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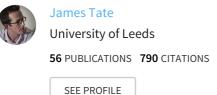
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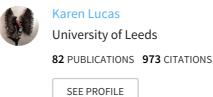
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# Exposure to Traffic-related Air Pollution and Risk of Development of Childhood Asthma: A Systematic Review and Meta-analysis

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#### **Background and Objective**

The question of whether children's exposure to trafficrelated air pollution (TRAP) contributes to their initial development of asthma is an unresolved one. We conducted a systematic review and performed a metaanalysis to examine the association between TRAP and asthma development in childhood.

### Study Eligibility Criteria, Participants and Interventions

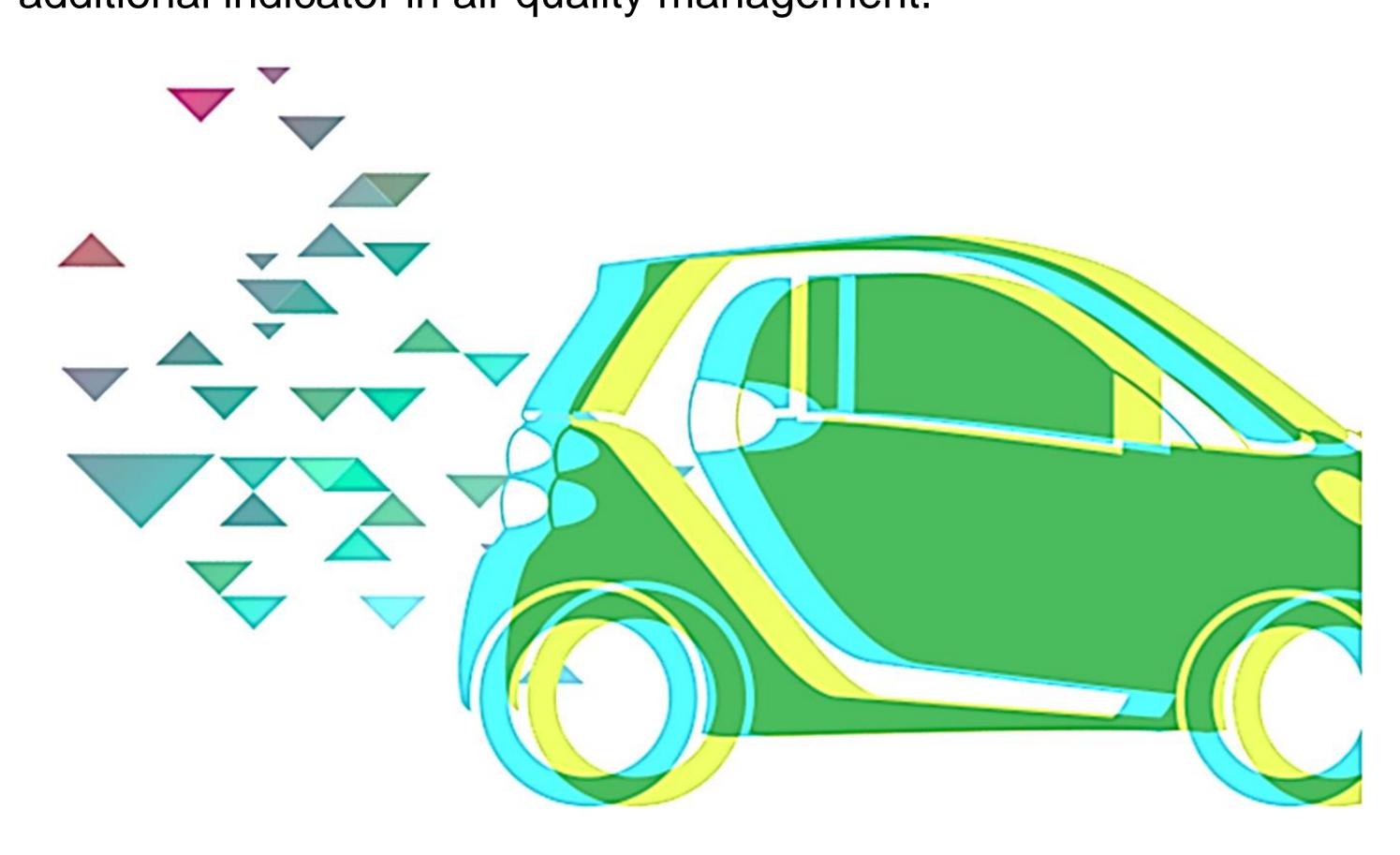
We included studies that examined the association between children's exposure to TRAP metrics and their subsequent risk of "asthma" development through birth to age 18 years old.

## **Key Findings**

Thirty-eight studies met our eligibility criteria. There was notable variability in asthma definitions, TRAP exposure assessment methods and selections for confounder adjustment. The summary overall random-effects ORs were 1.08 (95% CI 1.02, 1.14) per 0.5 x  $10^{-5}~\text{m}^{-1}$  black carbon (BC), 1.04 (95% CI 1.01, 1.08) per 4 µg/m³ NO2, 1.46 (95% CI 0.77, 2.78) per 30 µg/m³ NOx, 1.04 (95% CI 0.99, 1.08) per 1 µg/m³ PM2.5 and 1.05 (95% CI 1.01, 1.10) per 2 µg/m³ PM10. The least heterogeneity was seen for the BC and PM10 estimates whilst the most heterogeneity was seen for NO2 and NOx. Fixed-effects models and sensitivity analyses supported these findings. The age-specific models suggested that the effects were more robust in the older children where diagnosis is likely more reliable. There was suggestion that effects were different between sexes and that they may be limited to non-atopic asthma.

#### Conclusions and Implication of Key Findings

Recently, there has significant advances in the field, yet we highlight important gaps in the current state of research particularly in the exposure assessment, lack of outcome harmonization and systematic evaluation of subgroups and phenotypic characterization of asthma. Improvements in these areas, albeit challenging, are central to better understanding the role of TRAP in asthma pathogenesis. As it stands, the impact of TRAP on asthma prevalence could be considerable because of the high numbers of children exposed. Our findings underlie the need to reduce childhood exposures to TRAP and suggest a value of BC as an additional indicator in air quality management.



#### **Data Sources**

We systematically reviewed epidemiological studies published until 6<sup>th</sup> March 2016 and available in the Embase, Ovid MEDLINE (R), and Transport databases.

#### **Study Appraisal and Synthesis Methods**

We extracted and tabulated key characteristics of each included study using a predefined piloted data template. We used the Critical Appraisal Skills Programme checklists to assess the risk of bias for each included study. Where four or more independent odds ratios (OR) were available for a continuous pollutant exposure, we conducted random-effects and age-specific (below and above 6 years old) meta-analyses. We conducted four sensitivity analyses for each summary meta-analytic exposure-outcome association to test the robustness of findings.

			Odds Ratio		Odds Ratio		
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Rando	m, 95% CI	
Carlsten et al. 2010 - at 7 y.o.	0.0397	0.1061	6.5%	1.04 [0.85, 1.28]	· · · · · · · · · · · · · · · · · · ·	<del>-</del> ,	
Clark et al. 2010 LUR - at mean age of 4 y.o	0.0655	0.0312	75.6%	1.07 [1.00, 1.14]		-	
Gehring et al. 2015 b - BAMSE birth to 16 y.o.	-0.0105	0.1707	2.5%	0.99 [0.71, 1.38]	<del></del>		
Gehring et al. 2015 b - PIAMA birth to 14 y.o.	0.1662	0.0804	11.4%	1.18 [1.01, 1.38]		<u> </u>	
Gehring et al. 2015b - GINI&LISA South birth to 15	0.124	0.1831	2.2%	1.13 [0.79, 1.62]			
Gehring et al. 2105b - GINI&LISA North birth to 15	0.0322	0.2613	1.1%	1.03 [0.62, 1.72]		_	
Mölter et al. 2014 b - MAAS only birth to 8 y.o.	0.4293	0.344	0.6%	1.54 [0.78, 3.01]		<u>-</u>	<b>→</b>
Total (95% CI)			100.0%	1.08 [1.02, 1.14]		<b>*</b>	
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.90, df = 6 (P = 0 Test for overall effect: $Z = 2.82$ (P = 0.005)	.82); I²= 0%				0.5 0.7 1 Decreased risk	1.5 Increased risk	<u>−</u> 2

BC meta-analysis: Individual and summary random effects estimates for associations between BC per 0.5 x 10<sup>-5</sup> m<sup>-1</sup> and asthma at any age

				Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl	IV, Random, 95% CI
Carlsten et al. 2010 - at 7 y.o.	0.2253	0.1448	1.3%	1.25 [0.94, 1.66]	
Clark et al. 2010 LUR - at mean age of 4 y.o.	0.0489	0.0171	12.7%	1.05 [1.02, 1.09]	<del></del>
Dell et al. 2014 LUR - 5 to 9 y.o.	0.039	0.04	8.3%	1.04 [0.96, 1.12]	g <del>  ■</del>
Deng et al. 2015 - 3 to 6 y.o.	0.1712	0.0623	5.1%	1.19 [1.05, 1.34]	<del></del>
Gehring et al. 2015 b - BAMSE birth to 16 y.o.	0.0397	0.0498	6.7%	1.04 [0.94, 1.15]	y <del>-   =</del>
Gehring et al. 2015 b - PIAMA birth to 14 y.o.	0.0665	0.0246	11.2%	1.07 [1.02, 1.12]	
Gehring et al. 2015b - GINI&LISA North birth to 15	-0.0679	0.1235	1.8%	0.93 [0.73, 1.19]	, <del> </del>
Gehring et al. 2015b - GINI&LISA South birth to 15	-0.0252	0.0602	5.4%	0.98 [0.87, 1.10]	2 <del></del>
Kim et al. 2016 - at 6-7 y.o.	-0.0214	0.0219	11.8%	0.98 [0.94, 1.02]	<del>-= </del>
MacIntyre et al. 2014 - CAPPS&SAGE only birth to 8	0.1111	0.1268	1.7%	1.12 [0.87, 1.43]	
Mölter et al. 2014 b - MAAS only birth to 8 y.o.	0.574	0.2374	0.5%	1.78 [1.11, 2.83]	
Nishimura et al. 2013 - 8 to 21 y.o.	0.0632	0.0269	10.8%	1.07 [1.01, 1.12]	<del></del>
Oftedal et al. 2009 - birth to 10 y.o.	-0.0359	0.0196	12.2%	0.96 [0.93, 1.00]	-=-
Ranzi et al. 2014 - birth to 7 y.o.	0.0289	0.0701	4.4%	1.03 [0.90, 1.18]	<del>-   -  </del>
Shima et al. 2002 - 6 to 12 y.o.	0.1136	0.0534	6.2%	1.12 [1.01, 1.24]	
Total (95% CI)			100.0%	1.04 [1.01, 1.08]	•
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 38.32, df = 14 (P = 0.0005); $I^2$ = 63%					
Test for overall effect: $Z = 2.38$ (P = 0.02)	•.:				0.5 0.7 1 1.5 2
					Decreased risk Increased risk

NO<sub>2</sub> meta-analyses: Individual and summary random effects estimates for associations between NO<sub>2</sub> per 4 μg/m<sup>3</sup> and asthma at any age

Study or Subgroup	log[Odds Ratio]		Odds Ratio SE Weight IV, Random, 95		Odds Ratio Cl IV, Random, 95% Cl		
Carlsten et al. 2010 - at 7 y.o.	0.276	0.1082	3.9%	1.32 [1.07, 1.63]			
Clark et al. 2010 LUR - at mean age of 4 y.o.	0.01	0.0101	46.6%	1.01 [0.99, 1.03]		•	
Gehring et al. 2015 b - BAMSE birth to 16 y.o.	0.0259	0.0385	20.1%	1.03 [0.95, 1.11]		<del>-</del>	
Gehring et al. 2015 b - PIAMA birth to 14 y.o.	0.1093	0.0546	12.4%	1.12 [1.00, 1.24]		=	
Gehring et al. 2015b - GINI&LISA North birth to 15	0.066	0.1352	2.5%	1.07 [0.82, 1.39]		<del></del>	
Gehring et al. 2015b - GINI&LISA South birth to 15	-0.0266	0.0861	5.8%	0.97 [0.82, 1.15]			
Mölter et al. 2014 b - MAAS only birth to 8 y.o.	-0.1688	0.8068	0.1%	0.84 [0.17, 4.11]	+	-	<b>—</b>
Nishimura et al. 2013 - 8 to 21 y.o.	0.0296	0.0691	8.5%	1.03 [0.90, 1.18]			
Total (95% CI)			100.0%	1.04 [0.99, 1.08]		•	
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 9.59, df = 7 (P = 0 Test for overall effect: $Z = 1.66$ (P = 0.10)	l.21); l²= 27%				0.5	0.7 1 1.5 Decreased risk Increased risk	2

 $PM_{2.5}$  meta-analyses: Individual and summary random effects estimates for associations between  $PM_{2.5}$  per 1  $\mu$ g/m³ and asthma at any age

