PCB 178)			-	
Polychlorinated biphenyl 180 (PCB 180)	0	0		0
Polychlorinated biphenyl 183 (PCB 183)			-	
Polychlorinated biphenyl 187 (PCB 187)		0	-	
Polychlorinated biphenyl 194 (PCB 194)			-	
Polychlorinated biphenyl 195 (PCB 195)			-	
Polychlorinated biphenyl 196 (PCB 196)		0		
Polychlorinated biphenyl 196/203 (PCB 196/203)			-	

Polychlorinated biphenyl 199 (PCB 199)	-		
Polychlorinated biphenyl 206 (PCB 206)	0		
Polychlorinated biphenyl 209 (PCB 209)	-		
Polychlorinated biphenyl 28 (PCB 28)	0		
Polychlorinated biphenyl 52 (PCB 52)		0	
Polychlorinated biphenyl 66 (PCB 66)	0		
Polychlorinated biphenyl 74 (PCB 74)	-		
Polychlorinated biphenyl 77 (PCB 77)		0	
Polychlorinated biphenyl 84 (PCB 84)		0	
Polychlorinated biphenyl 91 (PCB 91)		0	
Polychlorinated biphenyl 95 (PCB 95)		0	
Polychlorinated biphenyl 99 (PCB 99)	0		
Polychlorinated biphenyls		0	
Polychlorinated dibenzo-p-dioxins and dibenzofurans		-	
Polycyclic aromatic hydrocarbon			0
Selenium			0
Sulfur dioxide (SO2)	+		0
Terbufos		0	
Three metabolites of di-(2-ethylhexyl) phthalate (DEHP)			0
Toluene			+

Trans-Nonachlor	0	0	
Trichloroethylene			+
Triclosan	0		
Vanadium			-
β-Hexachlorocyclohexane (β-HCH)	0	-	

+: Positive association; -: Negative association; 0: No association; NR: not reported

Table S4. Certainty of Evidence for meta-analyses individuals (quality)

Summary of findings:

Meta-analyses Individuals Quality

Patient or population: Autism

Setting:

Intervention: Pollution

Comparison:

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with	Risk with Pollution				
Cooper	The mean cooper was 0	0 (0 to 0)	-	(2 non-randomised studies)	⊕○○○ Very low ^a	
Mono-3-carboxypropyl phthalate	The mean mono-3-carboxypropyl phthalate was 0	0 (0 to 0)	-	(2 non-randomised studies)	⊕○○○ Very low ^a	
Monobutyl phthalate	The mean Monobutyl phthalate was 0	0 (0 to 0)	-	(2 non-randomised studies)	⊕○○○ Very low ^a	
Nitrogen Dioxide	The mean nitrogen Dioxide was 0	0 (0 to 0)	-	(6 non-randomised studies)	⊕⊕○○ Low	
Ozone	The mean ozone was 0	0 (0 to 0)	-	(4 non-randomised studies)	⊕⊕○○ Low	
Particular Matter	The mean particular Matter was 0	0 (0 to 0)	-	(5 non-randomised studies)	⊕⊕○○ Low	
Polychlorinated biphenyl 138	The mean polychlorinated biphenyl 138 was 0	0 (0 to 0)	-	(2 non-randomised studies)	⊕○○○ Very low ^a	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: confidence interval

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Publication bias considered high due to the number of studies (n = 2)

Table S5. Certainty of Evidence for meta-analyses individuals (instruments)

Summary of findings:

Meta-analises Individuals instrument

Patient or population: [problema de saúde e/ou população]

Setting:

Intervention: [intervenção]

Comparison: [comparação]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with [comparação]	Risk with [intervenção]				
Carbon monoxide	The mean carbon monoxide was 0	0 (0 to 0)	-	(2 non-randomised studies)	⊕○○○ Very low ^a	
Cooper	The mean cooper was 0	0 (0 to 0)	-	(2 non-randomised studies)	⊕○○○ Very low ^a	
Mono-3-carboxypropyl phthalate	The mean mono-3-carboxypropyl phthalate was 0	0 (0 to 0)	-	(2 non-randomised studies)	⊕○○○ Very low ^a	
Monobutyl phthalate	The mean Monobutyl phthalate was 0	0 (0 to 0)	-	(2 non-randomised studies)	⊕○○○ Very low ^a	
Nitrogen Dioxide	The mean nitrogen Dioxide was 0	0 (0 to 0)	-	(4 non-randomised studies)	⊕⊕○○ Low	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: confidence interval

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Publication bias considered high due to the number of studies (n = 2)

Table S6. Certainty of Evidence for meta-analyses subgroups (quality)

Summary of findings:

Subgroups Quality

Patient or population: [health problem and/or population]

Setting:

Intervention: Subgroups Quality

Comparison: [comparison]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with [comparison]	Risk with Subgroups Quality				
Particulate Matter ()	The mean particulate Matter was 0	0 (0 to 0)	-	(12 non-randomised studies)	⊕⊕○○ Low	
Carbon Monoxide	The mean carbon Monoxide was 0	0 (0 to 0)	-	(2 non-randomised studies)	⊕○○○ Very low ^a	
Nitrogen oxides	The mean nitrogen oxides was 0	0 (0 to 0)	-	(10 non-randomised studies)	⊕⊕○○ Low	
Dioxins, Furans, PCBs	The mean dioxins, Furans, PCBs was 0	0 (0 to 0)	-	(1 non-randomised study)	⊕○○○ Very low ^b	
Inorganic substances	The mean inorganic substances was 0	0 (0 to 0)	-	(3 non-randomised studies)	⊕⊕○○ Low	
Metals Elements	The mean metals Elements was 0	0 (0 to 0)	-	(2 non-randomised studies)	⊕○○○ Very low ^a	
Organophosphates and carbamates	The mean organophosphates and carbamates was 0	0 (0 to 0)	-	(2 non-randomised studies)	⊕○○○ Very low ^a	
Organophosphates and carbamates	The mean organophosphates and carbamates was 0	0 (0 to 0)	-	(3 non-randomised studies)	⊕⊕○○ Low	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: confidence interval

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Publication bias considered high due to the number of studies (n = 2)

b. Publication bias considered high due to the number of studies (n = 1) The same study presents several types of pollutants

Table S7. Certainty of Evidence for meta-analyses subgroups (instruments)

Summary of findings:

Meta-analyses instrument Subgroup

Patient or population: [health problem and/or population]

Setting:

Intervention: [intervention]

Comparison: [comparison]

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with [comparison]	Risk with [intervention]				
Particulate Matter	The mean particulate Matter was 0	0 (0 to 0)	-	(3 non-randomised studies)	⊕⊕○○ Low	
Nitrogen oxides	The mean nitrogen oxides was 0	0 (0 to 0)	-	(6 non-randomised studies)	⊕⊕○○ Low	
Metals Elements	The mean metals Elements was 0	0 (0 to 0)	-	(2 non-randomised studies)	⊕○○○ Very low ^a	
Organophosphates and carbamates	The mean organophosphates and carbamates was 0	0 (0 to 0)	-	(6 non-randomised studies)	⊕⊕○○ Low	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: confidence interval

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. **Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Publication bias considered high due to the number of studies (n = 2)

Figure S1. Quality of Studies included.



Interpretation: Most of the included studies (81.5%) showed high quality, a smaller proportion (18.5%) presented fair quality and none presented poor quality (Figure S1).

1. Was the research question or objective in this paper clearly stated? 2. Was the study population clearly specified and defined? 3. Was the participation rate of eligible persons at least 50%? 4. Were all the subjects selected or recruited from the same or similar populations (including the same time period) Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants? 5. Was a sample size justification, power description, or variance and effect estimates provided? 6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured? 7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed? 8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)? 9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? 10. Was the exposure(s) assessed more than once over time? 11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? 12. Were the outcome assessors blinded to the exposure status of participants? 13. Was loss to follow-up after baseline 20% or less? 14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s).

Figure S2. Mechanisms of major environmental pollutants causing autism.

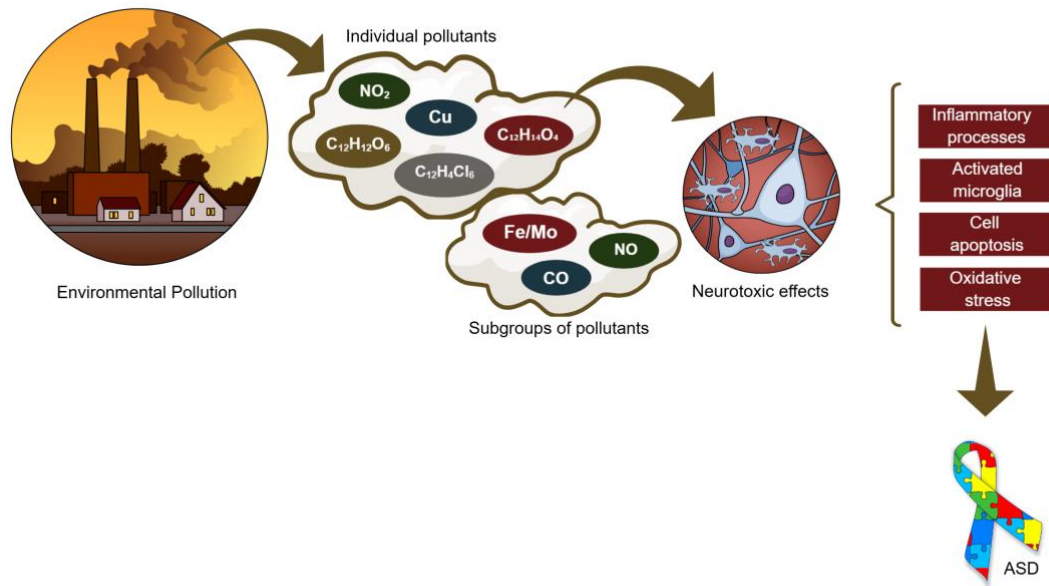
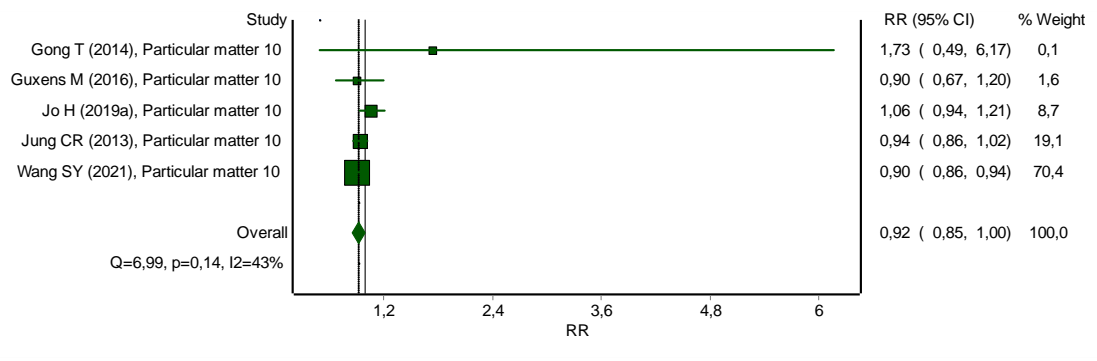
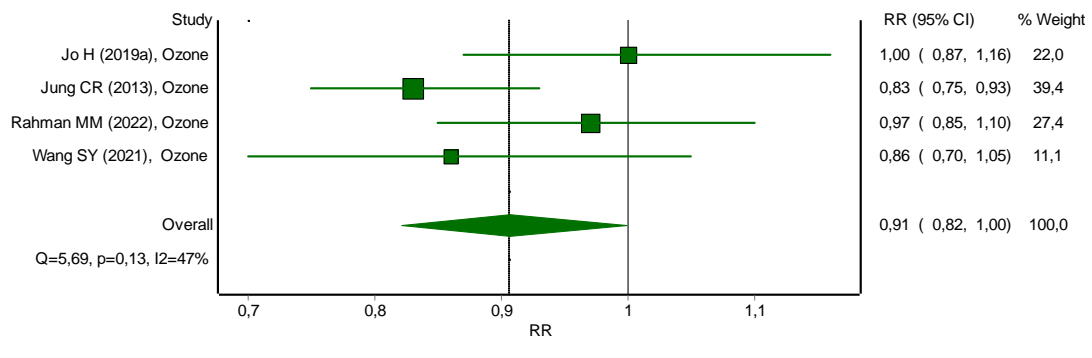


Figure S3. Meta-analysis association particulate matter 10 and autism.



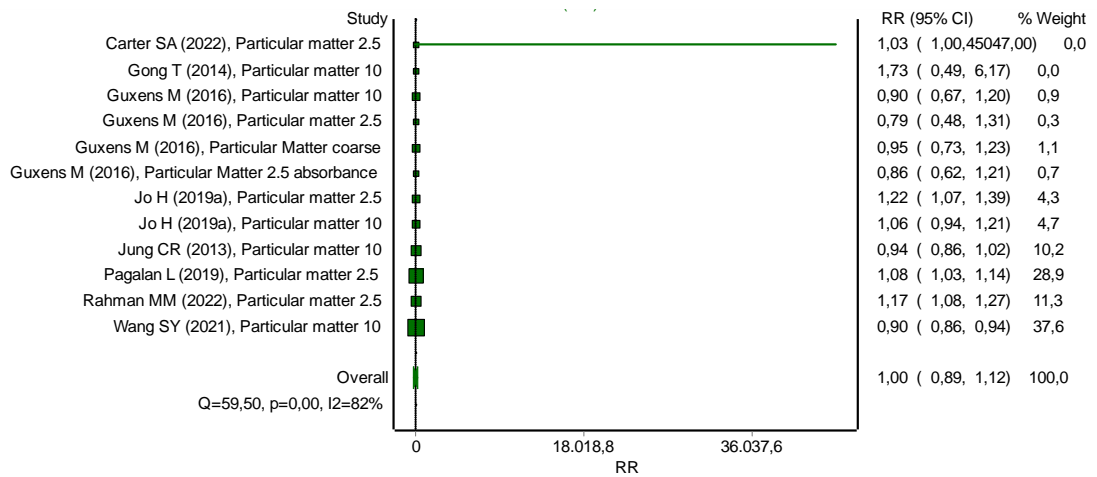
Interpretation: The association between particulate matter 10 and autism was RR = 0,92 (95% CI: 0,85 to 1,00) and the heterogeneity was moderate (I²: 43%) (Figure S3).

Figure S4. Meta-analysis association between ozone and autism.



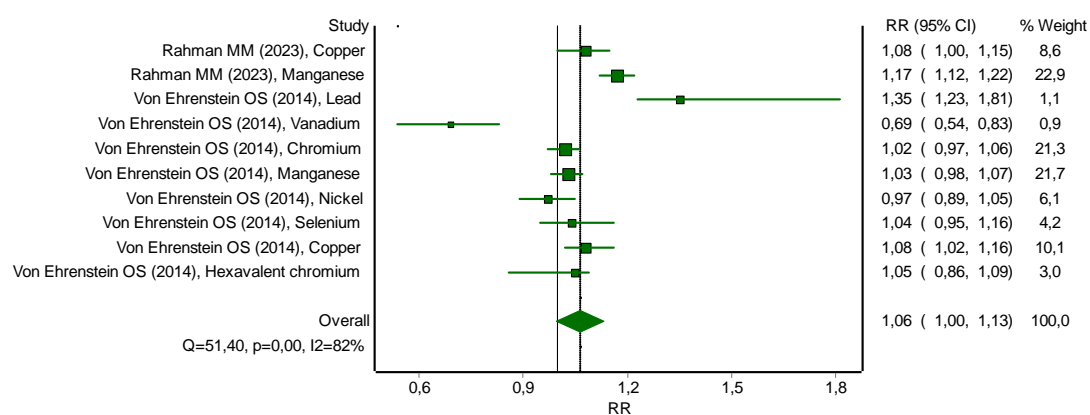
Interpretation: The association between ozone and autism was RR = ,91 (95% CI: 0,82 to 1,00) and the heterogeneity was moderated (I^2 : 47%) (Figure S4).

Figure S5. Meta-analysis association between particulate matter and autism.



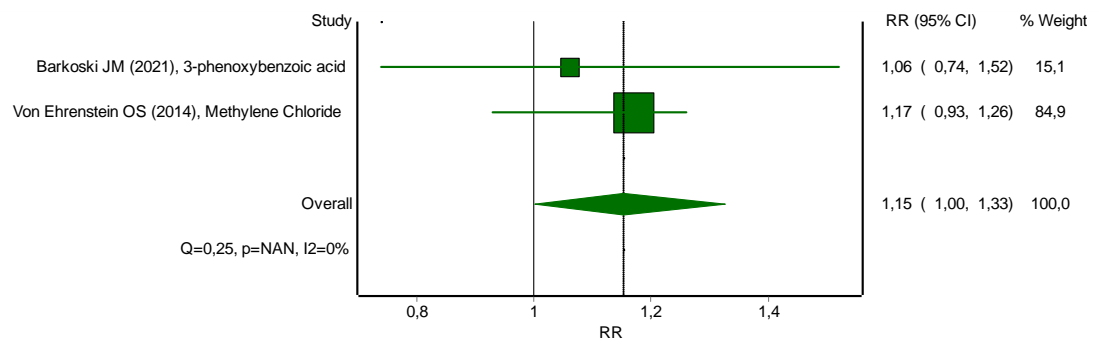
Interpretation: The association between particulate matter and autism was $RR = 1,00$ (95% CI: 0,89 to 1,12) and the heterogeneity was high (I^2 : 82%) (Figure S5).

Figure S6. Meta-analysis association between inorganic substances and autism.



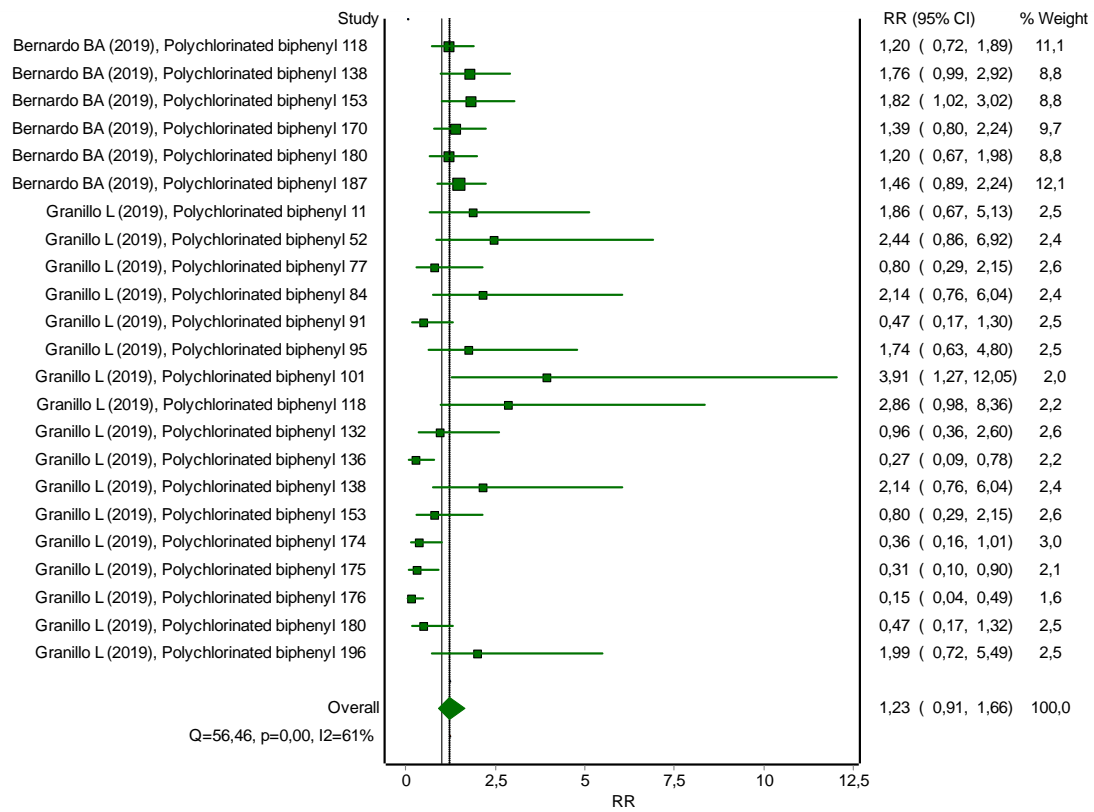
Interpretation: The association between inorganic substances and autism was RR = 1,06 (95% CI: 1,00 to 1,13) and the heterogeneity was high (I²: 82%) (Figure S6).

Figure S7. Meta-analysis association between pesticides and autism.



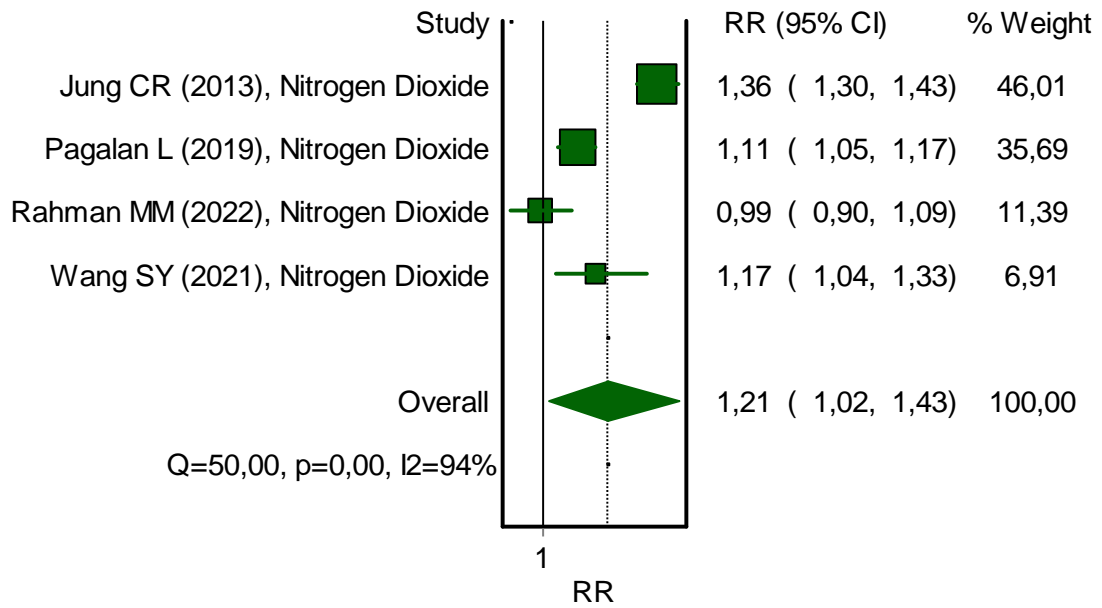
Interpretation: The association between pesticides and autism was RR = 1,15 (95% CI: 1,00 to 1,33) and the heterogeneity was low (I^2 : 0%) (Figure S7).

Figure S8. Meta-analysis association between dioxins, furans, PCBs and autism.



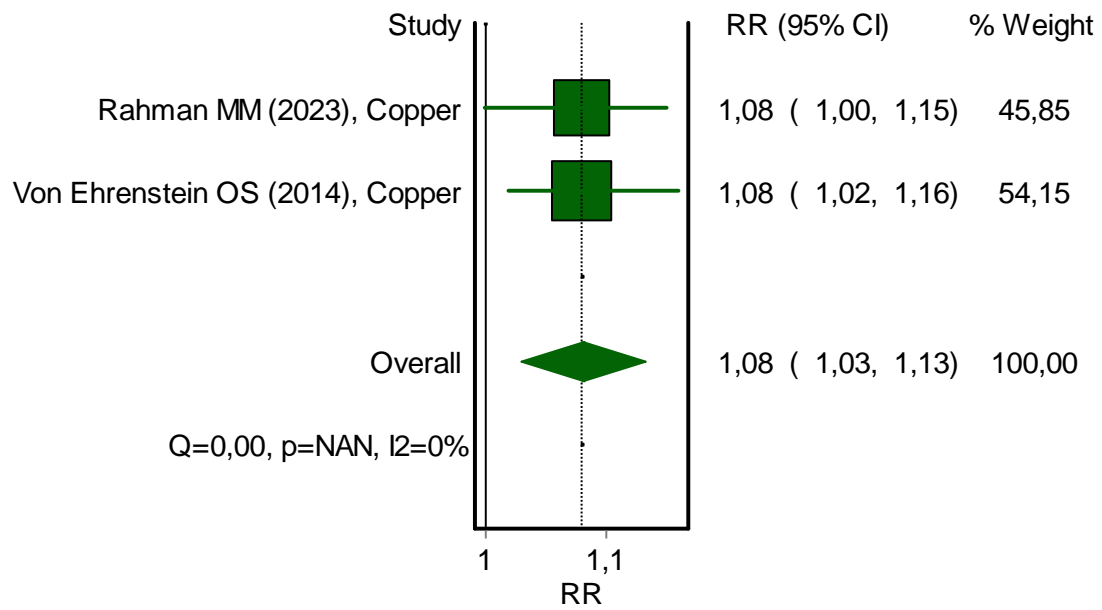
Interpretation: The association between dioxins, furans, PCBs and autism was RR = 1,23 (95% CI: 0,91 to 1,66) and the heterogeneity was moderated (I²: 61%) (Figure S8).

Figure S9. Meta-analysis association nitrogen dioxide and autism with diagnostic instruments.



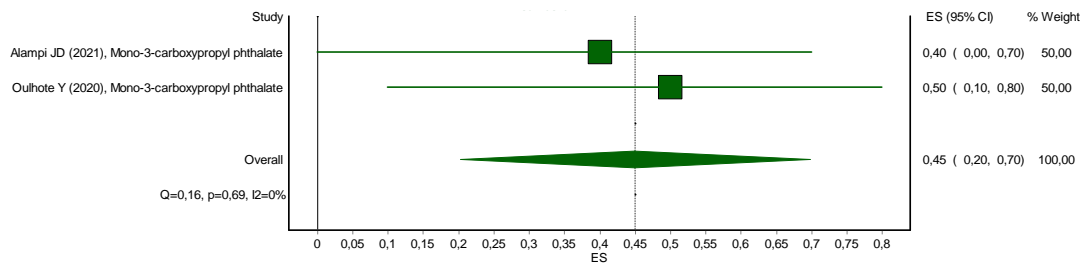
Interpretation: The association between nitrogen dioxide and autism was $RR = 1,21$ (95% CI: 1,02 to 1,43) and the heterogeneity was high ($I^2: 94\%$) (Figure S9).

Figure S10. Meta-analysis association between copper and autism with diagnostic instruments.



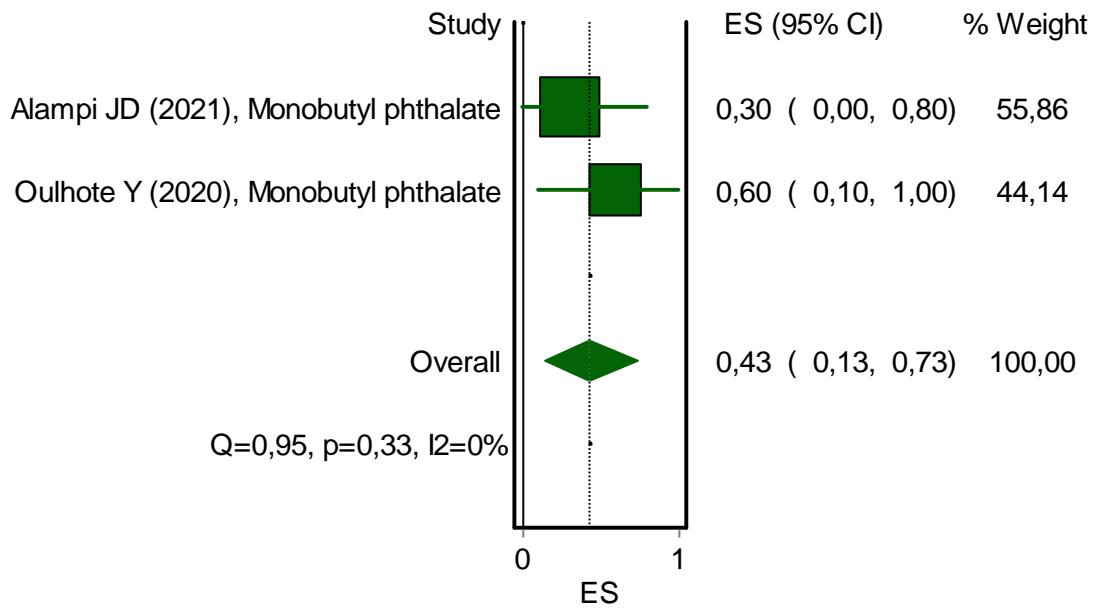
Interpretation: The association between copper and autism was RR = 1,08 (95% CI: 1,03 to 1,13) and the heterogeneity was low (I^2 : 0%) (Figure S10).

Figure S11. Meta-analysis association between mono-3-carboxypropyl phthalate and autism with screening instruments.



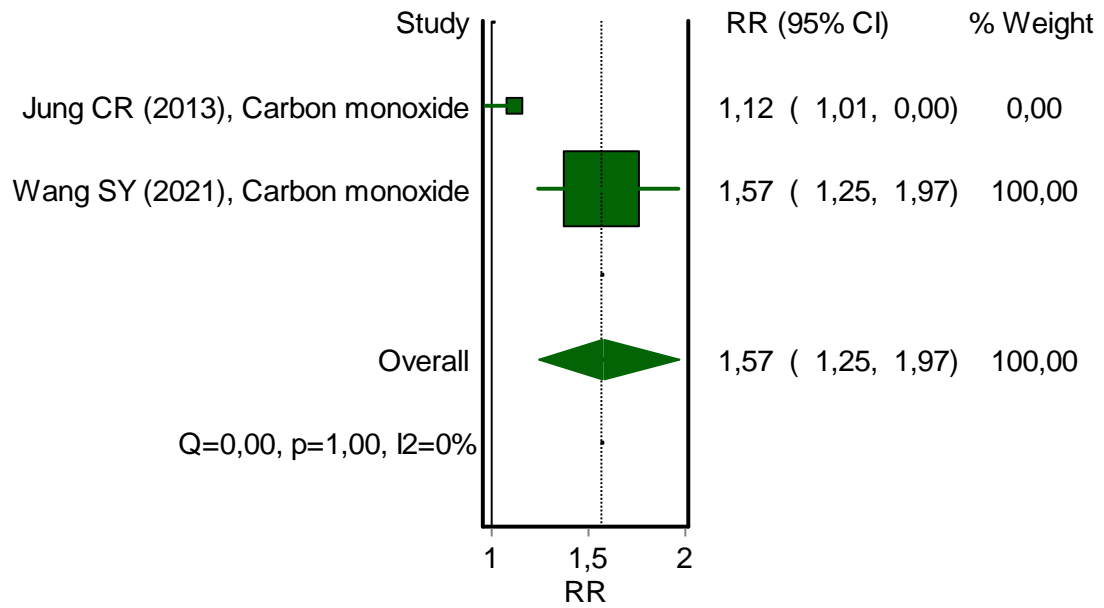
Interpretation: The association between mono-3-carboxypropyl phthalate and autism was $\beta= 0,45$ (95% CI: 0,20 to 0,70) and the heterogeneity was low ($I^2: 0\%$) (Figure S11).

Figure S12. Meta-analysis association between monobutyl phthalate and autism with screening instruments.



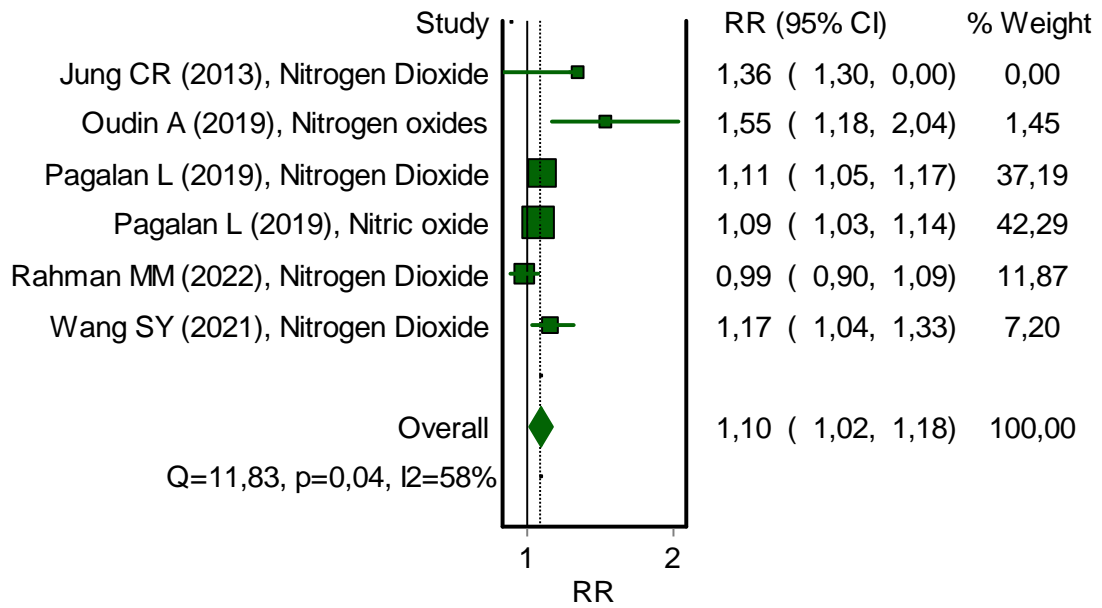
Interpretation: The association between monobutyl phthalate and autism was $\beta = 0,43$ (95% CI: 0,13 to 0,73) and the heterogeneity was low ($I^2: 0\%$) (Figure S12).

Figure S13. Meta-analysis association between carbon monoxide and autism with diagnostic instruments.



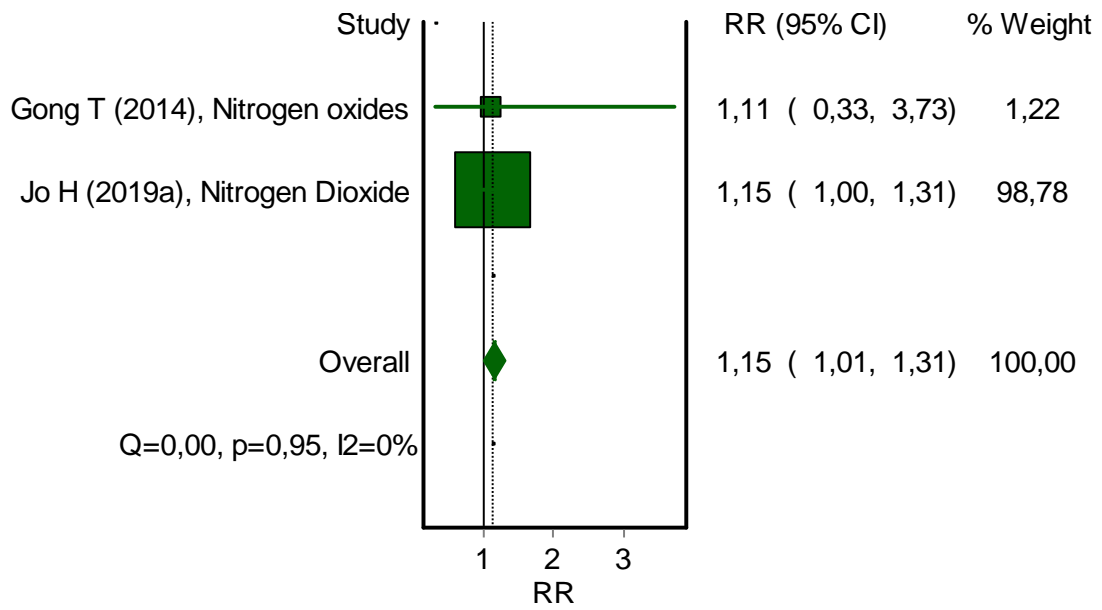
Interpretation: The association between carbon monoxide and autism was RR = 1,57 (95% CI: 1,25 to 1,97) and the heterogeneity was low (I²: 0%) (Figure S13).

Figure S14. Meta-analysis association between nitrogen oxides and autism with diagnostic instruments.



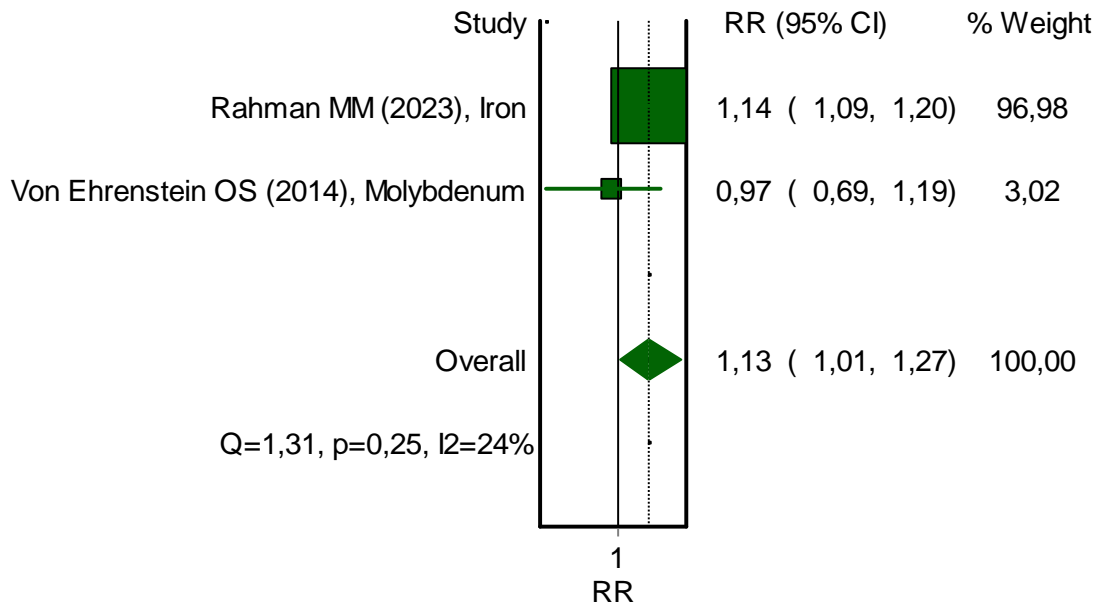
Interpretation: The association between nitrogen oxides and autism was RR = 1,10 (95% CI: 1,02 to 1,18) and the heterogeneity was moderated (I²: 58%) (Figure S14).

Figure S15. Meta-analysis association between nitrogen oxides and autism with screening instruments.



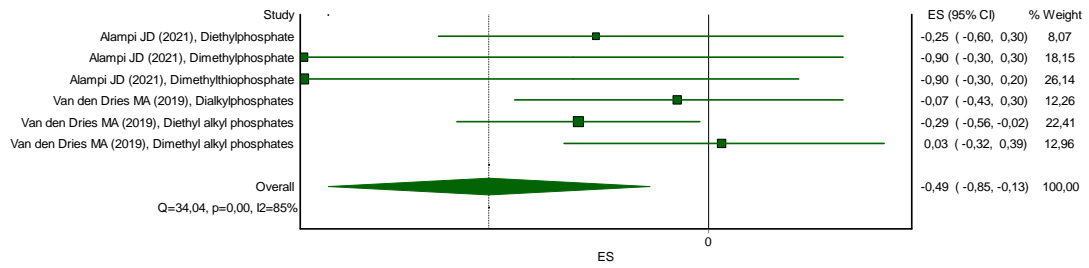
Interpretation: The association between nitrogen oxides and autism was RR = 1,15 (95% CI: 1,01 to 1,31) and the heterogeneity was low (I²: 0%) (Figure S15).

Figure S16. Meta-analysis association between metals elements and autism with diagnostic instruments.



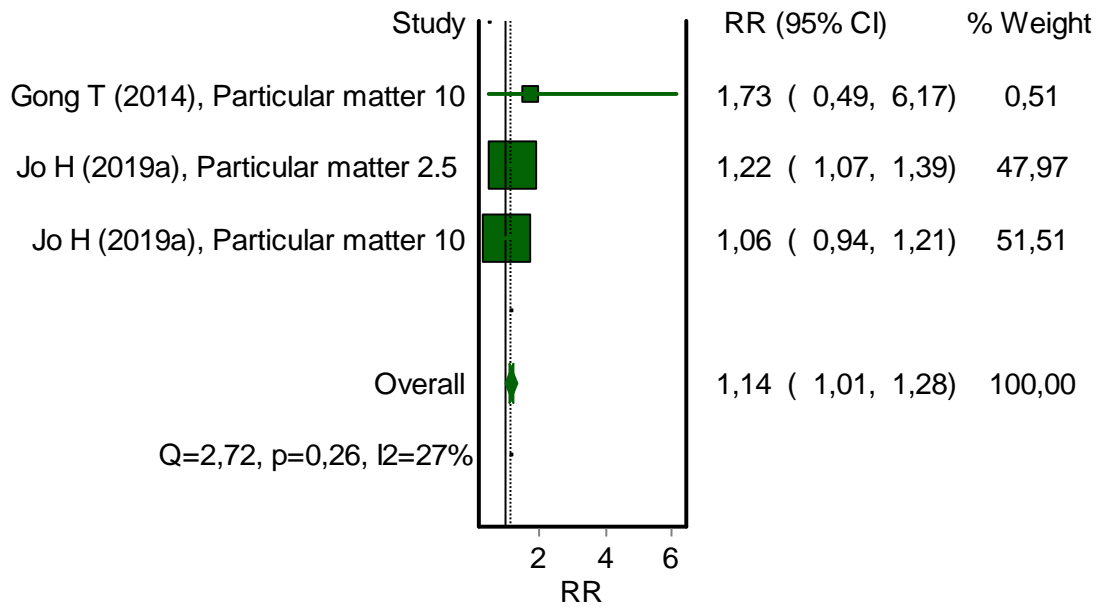
Interpretation: The association between metals elements and autism was RR = 1,13 (95% CI: 1,01 to 1,27) and the heterogeneity was low (I²: 24%) (Figure S16).

Figure S17. Meta-analysis association between organophosphates and carbamates and autism with screening instruments.



Interpretation: The association between organophosphates and carbamates and autism was $RR = -0,49$ (95% CI: $-0,85$ to $-0,13$) and the heterogeneity was high (I^2 : 85%) (Figure S17).

Figure S18. Meta-analysis association between particulate matter and autism with screening instruments.



Interpretation: The association between particulate matter and autism was RR = 1,14 (95% CI: 1,01 to 1,28) and the heterogeneity was moderated (I^2 : 27%) (Figure S18).