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Risk of childhood leukemia and exposure to outdoor air pollution. Updated review and dose-response meta-analysis

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Background

Leukemia is the most frequent our previous review and meta-Most epidemiologic studies have now available, and we also suggested that exposure to traffic performed a dose-response metapollutants may increase the risk of analysis using traffic estimators. childhood leukemia. We updated

malignant disease of childhood. analysis as some recent studies have

Methods

performed a systematic leukemia subtype (ALL: acute We 2016, lymphoblastic leukemia, PubMed search in July AML: MeSH Terms acute myeloid leukemia). We used including as "childhood leukemia", "traffic" and the highest versus the lowest "benzene". We extracted the category estimates for meta-analysis following data: study estimates, type of the effect of traffic density and

Results

Summary RR (sRR) associated with traffic density were 1.05 (95% CI alternatively one study from each 0.97 to 1.14) for all leukemia, 1.03 summary estimate did not alter (1.00 to 1.06) for ALL and 1.04 substantially the results. A dose-(0.81 to 1.34) for AML. For response meta-analysis indicated an benzene, sRR were 1.29 (0.98 to approximately linear association 1.70) for all leukemia, 1.04 (0.87 to between number of vehicles per 1.24) for ALL and 1.75 (1.20 to day and disease risk. Similar results 2.56) for AML. sRR for NO_2 were were found for NO_2 estimator with 1.05 (0.86 to 1.28) for all leukemia, increasing risk approximately from 1.04 (0.83 to 1.31) for ALL and $40 \,\mu\text{g/m}^3$ level, and for benzene for 0.97 (0.77 to 1.23) for AML). which risk star increasing after 3 Finally sRR for 1-3 butadiene was $\mu g/m^3$. 1.45 (1.08 to 1.95).

Sensitivity analysis removing

of exposure assessment (traffic benzene exposure on disease risk. density, generally coded as numbers For dose-response meta-analysis of vehicles per day, distance and/or the number of vehicles per day was length of major roads near subjects used as continuous estimator of address; benzene exposure) and traffic exposure.



Figure 1. Summary RR for traffic density, NO₂ and benzene for all leukemia and divided by subtypes(ALL and AML).

	Traffic density Weight			NO_2				Be	Benzene		%	
Reference	Region	RR (95% CI)	(D+L)		-	•	%	Reference	Region		RR (95% CI)	Weight
Harrison 1999	United Kindom	1.61 (0.90, 2.87)	1.87	Reference	Region	RR (95% CI)	Weight (D+L)			1!		
Raaschou-Nielsen 200	1 Denmark	1 10 (0 60 2 20)	1 52					Raaschou-Nielsen 2	2001 Denmark (=		0.40 (0.10, 1.60)	3.43
l angholz 2002		1 40 (0 90 2 30)	2 73	Feytching 1998	Sweden —	● → 2.70 (0.33, 22.3	7) 0.86					
Steffen 2004		1.30 (0.60, 2.90)	1.06	Raaschou-Nielsen 2	001 Denmark 🛛 👘	0.40 (0.11, 1.44) 2.18	Crosignani 2004	Italy		→ 3.91 (1.36, 11.26	5) 5.42
Reynolds 2004	California –	0.92 (0.73, 1.15)	8.22	Weng 2008	Taiwan –	2.29 (1.44, 3.64) 10.03	Vinceti 2012	Italy		1.70 (0.80, 3.61)	8.99
Crosignani 2004	Italy	2.09 (0.85, 5.12)	0.82	Badaloni 2013	Italy 😽	0.85 (0.61, 1.18) 13.68			i	, , , , , , , , , , , , , , , , , , ,	
Von Behren 2008 (ALL) California	1.17 (0.76, 1.81)	3.12	Ghosh 2013 (ALL)	California 🗧	1.23 (0.98, 1.54) 17.17	Heck 2014 (ALL)	California –		1.23 (0.62, 2.44)	10.19
Badaloni 2013	ltaly	0.91 (0.68, 1.21)	5.98	Ghosh 2013 (AML)	California 🚽 📕	0.71 (0.39, 1.30) 7.32	Heck 2014 (AML)	California		- 2 61 (0 97 7 01)	6 04
Heck 2013 (ALL)	California	1.03 (1.00, 1.07)	20.65	Houot 2015 (ALL)	France	0.90 (0.80, 1.01) 20.44		California		2.01 (0.07, 1.01)	0.04
Heck 2013 (AML)	California 🗾	0.89 (0.79, 1.00)	14.94	Houot 2015 (AML)	France	1.00 (0.76, 1.31) 15.62	Houot 2015 (ALL)	France	-	0.90 (0.75, 1.08)	24.79
Houot 2015 (ALL)	France	1.00 (0.90, 1.10)	16.29	Janitz 2016	Oklahoma	1 08 (0 75 1 55) 12.69		Frence		4 00 (4 00 0 40)	40.04
Houot 2015 (AML)	France	1.20 (1.00, 1.30)	13.94	D+L Overall (I-squar	red = 66.6% $p = 0.002$	1 05 (0 86 1 28) 100.00	HOUOL 2015 (AML)	France		1.60 (1.03, 2.46)	10.24
Spycher 2015	Switzerland 🚽 📧 🚽	1.43 (0.79, 2.61)	1.77	NOS>7 Overall (I-so	$\mu ared = 69.8\%$ $p = 0.002)$	1.09 (0.86, 1.26)	Symanski 2016	Texas	•	1.17 (0.98, 1.39)	24.90
Janitz 2016	Oklahoma –	0.99 (0.76, 1.29)	6.74		uared = 00.070, p = 0.002)	1.00 (0.00, 1.00))			↓ ↓	, , , , , , , , , , , , , , , , , , ,	
D+L Overall (I-squared	d = 53.6%, p = 0.007)	1.05 (0.97, 1.14)	100.00					Overall (I-squared =	= 65.1%, p = 0.005)	$\langle \mathbf{v} \rangle$	1.29 (0.98, 1.70)	100.00
NOS≥7 Overall (I-squa	red = 56.9%, p = 0.008) 🚯	1.04 (0.95, 1.13)			.3 1	10						
		10							.3	1	10	
D (_ ·		%				%					%
Reference	Region	RR (95% CI)	vveight	Reference Regi	ion	RR (95%)	CI) Weight	Reference	Region		RR (95% CI)	Weight
ALL												
Savitz 1989	Colorado +	1.60 (0.78, 3.30)	0.19	ALL				ALL				
Von Behren 2008 (ALL)	California	1.17 (0.76, 1.81)	0.53	Ghosh 2013 (ALL) Calif	fornia	1.23 (0.98	, 1.54) 34.73	Vinceti 2012 (ALL)	Italy		0.97 (0.49, 1.93)	6.12
Heck 2013 (ALL)	California	1.03 (1.00, 1.07)	87.97	Houot 2015 (ALL) Fran	ice	0.90 (0.80	, 1.01) 45.66	Heck 2014 (ALL)	California		1.23 (0.62, 2.44)	6.16
Houot 2015 (ALL)	France	1.00 (0.90, 1.11)	10.00	Janitz 2016 (ALL) Okla	ihoma 🚽 🖉 🖉	1.09 (0.72	, 1.65) 19.6 <mark>1</mark>	Houot 2015 (ALL)	France		0.90 (0.75, 1.08)	43.47
Spycher 2015	Switzerland	1.50 (0.77, 2.92)	0.23	Subtotal (I-squared = 6	8.7%, p = 0.041)	1.04 (0.83	, 1.31) 100.00	Symanski 2016	Texas		1.17 (0.98. 1.39)	44,25
Janitz 2016 (ALL)	Oklahoma —	0.96 (0.71, 1.30)	1.07					Subtotal (I-squared =	33.8% n = 0.210)	5	1 04 (0 87 1 24)	100.00
Subtotal (I-squared = 0.0	0%, p = 0.622)	1.03 (1.00, 1.06)	100.00	AML				Cubicial (1-54ualeu -	00.070, p 0.210)	Y	1.04 (0.07, 1.24)	100.00
				Ghosh 2013 (AML)Calif	fornia (🔹 🔹 🗌 –	0.71 (0.39	, 1.30) 15.18	AMI				





Conclusions

Our results confirmed previous findings butadiene increased leukemia risk, especially about an excess risk of childhood leukemia AML risk for benzene. Dose-response in area with high traffic density, especially analysis revealed a linear risk increase for for the ALL subtype. When considering exposure air pollutants, namely nitrogen specific pollutants, both benzene and 1,3 dioxide and benzene.





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