

ADDITIONAL MATERIALS AVAILABLE ON THE HEI WEBSITE

Special Report 23

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

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

Chapter 8: Traffic-Related Air Pollution and Birth Outcomes Additional Materials 8.1 to 8.4

These Additional Materials were not formatted or edited by HEI. This document was part of the HEI Panel's review process.

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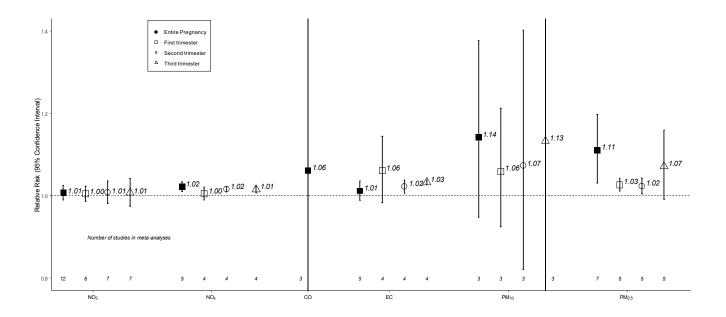
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Chapter 8: Traffic-Related Air Pollution and Birth Outcomes Additional Materials: All Analyses

- 8.1 Term low birth weight
- 8.2 Term birth weight
- 8.3 Small for gestational age
- 8.4 Preterm birth

8.1 Term low birth weight (TLBW)

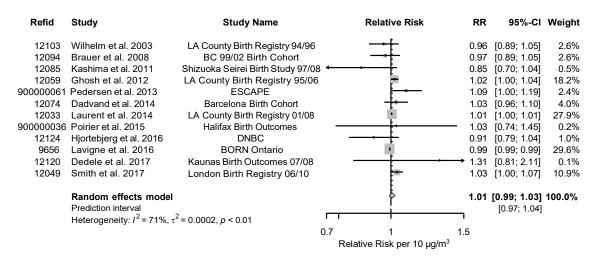
Summary of meta-analysis

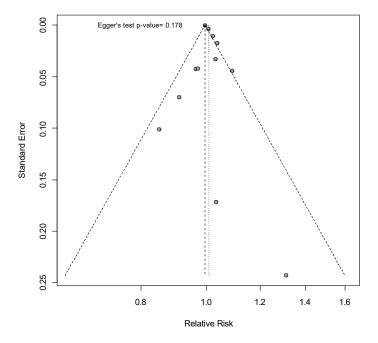


Footnote: The following increments were used: $10 \, \mu g/m^3$ for NO_2 , $20 \, \mu g/m^3$ for NO_x , $1 \, mg/m^3$, $1 \, \mu g/m^3$ for EC, $10 \, \mu g/m^3$ for $PM_{2.5}$ and $5 \, \mu g/m^3$ for $PM_{2.5}$. Effect estimates cannot be directly compared across the different traffic-related pollutants because the selected increments do not necessarily represent the same contrast in exposure.

NO2- Entire pregnancy exposure - primary meta-analysis - TLBW

NO₂ entire pregnancy exposure and TLBW



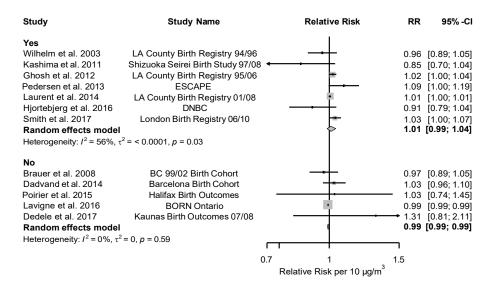


Footnote: The vertical lines in the funnel plots represent the pooled fixed and random effect estimates. The vertical dashed line in the middle of the funnel shows the fixed effect estimate. As the Panel applied a random-effects model, the funnel plot also presents the random-effects estimate with the dotted line.

Subgroup analysis – entire pregnancy exposure

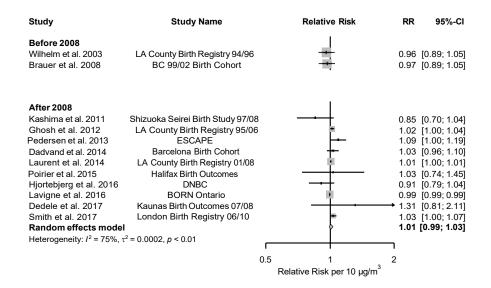
By gestational age adjustment

NO2 - TLBW by gestational age

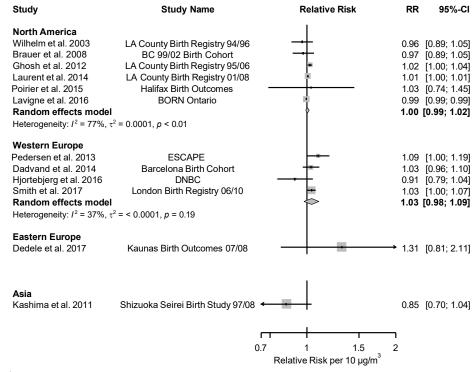


By publication year

NO2 - TLBW by publication year

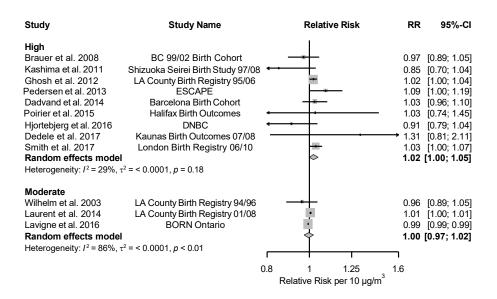


NO₂ - TLBW by region



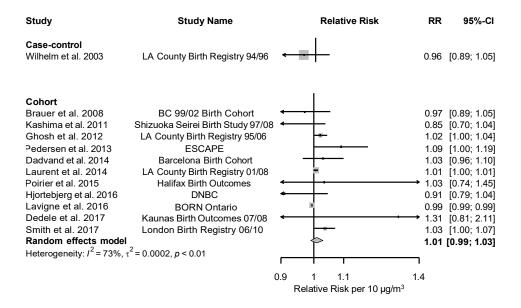
By traffic specificity

NO2 - TLBW by Traffic Specificity



By study design

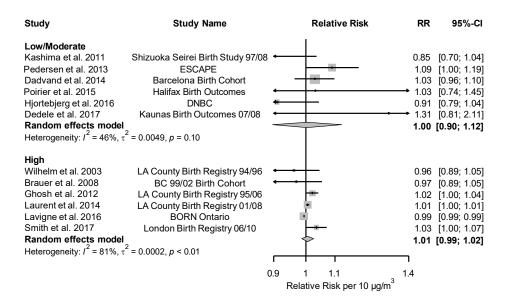
NO₂ - TLBW by study design



By risk of bias

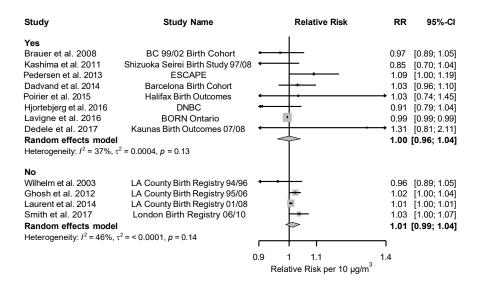
Plots not shown for risk of bias domains if all studies were rated low or moderate

NO₂ - TLBW by Risk of bias assessment on confounding



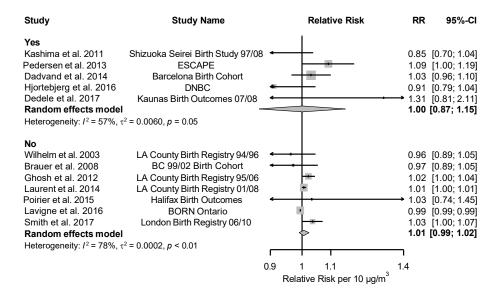
By smoking adjustment

NO₂ - TLBW by smoking adjustment



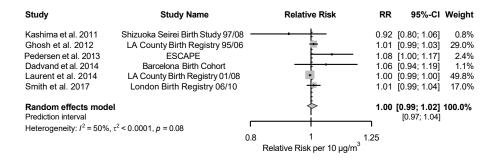
By BMI adjustment

NO₂ - TLBW by BMI



NO₂ First trimester exposure - primary meta-analysis - TLBW

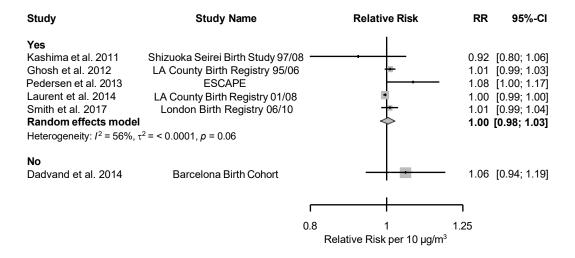
NO₂ first trimester exposure and TLBW



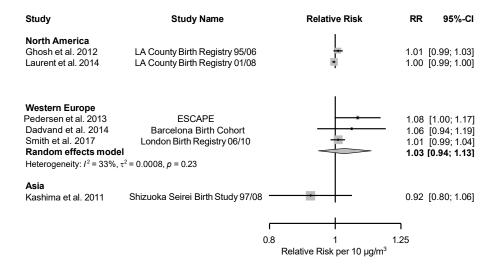
Subgroup analysis

By gestational age adjustment

NO₂ - first trimester and TLBW by gestational age

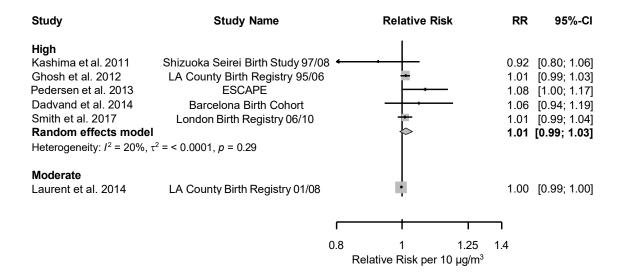


NO₂-first trimester exposure and TLBW by region



By traffic specificity

NO₂ first trimester - TLBW by Traffic Specificity

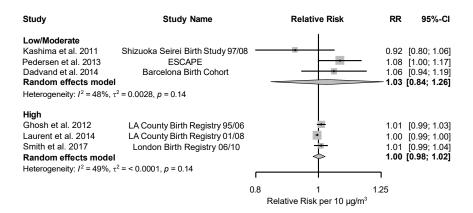


By study design- all cohort studies

By risk of bias

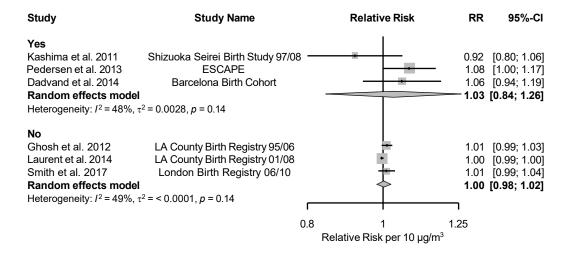
Plots not shown for risk of bias domains if all studies were rated low or moderate

NO2 first trimester - TLBW by Risk of bias assessment on confounding



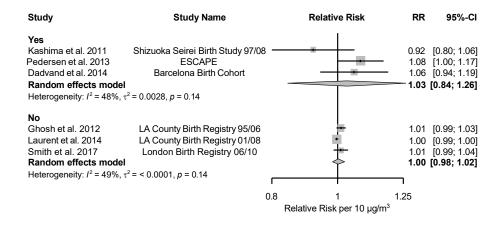
By smoking adjustment

NO₂ first trimester - TLBW by smoking adjustment

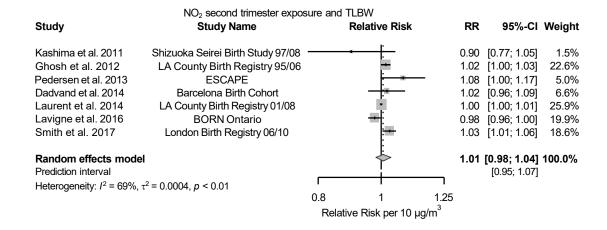


By BMI adjustment

NO_2 - TLBW by BMI



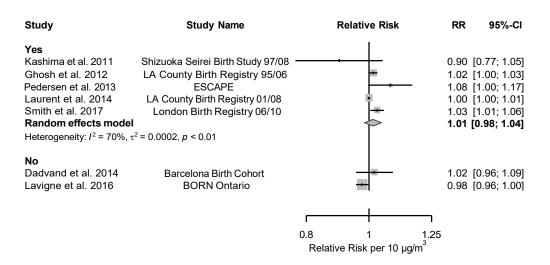
NO₂ Second trimester exposure - primary meta-analysis - TLBW



Subgroup analysis

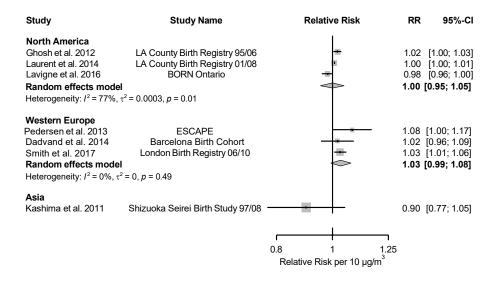
By gestational age adjustment

 $\ensuremath{\text{NO}_2}\xspace$ - second trimester and TLBW by gestational age



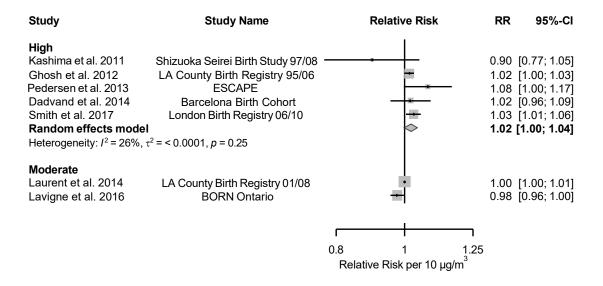
By study design - all cohort studies

NO₂ second trimester exposure and TLBW by region



By traffic specificity

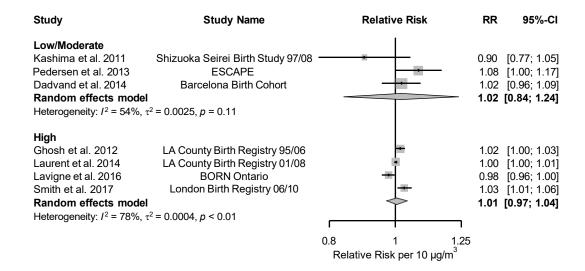
NO₂ second trimester - TLBW by Traffic Specificity



By risk of bias

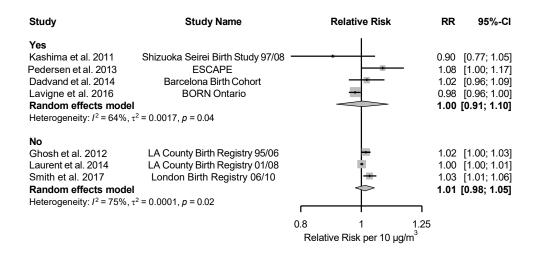
Plots not shown for risk of bias domains if all studies were rated low or moderate

NO₂ second trimester - TLBW by Risk of bias assessment on confounding



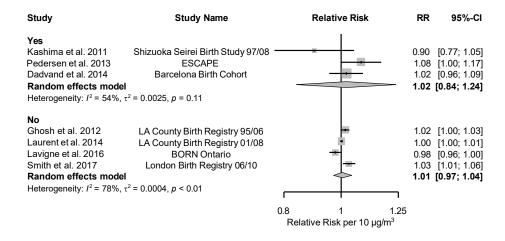
By smoking adjustment

NO₂ second trimester - TLBW by smoking adjustment



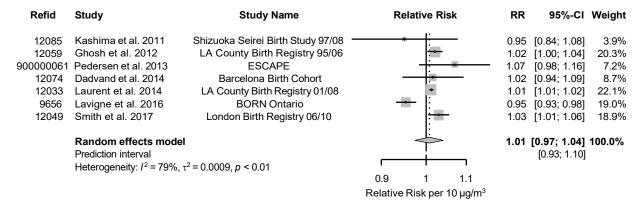
By BMI adjustment

NO_2 second trimester - TLBW by BMI



NO₂ Third trimester exposure - primary meta-analysis - TLBW

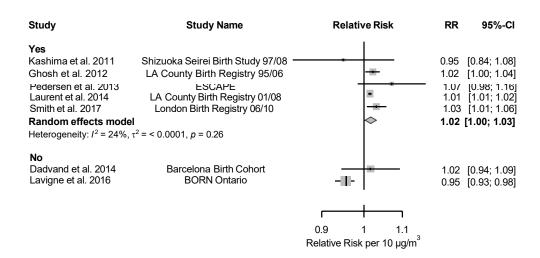
NO₂ third trimester exposure and TLBW



Subgroup analysis – third trimester exposure

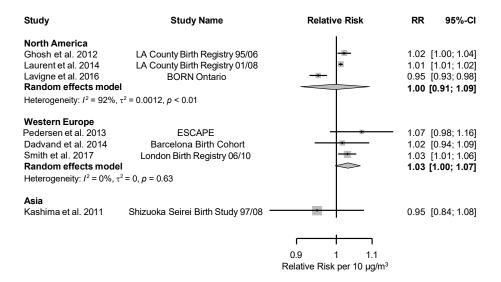
By gestational age adjustment

NO₂ - third trimester and TLBW by gestational age



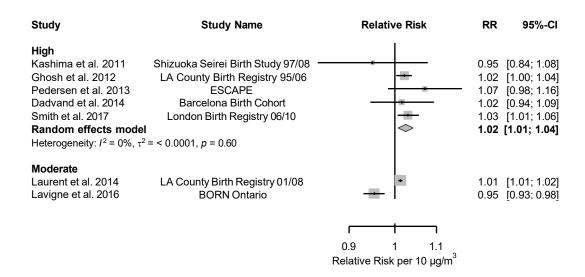
By study design - all cohort studies

NO₂ third trimester exposure and TLBW by region



By traffic specificity

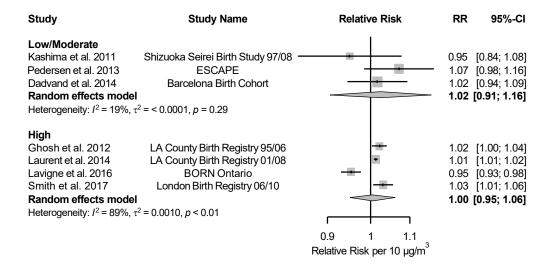
NO₂ third trimester - TLBW by Traffic Specificity



By risk of bias

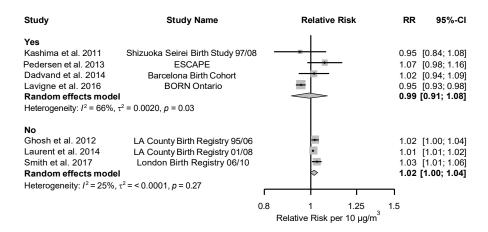
Plots not shown for risk of bias domains if all studies were rated low or moderate

NO₂ third trimester - TLBW by Risk of bias assessment on confounding



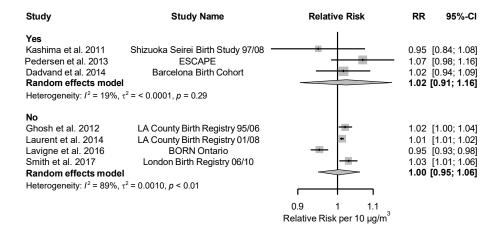
By smoking adjustment

NO₂ third trimester - TLBW by smoking adjustment



By BMI adjustment

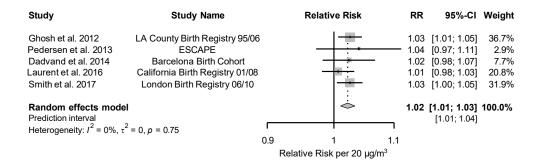
NO2 third trimester - TLBW by BMI



NO - entire pregnancy only 2 independent cohorts for TLBW (Brauer et al. 2008, Gosh et al. 2012); hence no meta-analysis.

NO_x Entire pregnancy exposure - primary meta-analysis - TLBW

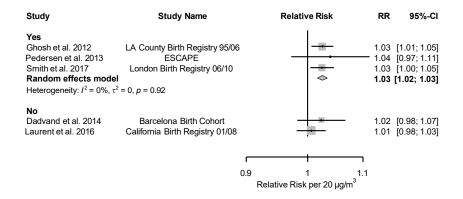
NO_x entire pregnancy exposure and TLBW



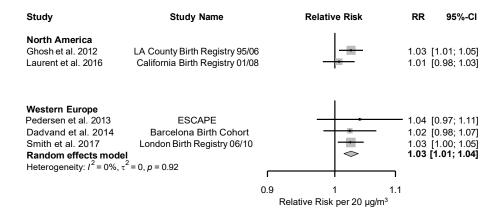
Subgroup analysis – entire pregnancy exposure

By gestational age adjustment

NO_x entire pregnancy and TLBW by gestational age



NO_x entire pregnancy and TLBW by region

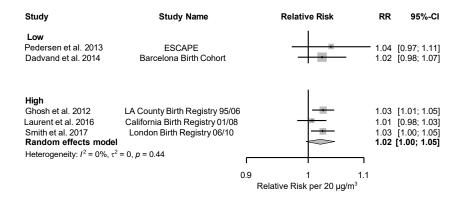


By traffic specificity - all rated high

By risk of bias

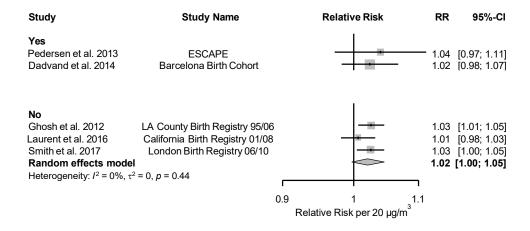
Plots not shown for risk of bias domains if all studies were rated low or moderate

NO_x entire pregnancy - TLBW by Risk of bias assessment on confounding



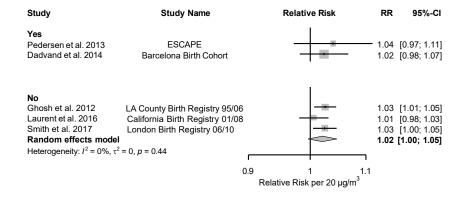
By smoking adjustment

NO_x entire pregnancy - TLBW by smoking adjustment



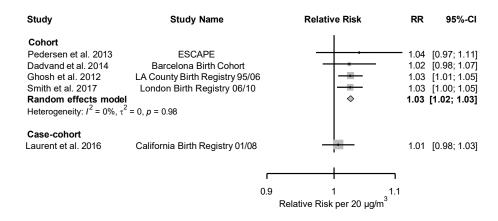
By BMI adjustment

NO_{x} entire pregnancy - TLBW by BMI



By study design

NO_x entire pregnancy - TLBW by Study Design



NO_x First trimester exposure - primary meta-analysis - TLBW

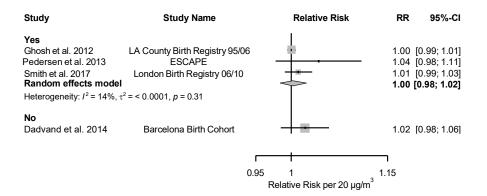
NO_x first trimester exposure and TLBW



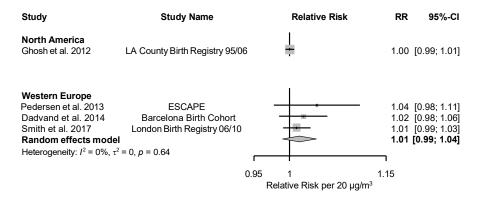
Subgroup analysis – first trimester exposure

By gestational age adjustment

NO_x first trimester and TLBW by gestational age



NO_x first trimester and TLBW by region



By traffic specificity - all high

By study design - all cohort studies

By risk of bias

Ghosh et al. 2012 and Smith et al. 2017 high risk of bias for confounding, Dadvand et al. 2014 and Pedersen et al. 2013 low risk of bias for confounding.

By smoking adjustment

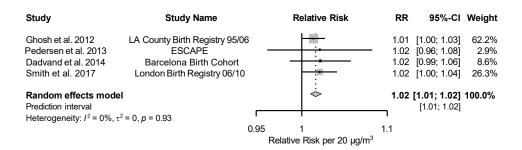
Dadvand et al. 2014 and Pedersen et al. 2013 adjusted for smoking, Ghosh et al. 2012 and Smith et al. 2017 did not adjust for smoking.

By BMI adjustment

Dadvand et al. 2014 and Pedersen et al. 2013 adjusted for BMI, Ghosh et al. 2012 and Smith et al. 2017 did not adjust for BMI.

NO_x Second trimester exposure - primary meta-analysis - TLBW

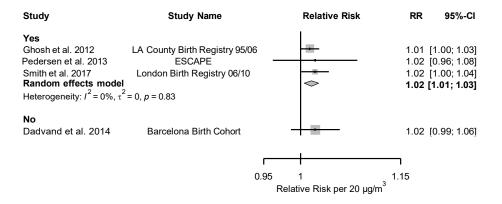
NO_x second trimester exposure and TLBW



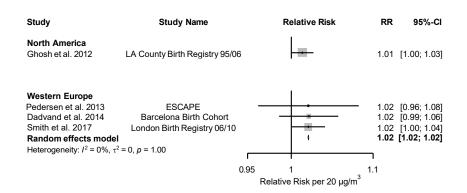
Subgroup analysis – second trimester exposure

By gestational age adjustment

NO_x second trimester and TLBW by gestational age



NO_x second trimester and TLBW by region



By traffic specificity - all high

By study design- all cohort studies

By risk of bias

Ghosh et al. 2012 and Smith et al. 2017 high risk of bias for confounding, Dadvand et al. 2014 and Pedersen et al. 2013 low risk of bias for confounding.

By smoking adjustment

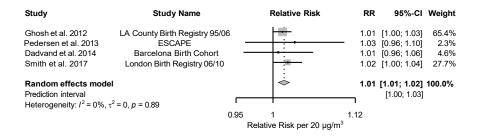
Dadvand et al. 2014 and Pedersen et al. 2013 adjusted for smoking, Ghosh et al. 2012 and Smith et al. 2017 did not adjust for smoking.

By BMI adjustment

Dadvand et al. 2014 and Pedersen et al. 2013 adjusted for BMI, Ghosh et al. 2012 and Smith et al. 2017 did not adjust for BMI.

NO_x Third trimester exposure - primary meta-analysis - TLBW

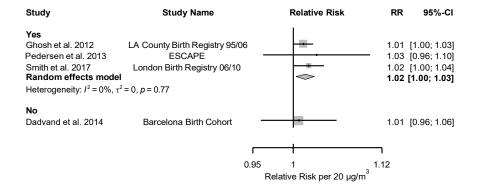
NO_x third trimester exposure and TLBW



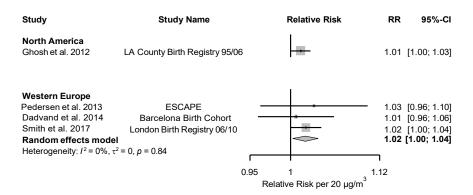
Subgroup analysis – third trimester exposure

By gestational age adjustment

NO_x third trimester and TLBW by gestational age



$NO_{\scriptscriptstyle X}$ third trimester and TLBW by region



By traffic specificity- all high

By study design- all cohorts

By risk of bias

Ghosh et al. 2012 and Smith et al. 2017 high risk of bias for confounding, Dadvand et al. 2014 and Pedersen et al. 2013 low risk of bias for confounding.

By smoking adjustment

Dadvand et al. 2014 and Pedersen et al. 2013 adjusted for smoking, Ghosh et al. 2012 and Smith et al. 2017 did not adjust for smoking.

By BMI adjustment

Dadvand et al. 2014 and Pedersen et al. 2013 adjusted for BMI, Ghosh et al. 2012 and Smith et al. 2017 did not adjust for BMI.

EC Entire pregnancy exposure - primary meta-analysis - TLBW

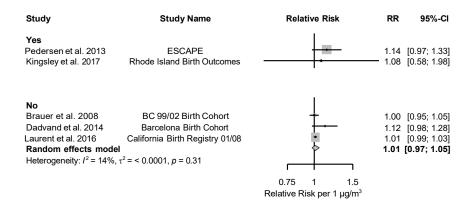
EC entire pregnancy exposure and TLBW

Study	Study Name	pollutant	Relative Risk	RR	95%-CI	Weight
Brauer et al. 2008 Pedersen et al. 2013 Dadvand et al. 2014	BC 99/02 Birth Cohort ESCAPE Barcelona Birth Cohort	PM2.5 abs PM2.5 abs PM2.5 abs	+	1.14	[0.95; 1.05] [0.97; 1.33] [0.98; 1.28]	10.2% 1.0% 1.3%
Laurent et al. 2016 Kingsley et al. 2017	California Birth Registry 01/08 Rhode Island Birth Outcomes	EC BC			[0.99; 1.03] [0.58; 1.98]	87.4% 0.1%
Random effects model Prediction interval Heterogeneity: $I^2 = 12\%$, $\tau^2 = 0$, $p = 0.34$		 	1.01	[0.99; 1.04] [0.98; 1.04]	100.0%	
,			0.75 1 1.5 Relative Risk per 1 µg/m³			

Subgroup meta-analysis

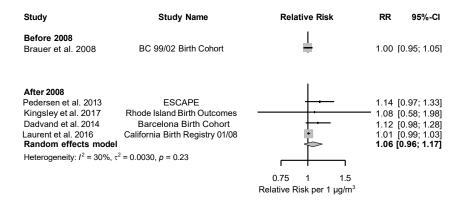
By gestational age adjustment

EC entire pregnancy exposure and TLBW by gestational age



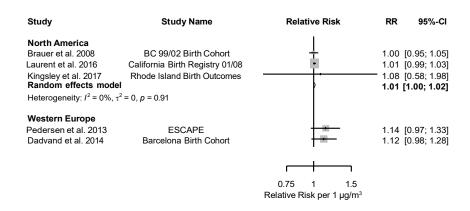
By publication year

EC entire pregnancy exposure and TLBW by publication year



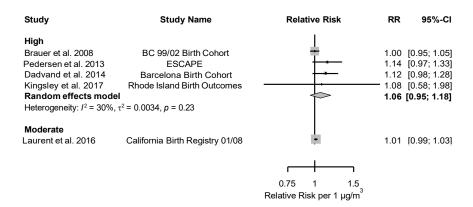
By region

EC entire pregnancy exposure and TLBW by region



By traffic specificity

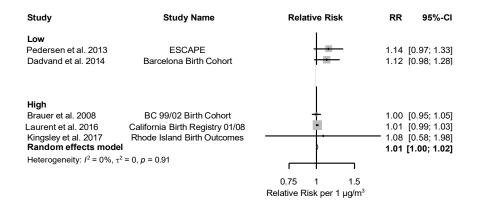
EC entire pregnancy exposure and TLBW by Traffic Specificity



By risk of bias

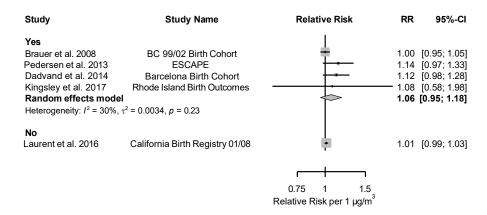
Plots not shown for risk of bias domains if all studies were rated low or moderate

EC entire pregnancy exposure and TLBW by Risk of bias assessment on confounding



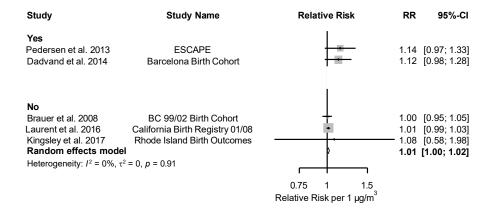
By smoking adjustment

EC entire pregnancy exposure and TLBW by smoking adjustment



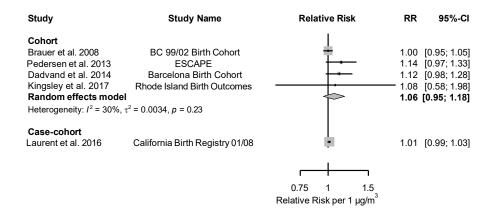
By BMI adjustment

EC entire pregnancy exposure and TLBW by BMI



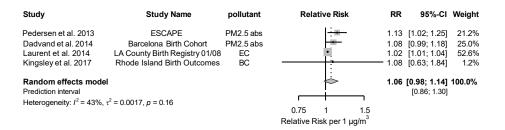
By study design

EC entire pregnancy exposure and TLBW by study design



EC First trimester exposure - primary meta-analysis - TLBW

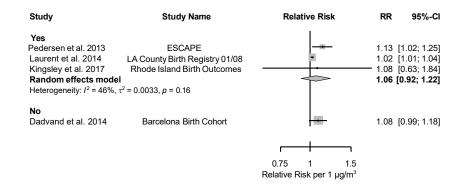
EC first trimester exposure and TLBW



Subgroup meta-analysis

By gestational age adjustment

EC first trimester - and TLBW by gestational age



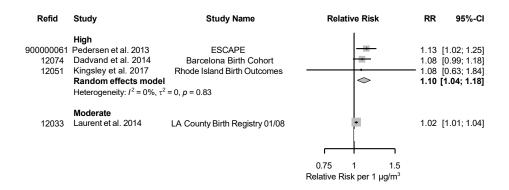
By region

Laurent et al. 2014 and Kingsley et al. 2017 from North America, Dadvand et al. 2014 and Pedersen et al. 2013 from Western Europe.

By study design - all cohort studies

By traffic specificity

EC first trimester - and TLBW by Traffic Specificity

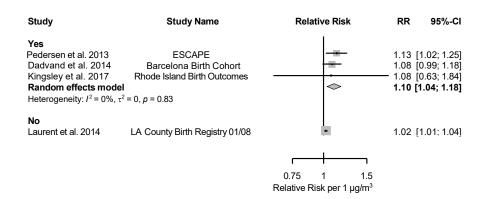


By risk of bias

Laurent et al. 2014 and Kingsley et al. 2017 high risk of bias for confounding, Dadvand et al. 2014 and Pedersen et al. 2013 low risk of bias for confounding.

By smoking adjustment

EC first trimester - and TLBW by smoking adjustment



By BMI adjustment

Dadvand et al. 2014 and Pedersen et al. 2013 adjusted for BMI, Laurent et al. 2014 and Kingsley et al. 2017 did not adjust for BMI.

EC Second trimester exposure - primary meta-analysis - TLBW

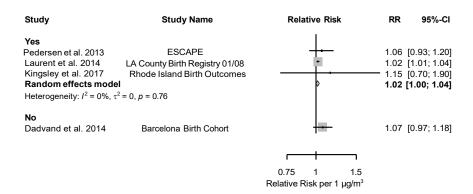
EC second trimester exposure and TLBW

Study	Study Name	pollutant	Rela	ative Risk	RR	95%-CI	Weight
Pedersen et al. 2013 Dadvand et al. 2014 Laurent et al. 2014 Kingsley et al. 2017 Random effects mode Prediction interval Heterogeneity: 1 ² = 0%, τ ²			0.75		1.07 1.02 1.15 1.02	[0.93; 1.20] [0.97; 1.18] [1.01; 1.04] [0.70; 1.90] [1.01; 1.04] [1.00; 1.04]	1.3% 2.2% 96.4% 0.1% 100.0%
			Relative F	Risk per 1 µg/r	m ³		

Subgroup meta-analysis

By gestational age adjustment

EC second trimester - and TLBW by gestational age



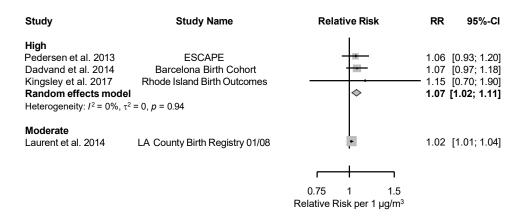
By region

Laurent 2014 and Kingsley from North America, Dadvand 2014 and Pedersen 2013 from Western Europe.

By study design - all cohort studies

By traffic specificity

EC second trimester - and TLBW by Traffic Specificity

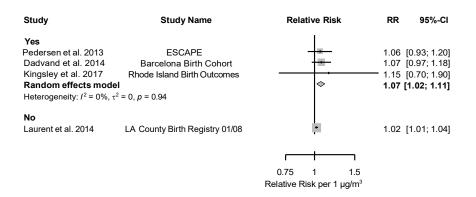


By risk of bias

Laurent et al. 2014 and Kingsley et al. 2017 high risk of bias for confounding, Dadvand et al. 2014 and Pedersen et al. 2013 low risk of bias for confounding.

By smoking adjustment

EC second trimester - and TLBW by smoking adjustment

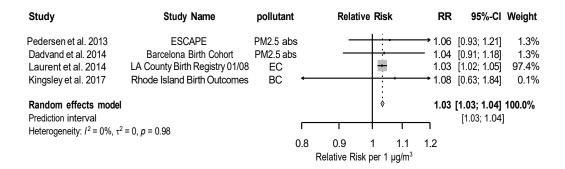


BMI adjustment

Dadvand et al. 2014 and Pedersen et al. 2013 adjusted for BMI, Laurent et al. 2014 and Kingsley et al. did not adjust for BMI.

EC Third trimester exposure - primary meta-analysis - TLBW

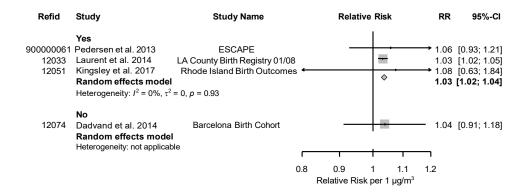
EC third trimester exposure and TLBW



Subgroup meta-analysis

By gestational age adjustment

EC third trimester - and TLBW by gestational age

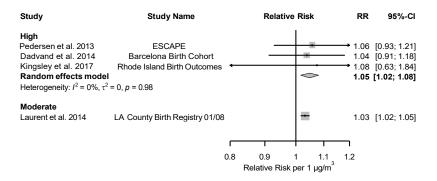


By region

Laurent et al. 2014 and Kingsley et al. 2017 from North America, Dadvand et al. 2014 and Pedersen et al. 2013 from Western Europe.

By traffic specificity

EC third trimester - and TLBW by Traffic Specificity



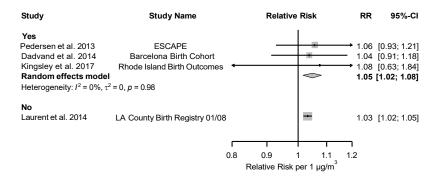
By study design - all cohort studies

By risk of bias

Laurent et al. 2014 and Kingsley et al. 2017 high risk of bias for confounding, Dadvand et al. 2014 and Pedersen et al. 2013 low risk of bias for confounding.

By smoking adjustment

EC third trimester - and TLBW by smoking adjustment

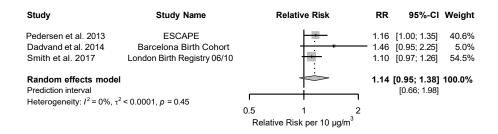


By BMI adjustment

Dadvand et al. 2014 and Pedersen et al. 2013 adjusted for BMI, Laurent et al. 2014 and Kingsley et al. did not adjust for BMI.

PM₁₀ Entire pregnancy exposure - primary meta-analysis - TLBW

PM₁₀ entire pregnancy exposure and TLBW



Subgroup analysis

All Western European cohort studies.

By gestational age: Dadvand et al. 2014 did not adjust for gestational age.

By traffic specificity: all rated moderate.

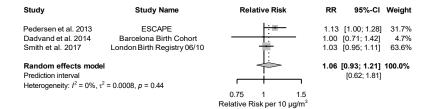
By risk of bias: all rated moderate for exposure domain, low for other domains and for confounding Smith et al. 2017 rated high and the other 2 studies low.

By smoking adjustment: Smith et al. 2017 did not adjust for smoking.

By BMI adjustment: Smith et al. 2017 did not adjust for BMI.

PM₁₀ First trimester exposure - primary meta-analysis - TLBW

PM₁₀ first trimester pregnancy exposure and TLBW



PM₁₀ Second trimester exposure - primary meta-analysis - TLBW

PM₁₀ Second trimester pregnancy exposure and TLBW

Study	Study Name	Re	lative Ris	sk	RR	95%-CI	Weight
Pedersen et al. 2013 Dadvand et al. 2014	ESCAPE Barcelona Birth Cohort		=			[0.97; 1.29] [0.94; 2.04]	34.9% 7.7%
Smith et al. 2017	London Birth Registry 06/10		Ė			[0.94; 1.08]	57.4%
Random effects mode Prediction interval Heterogeneity: $I^2 = 49\%$,		_		_	1.07	[0.82 ; 1.40] [0.33; 3.44]	100.0%
		0.5 Relative I	1 Risk per 1	2 10 µg/m³			

PM₁₀ Third trimester exposure - primary meta-analysis - TLBW

PM₁₀ Third trimester pregnancy exposure and TLBW

Study	Study Name	Relative Risk	RR	95%-CI Weight
Pedersen et al. 2013 Dadvand et al. 2014 Smith et al. 2017	ESCAPE Barcelona Birth Cohort London Birth Registry 06/10		1.56	[0.96; 1.27] 37.0% [1.11; 2.19] 16.0% [0.98; 1.11] 47.0%
Random effects mode Prediction interval Heterogeneity: $I^2 = 64\%$,		0.2 0.5 1 2 5 Relative Risk per 10 µg/m ³	1.13	[0.74; 1.74] 100.0% [0.16; 8.14]

PM_{2.5} Entire pregnancy exposure - primary meta-analysis - TLBW

PM_{2.5} entire pregnancy exposure and TLBW

Study	Study Name	Relative Risk	RR	95%-CI	Weight
Brauer et al. 2008 Coker et al. 2015 Laurent et al. 2016 Kingsley et al. 2017 Pedersen et al. 2013 Dadvand et al. 2014	BC 99/02 Birth Cohort LA County Birth Registry 95/06 California Birth Registry 01/08 Rhode Island Birth Outcomes ESCAPE Barcelona Birth Cohort	# H	1.13 0.99 - 1.10 1.18	L ,	9.4% 22.9% 26.9% 2.7% 16.5% 5.5%
Smith et al. 2017	London Birth Registry 06/10	-		[1.02; 1.28]	16.1%
Random effects mode Prediction interval Heterogeneity: I^2 = 84%,	-	0.75 1 1.5	1.11	[1.03; 1.20] [0.91; 1.36]	100.0%
		Relative Risk per 5 µg/m³			

Subgroup meta-analysis

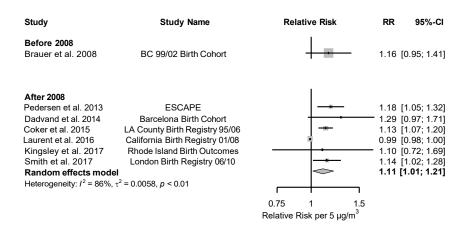
By gestational age adjustment

PM_{2.5} - TLBW by gestational age

Study	Study Name	Relative Risk	RR	95%-CI
No Brauer et al. 2008 Dadvand et al. 2014 Laurent et al. 2016 Random effects mode Heterogeneity: $I^2 = 65\%$,		*		[0.95; 1.41] [0.97; 1.71] [0.98; 1.00] [0.79; 1.50]
Yes Pedersen et al. 2013 Coker et al. 2015 Kingsley et al. 2017 Smith et al. 2017 Random effects mode Heterogeneity: I ² = 0%, a		0.75 1 1.5 Relative Risk per 5 μg/m ³	1.13 - 1.10 1.14	[1.05; 1.32] [1.07; 1.20] [0.72; 1.69] [1.02; 1.28] [1.11; 1.18]

By publication year

PM_{2.5} - TLBW by publication year



By region

PM_{2.5} - TLBW by region

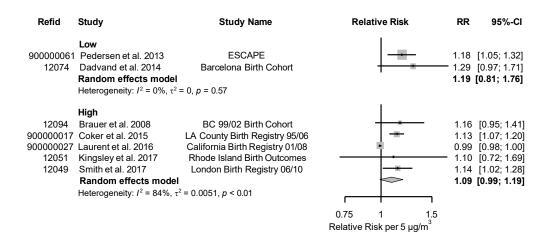
Study	Study Name	Relative Risk	RR	95%-CI
North America Brauer et al. 2008 Coker et al. 2015 Laurent et al. 2016 Kingsley et al. 2017 Random effects model Heterogeneity: 1² = 85%		-	0.99 - 1.10	[0.95; 1.41] [1.07; 1.20] [0.98; 1.00] [0.72; 1.69] [0.95; 1.22]
Western Europe Pedersen et al. 2013 Dadvand et al. 2014 Smith et al. 2017 Random effects mode Heterogeneity: I ² = 0%,		0.75 1 1.5 Relative Risk per 5 µg/m ³	- 1.29 1.14	[1.05; 1.32] [0.97; 1.71] [1.02; 1.28] [1.06; 1.29]

By traffic specificity – all rated moderate

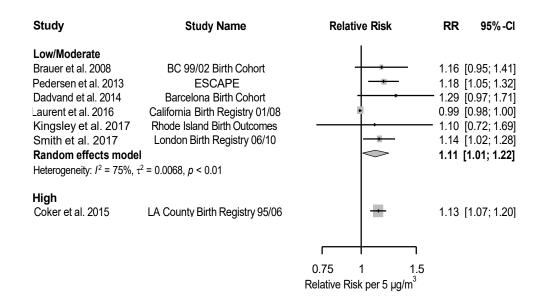
By risk of bias

Plots not shown for risk of bias domains if all studies were rated low or moderate

PM_{2.5} - TLBW by Risk of bias assessment on confounding



PM_{2.5} - TLBW by Risk of bias assessment on exposure assessment



 $\ensuremath{\mathsf{PM}}_{2.5}\text{-}\operatorname{TLBW}$ by smoking adjustment

Study	Study Name	Relative Risk	RR	95%-CI
Yes Brauer et al. 2008 Pedersen et al. 2013 Dadvand et al. 2014 Kingsley et al. 2017 Random effects model Heterogeneity: I² = 0%, τ	· ·	*	1.18 - 1.29 - 1.10	[0.95; 1.41] [1.05; 1.32] [0.97; 1.71] [0.72; 1.69] [1.11; 1.26]
No Coker et al. 2015 Laurent et al. 2016 Smith et al. 2017 Random effects mode Heterogeneity: $I^2 = 91\%$,	•	0.75 1 1.5 Relative Risk per 5 µa/m³	0.99 1.14	[1.07; 1.20] [0.98; 1.00] [1.02; 1.28] [0.88; 1.32]

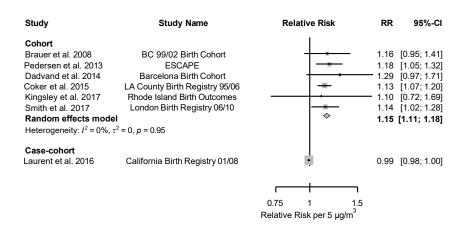
By BMI adjustment

PM_{2.5} - TLBW by BMI

Study	Study Name	Relative Risk	RR	95%-CI
Yes Pedersen et al. 2013 Dadvand et al. 2014	ESCAPE Barcelona Birth Cohort		1.18 - 1.29	[1.05; 1.32] [0.97; 1.71]
No Brauer et al. 2008 Coker et al. 2015 Laurent et al. 2016 Kingsley et al. 2017 Smith et al. 2017 Random effects mod Heterogeneity: J ² = 84%	**	**************************************	1.13 0.99 - 1.10 1.14	[0.95; 1.41] [1.07; 1.20] [0.98; 1.00] [0.72; 1.69] [1.02; 1.28] [0.99; 1.19]
		0.75 1 1.5 Relative Risk per 5 μ g/m ³		

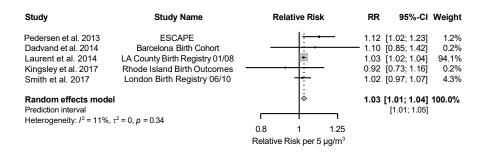
By study design

 $\ensuremath{\mathsf{PM}}_{2.5}$ - TLBW by study design



PM_{2.5} First trimester exposure - primary meta-analysis - TLBW

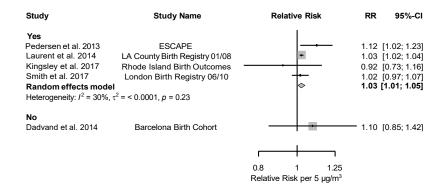
PM_{2.5} first trimester exposure and TLBW



Subgroup meta-analysis

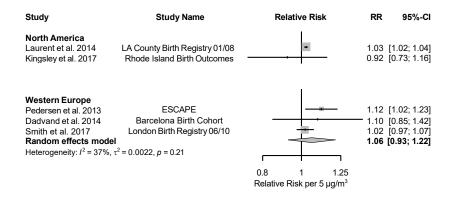
By gestational age adjustment

 $\ensuremath{\mathsf{PM}}_{2.5}$ first trimester exposure and TLBW by gestational age



By region

PM_{2.5} first trimester exposure and TLBW by region

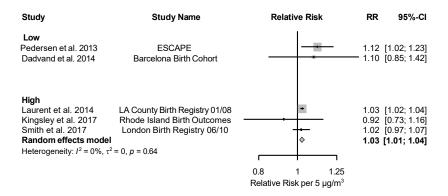


By traffic specificity - all rated moderate

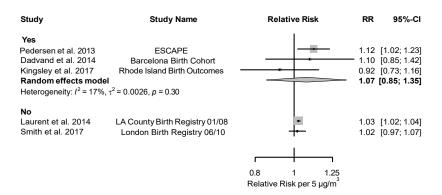
By risk of bias

Plots not shown for risk of bias domains if all studies were rated low or moderate

PM_{2.5} first trimester exposure and TLBW by Risk of bias assessment on confounding

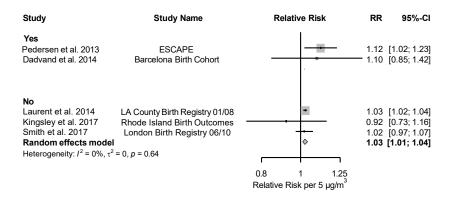


 $\ensuremath{\mathsf{PM}}_{2.5} \ensuremath{\mathsf{first}} \, trimester \, exposure \, and \, TLBW \, by \, smoking \, adjustment$



By BMI adjustment

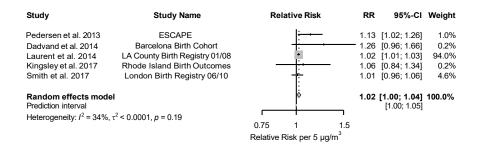
PM_{2.5} first trimester exposure and TLBW by BMI



By study design - all cohort studies

PM_{2.5} Second trimester exposure - primary meta-analysis - TLBW

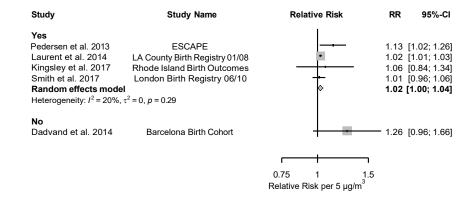
PM_{2.5} second trimester exposure and TLBW



Subgroup meta-analysis

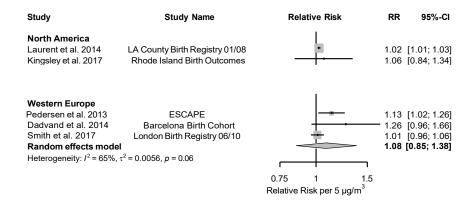
By gestational age adjustment

PM_{2.5} second trimester exposure and TLBW by gestational age



By region

PM_{2.5} second trimester exposure and TLBW by region



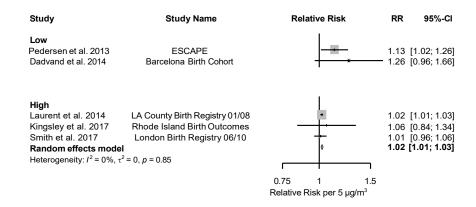
By traffic specificity - all rated moderate

By study design - all cohort studies

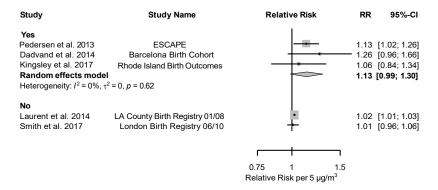
By risk of bias

Plots not shown for risk of bias domains if all studies were rated low or moderate

PM_{2.5} second trimester exposure and TLBW by Risk of bias assessment on confounding

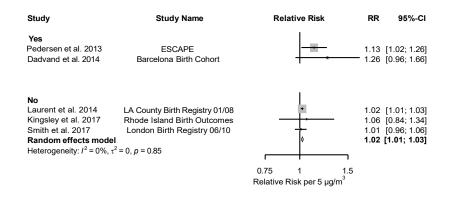


PM_{2.5} second trimester exposure and TLBW by smoking adjustment



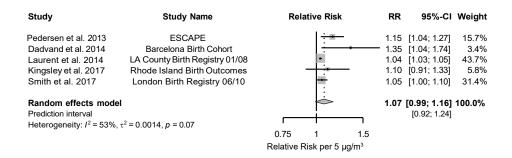
By BMI adjustment

 $\ensuremath{\mathsf{PM}}_{2.5}\,\ensuremath{\mathsf{second}}$ trimester exposure and TLBW by BMI



PM_{2.5} Third trimester exposure - primary meta-analysis - TLBW

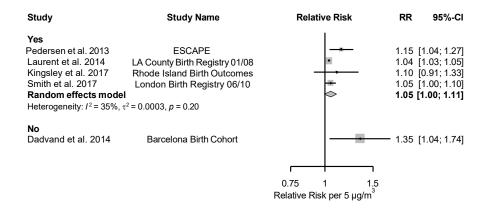
PM_{2.5} third trimester exposure and TLBW



Subgroup meta-analysis

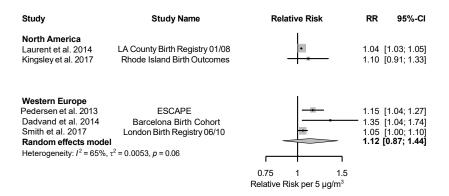
By gestational age adjustment

PM_{2.5} third trimester exposure and TLBW by gestational age



By region

PM_{2.5} third trimester exposure and TLBW by region



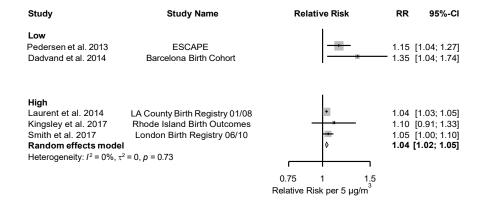
By traffic specificity - all rated moderate

By study design- all cohort studies

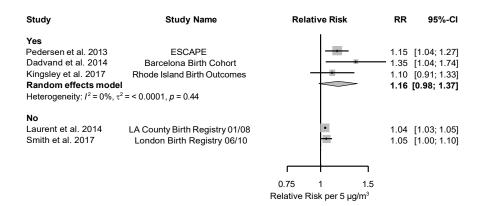
By risk of bias

Plots not shown for risk of bias domains if all studies were rated low or moderate

 $\mathrm{PM}_{2.5}$ third trimester exposure and TLBW by Risk of bias assessment on confounding

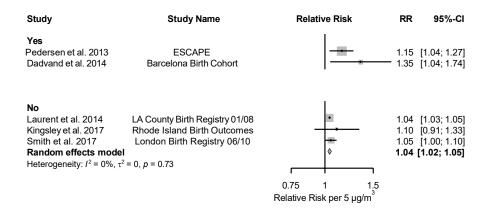


PM_{2.5} third trimester exposure and TLBW by smoking adjustment



By BMI adjustment

PM_{2.5} third trimester exposure and TLBW by BMI



CO Entire pregnancy exposure - primary meta-analysis - TLBW

CO entire pregnancy exposure and TLBW

Study	Study Name	Relative Risk	RR	95%-CI	Weight
Wilhelm et al. 2003 Laurent et al. 2013 Laurent et al. 2016	LA County Birth Registry 94/96 South Coast Births 97/06 California Birth Registry 01/08		0.64	[1.03; 1.38] [0.29; 1.41] [0.81; 1.20]	52.1% 5.5% 42.3%
Random effects mode Prediction interval Heterogeneity: $I^2 = 52\%$		0.2 0.5 1 2 5 Relative Risk per 1 mg/m³		[0.67; 1.68] [0.15; 7.74]	100.0%

Subgroup analysis

Laurent et al. 2016 did not adjust for gestational age.

All three studies did not adjust for smoking and BMI.

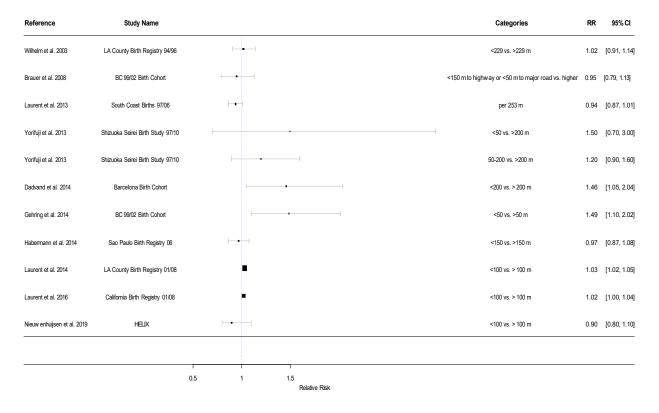
Traffic specificity: Wilhelm et al. 2003 was rated moderate the other 2 studies high.

Risk of bias: all three studies rated low for domains, except for exposure where all rated moderate and for confounding where all rated high risk of bias.

Wilhelm et al. 2003 was classified as a case-control, Laurent et al. 2013 as a cohort and Laurent et al. 2016 as a case-cohort.

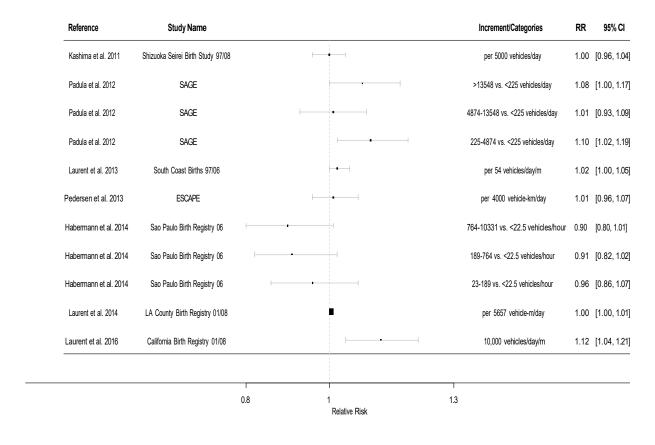
Distance measures

Traffic Distance measures - Term Low birth weight



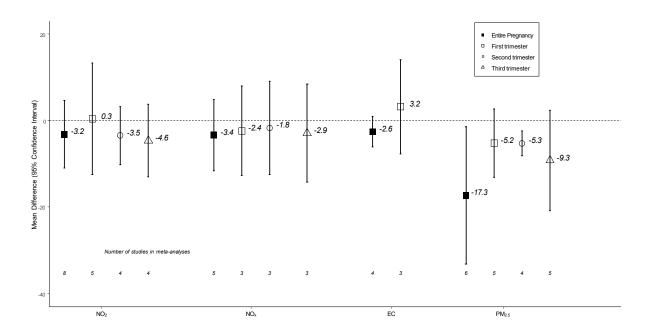
Density measures

Traffic Density measures - Term Low birth weight



8.2 Term birth weight (TBW)

Summary of meta-analysis

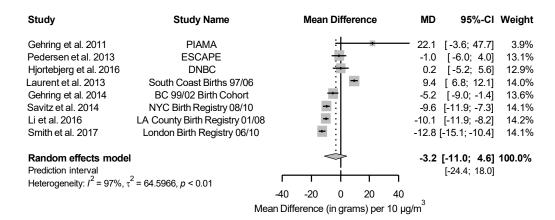


Footnote: The following increments were used: $10 \, \mu g/m^3$ for NO_2 , $20 \, \mu g/m^3$ for NO_x , $1 \, \mu g/m^3$ for EC, $5 \, \mu g/m^3$ for $PM_{2.5}$. Effect estimates cannot be directly compared across the different traffic-related pollutants because the selected increments do not necessarily represent the same contrast in exposure.

By gestational age - all term birth weight studies adjusted for gestational age

NO₂ Entire pregnancy exposure - primary meta-analysis - TBW

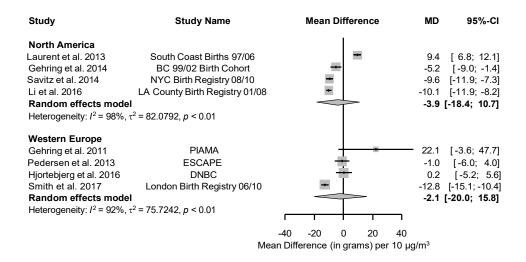
NO₂ entire pregnancy exposure and Term Birth Weight



Subgroup analysis – entire pregnancy exposure

By region

NO₂ - TBW by region



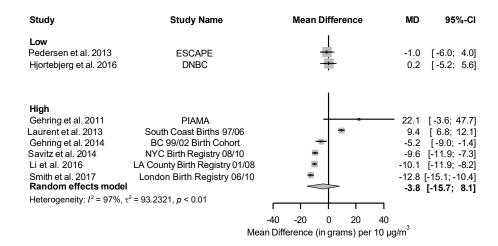
By traffic specificity - all high

By study design – all cohort studies

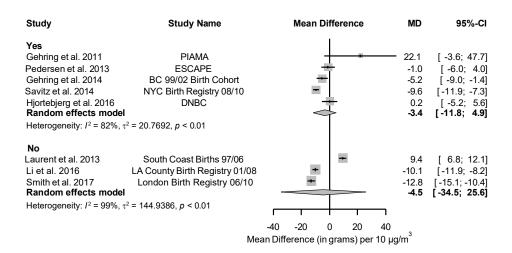
By risk of bias

Plots not shown for risk of bias domains if all studies where rated low or moderate

NO2 - TBW by Risk of bias assessment on confounding

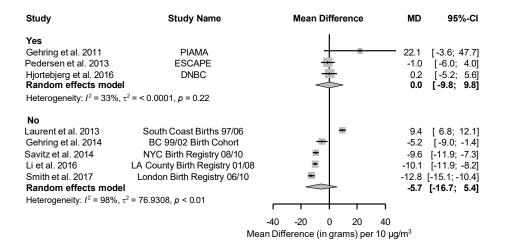


NO₂ - TBW by smoking adjustment



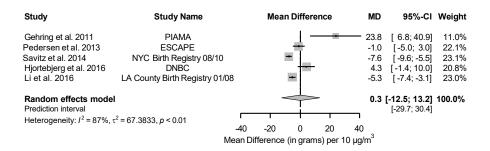
By BMI adjustment

NO₂ - TBW by BMI



NO₂ First trimester exposure - primary meta-analysis - TBW

 $\ensuremath{\mathsf{NO}}_2$ first trimester exposure and Term Birth Weight



Subgroup analysis

By region

NO₂ - first trimester TBW by region

Study	Study Name	Mean Diffe	erence	MD	95%-CI
North America Savitz et al. 2014 Li et al. 2016	NYC Birth Registry 08/10 LA County Birth Registry 01/08			-7.6 -5.3	,
Western Europe Gehring et al. 2011 Pedersen et al. 2013 Hjortebjerg et al. 2016 Random effects model Heterogeneity: $l^2 = 78\%$, r	PIAMA ESCAPE DNBC ² = 94 6851 p = 0.01	-	-		[6.8; 40.9] [-5.0; 3.0] [-1.4; 10.0] [-22.6; 35.9]
riotorogonomy. 7 7070, t	04.0001, p 0.01		1	ר	
		-40 -20 0 ean Difference (in gr		10 1a/m ³	

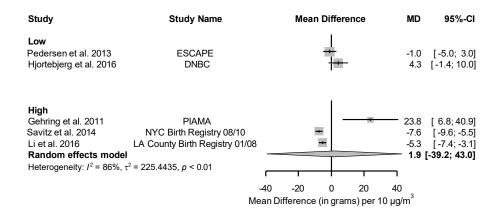
By traffic specificity – all high

By study design - all cohort studies

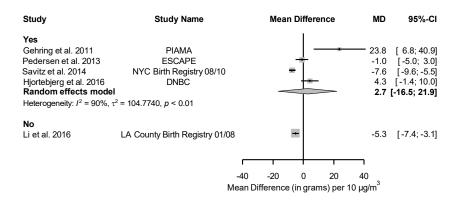
By risk of bias

Plots not shown for risk of bias domains if all studies were rated low or moderate

NO₂ - first trimester TBW by Risk of bias assessment on confounding

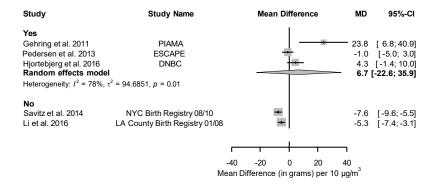


NO₂ - first trimester TBW by smoking adjustment



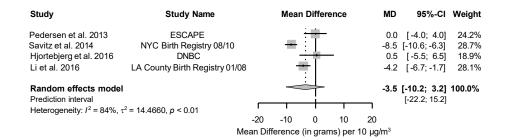
By BMI adjustment

NO₂ - first trimester TBW by BMI



NO₂ Second trimester exposure - primary meta-analysis - TBW

NO2 second trimester exposure and Term Birth Weight



Subgroup analysis

By region

Savitz et al. 2014 and Li et al. 2016 from North America, Hjorteberg et al. 2016 and Pedersen et al. 2013 from Western Europe.

By traffic specificity - all high

By study design - all cohort studies

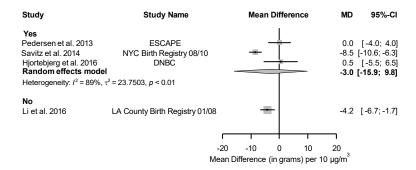
By risk of bias

Savitz et al. 2014 and Li et al. 2016 high risk of bias for confounding, Hjorteberg et al. 2016 and Pedersen et al. 2013 low risk of bias for confounding.

By BMI adjustment

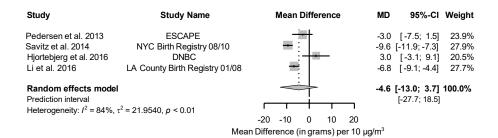
Savitz et al. 2014 and Li et al. 2016 did not adjust for BMI, Hjorteberg et al. 2016 and Pedersen et al. 2013 did adjust for BMI.

NO₂ - second trimester TBW by smoking adjustment



NO₂ Third trimester exposure - primary meta-analysis - TBW

NO₂ third pregnancy exposure and Term Birth Weight



Subgroup analysis - third trimester exposure

By region

Savitz et al. 2014 and Li et al. 2016 from North America, Hjorteberg et al. 2016 and Pedersen et al. 2013 from Western Europe.

By traffic specificity - all high

By study design - all cohort studies

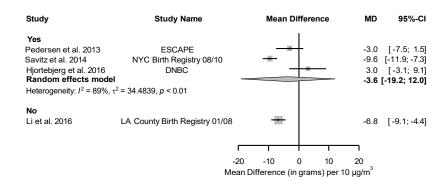
By risk of bias

Savitz et al. 2014 and Li et al. 2016 high risk of bias for confounding, Hjorteberg et al. 2016 and Pedersen et al. 2013 low risk of bias for confounding.

By BMI adjustment

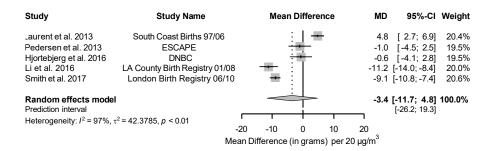
Savitz et al. 2014 and Li et al. 2016 did not adjust for BMI, Hjorteberg et al. 2016 and Pedersen et al. 2013 did adjust for BMI.

NO₂ - third trimester TBW by smoking adjustment



NO_x Entire pregnancy exposure - primary meta-analysis - TBW

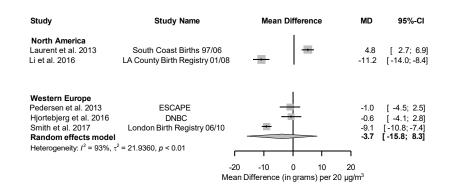
 NO_x entire pregnancy exposure and Term Birth Weight



Subgroup analysis – entire trimester exposure

By region

NO_x - TBW by region



By traffic specificity - all high

By study design - all cohort studies

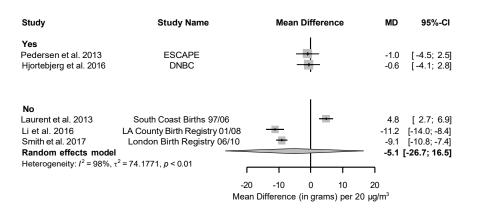
Plots not shown for risk of bias domains if all studies were rated low or moderate

 $\ensuremath{\mathsf{NO_x}}\xspace$ - TBW by Risk of bias assessment on confounding

Study	Study Name	Mean	Difference	MD	95%-CI
Low Pedersen et al. 2013 Hjortebjerg et al. 2016	ESCAPE DNBC		+	-1.0 -0.6	[-4.5; 2.5] [-4.1; 2.8]
High Laurent et al. 2013 Li et al. 2016 Smith et al. 2017 Random effects model Heterogeneity: l² = 98%, r		+	+	-9.1	[2.7; 6.9] [-14.0; -8.4] [-10.8; -7.4] [-26.7; 16.5]
	1	ı	1 1		
	-2 Mea		0 10 (in grams) per 2	20 0 μg/m³	

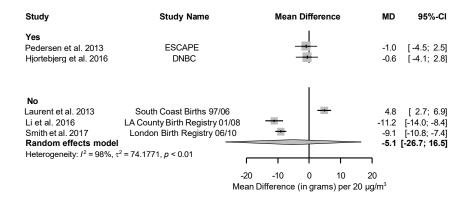
By smoking adjustment

NO_x - TBW by smoking adjustment



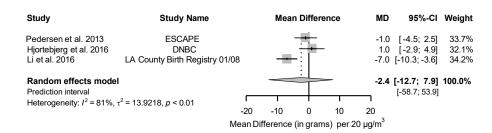
By BMI adjustment

NO_x - TBW by BMI



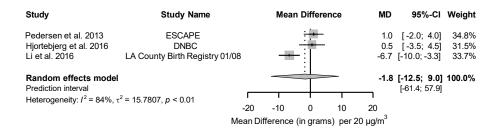
NO_x First trimester exposure – primary meta-analysis - TBW

NO_x first trimester exposure and Term Birth Weight



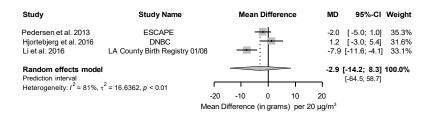
NO_x Second trimester exposure – primary meta-analysis - TBW

NO_x second trimester exposure and Term Birth Weight



NO_x Third trimester exposure - primary meta-analysis - TBW

NO_x third pregnancy exposure and Term Birth Weight



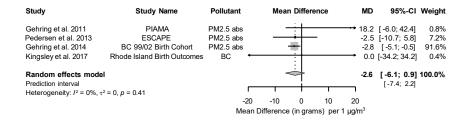
Li et al. 2016 is North American cohort and did not adjust for smoking or BMI, the other two studies Western European studies and did adjust for smoking and BMI.

Thus Li et al. 2016 rated high for risk of bias confounding, while the other 2 rated low. Li et al. 2016 rated moderate for risk of bias selection bias, while the other two studies were low risk of bias. Li et al. 2016 and Pedersen et al. 2013 rated moderate for risk of bias in exposure, while the other one rated low.

All high traffic specificity.

EC Entire pregnancy exposure - primary meta-analysis - TBW

EC entire pregnancy exposure and Term Birth Weight



Subgroup analysis

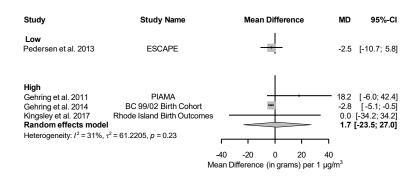
By region

Gehring et al. 2014 and Kingsley et al. 2017 from North America, Gehring et al. 2011 and Pedersen et al. 2013 from Western Europe.

By traffic specificity - all high

Plots not shown for risk of bias domains if all studies were rated low or moderate

EC - TBW by Risk of bias assessment on confounding



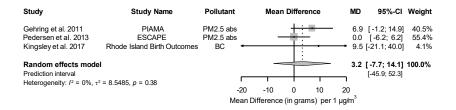
By smoking adjustment – all adjusted for smoking

By BMI adjustment

Gehring et al. 2014 and Kingsley et al. 2017 did not adjust for BMI, Gehring et al. 2011 and Pedersen et al. 2013 did adjust for BMI.

EC First trimester exposure - primary meta-analysis - TBW

EC first trimester exposure and Term Birth Weight



Subgroup analysis

Kingsley et al. 2017 is North American cohort and did not adjust for BMI, the other 2 Western European studies adjusted for BMI.

Gehring et al. 2011 and Kingsley et al. 2017 rated high risk of bias for confounding while the other low risk of bias. All rated moderate risk of bias for exposure. Gehring et al. 2011 rated moderate in risk of bias outcome assessment, and the other two studies low risk of bias.

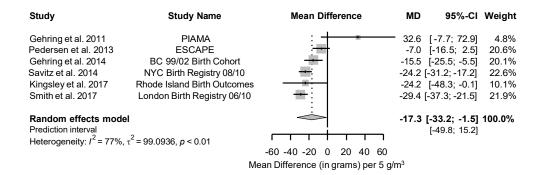
All rated high traffic specificity

Kingsley et al. 2017 did not report second and third trimester exposure hence no metaanalysis, as only 2 effect estimates.

PM₁₀ - Not enough TBW studies for meta-analysis

PM_{2.5} Entire pregnancy exposure - primary meta-analysis - TBW

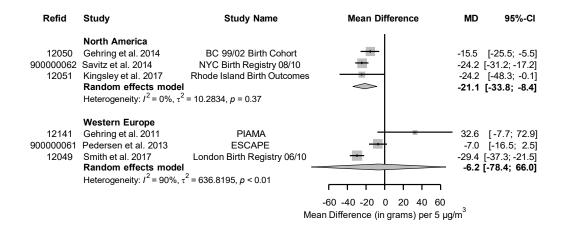
PM_{2.5} entire pregnancy exposure and Term Birth Weight



Subgroup analysis

By region

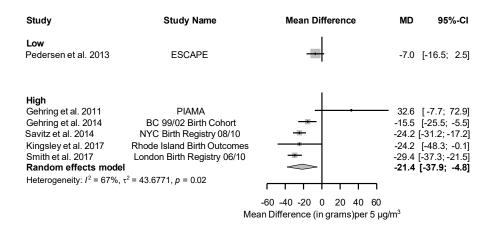
 $\ensuremath{\mathsf{PM}}_{2,5}$ - TBW by region



By traffic specificity – all rated moderate

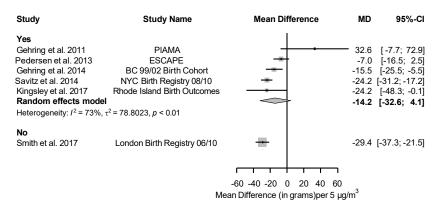
Plots not shown for risk of bias domains if all studies were rated low or moderate

PM_{2.5} - TBW by Risk of bias assessment on confounding



By smoking adjustment

PM_{2.5} - TBW by smoking adjustment



By BMI adjustment

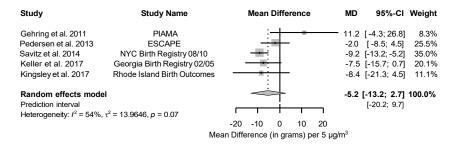
 $\mathsf{PM}_{2.5}$ - TBW by BMI

Study	Study Name	Mean Difference	MD	95%-CI
Yes Gehring et al. 2011 Pedersen et al. 2013	PIAMA ESCAPE	*	- 32.6 -7.0	[-7.7; 72.9] [-16.5; 2.5]
No Gehring et al. 2014 Savitz et al. 2014 Kingsley et al. 2017 Smith et al. 2017 Random effects mode Heterogeneity: $I^2 = 35\%$,	$\tau^2 = 17.7563, p = 0.21$	-60 -40 -20 0 20 40 60 ean Difference (in grams)per 5 µ		[-25.5; -5.5] [-31.2; -17.2] [-48.3; -0.1] [-37.3; -21.5] [-33.3; -14.1]

By study design - all cohort studies

PM_{2.5} First trimester exposure - primary meta-analysis - TBW

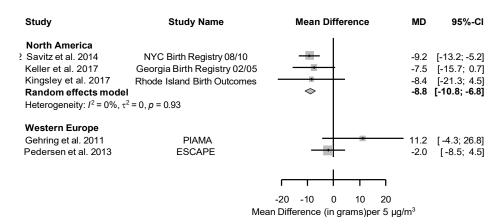
PM_{2.5} first trimester exposure and Term Birth Weight



Subgroup analysis

By region

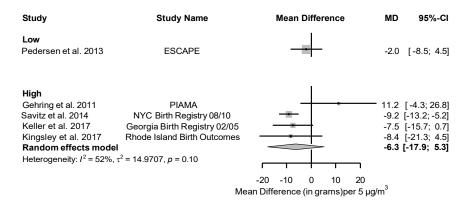
 $\mathsf{PM}_{2.5}$ first trimester exposure - TBW by region



By traffic specificity – all rated moderate

Plots not shown for risk of bias domains if all studies were rated low or moderate

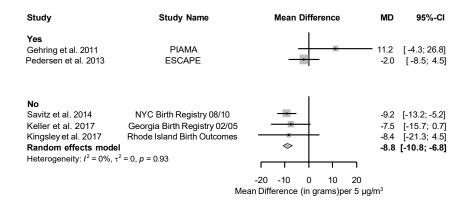
PM_{2.5} first trimester exposure - TBW by Risk of bias assessment on confounding



By smoking adjustment – all studies adjusted for smoking

By BMI adjustment

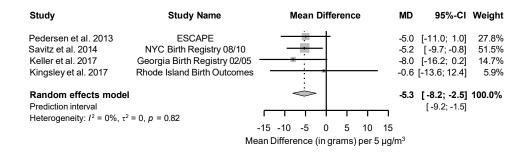
 $\ensuremath{\mathsf{PM}}_{2.5}$ first trimester exposure - TBW by BMI



PM_{2.5} Second trimester exposure - primary meta-analysis - TBW

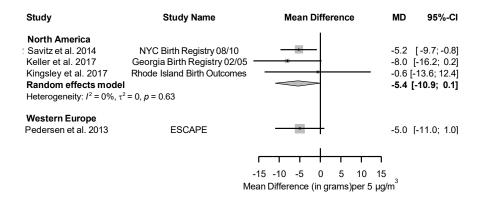
Subgroup analysis

PM_{2.5} second trimester exposure and Term Birth Weight



By region

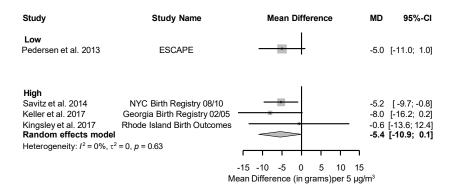
 ${\rm PM}_{2.5}$ second trimester exposure - TBW by region



By traffic specificity – all rated moderate

Plots not shown for risk of bias domains if all studies were rated low or moderate

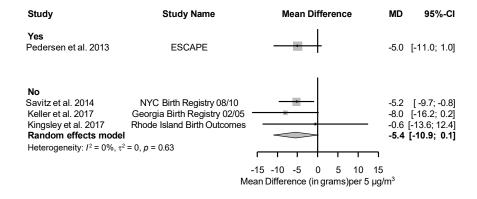
PM_{2.5} second trimester exposure - TBW by Risk of bias assessment on confounding



By smoking adjustment – all studies adjusted for smoking

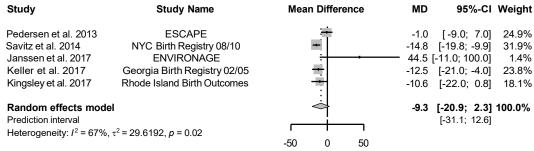
By BMI adjustment

 $\ensuremath{\mathsf{PM}}_{2.5}$ second trimester exposure - TBW by BMI



PM_{2.5} Third trimester exposure - primary meta-analysis - TBW

PM_{2.5} third trimester exposure and Term Birth Weight

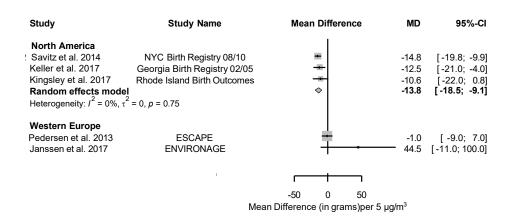


Mean Difference (in grams) per 5 $\mu g/m^3$

Subgroup analysis

By region

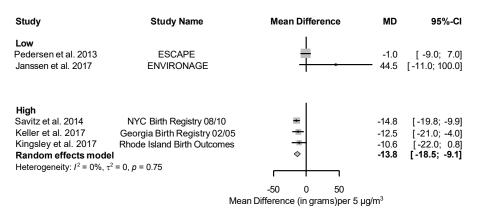
PM_{2.5} third trimester exposure - TBW by region



By traffic specificity – all rated moderate

Plots not shown for risk of bias domains if all studies were rated low or moderate

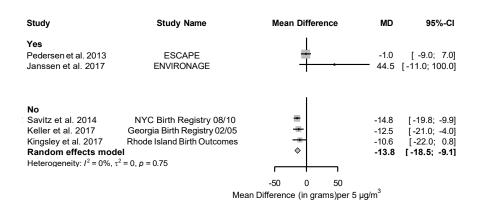
 $\mathrm{PM}_{2,6}$ third trimester exposure - TBW by Risk of bias assessment on confounding



By smoking adjustment – all studies adjusted for smoking

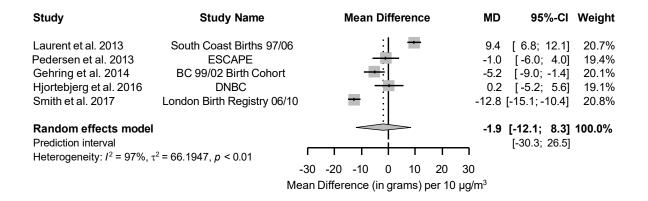
By BMI adjustment

PM_{2.5} third trimester exposure - TBW by BMI



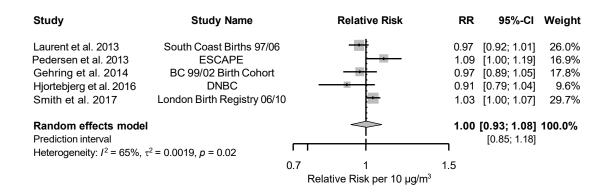
NO2 - TBW

NO₂ entire pregnancy exposure and Term Birth Weight



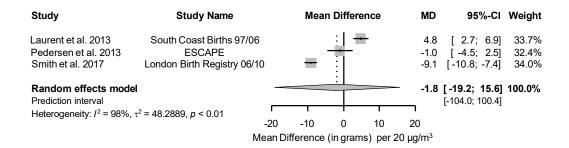
NO2 - TLBW

NO₂ entire pregnancy exposure and TLBW



NOx - TBW

NO_x entire pregnancy exposure and Term Birth Weight



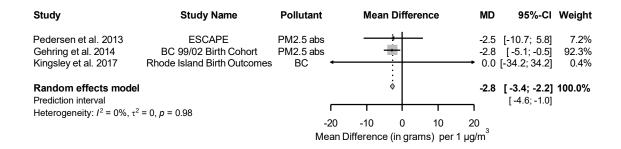
NOx - TLBW

NO_x entire pregnancy exposure and TLBW



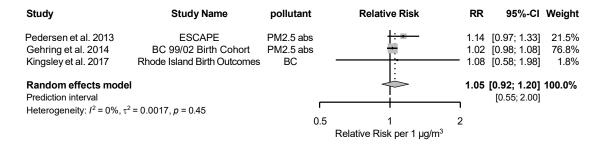
EC - TBW

EC entire pregnancy exposure and Term Birth Weight



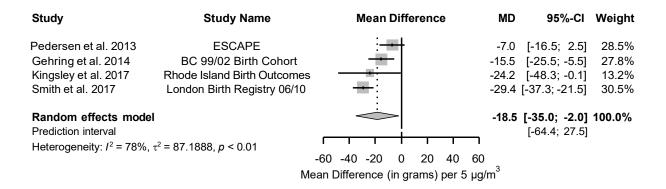
EC - TLBW

EC entire pregnancy exposure and TLBW



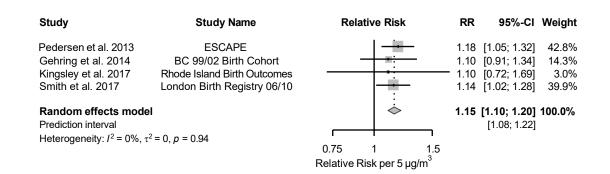
PM2.5 - TBW

PM_{2.5} entire pregnancy exposure and Term Birth Weight



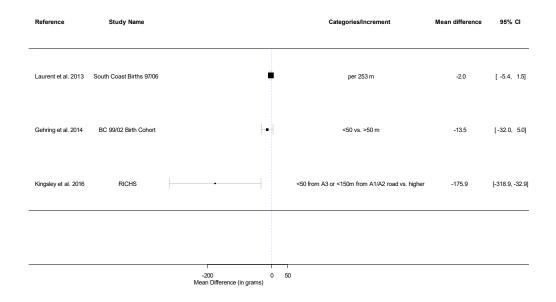
PM2.5 - TLBW

PM_{2.5} entire pregnancy exposure and TLBW



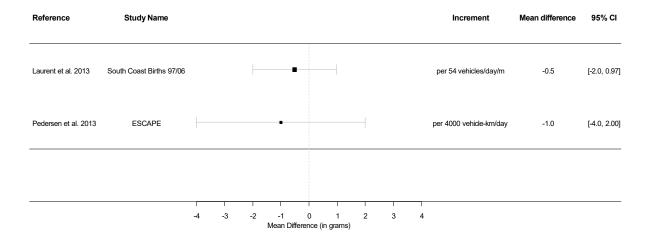
Distance measures

Traffic Distance measures - Term Birth weight



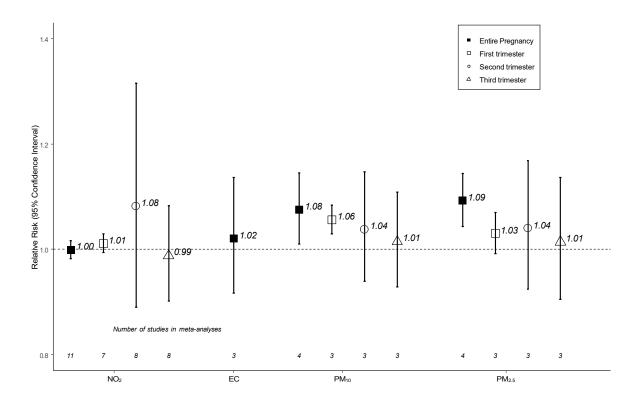
Density measures

Traffic Density measures - Term Birth weight



8.3 Small for gestational age (SGA)

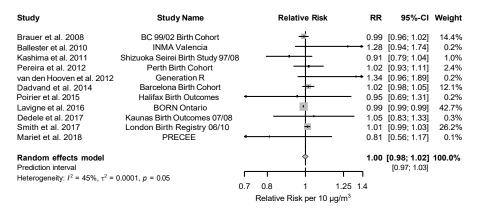
Summary of meta-analysis



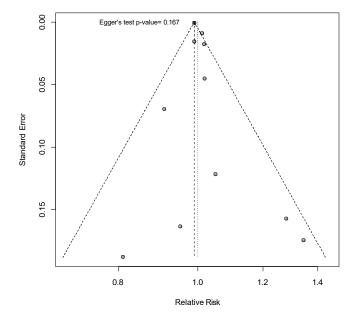
Footnote: The following increments were used: $10\,\mu g/m^3$ for NO₂, $1\,\mu g/m^3$ for EC, $10\,\mu g/m^3$ for PM₁₀ and $5\,\mu g/m^3$ for PM_{2.5}. Effect estimates cannot be directly compared across the different traffic-related pollutants because the selected increments do not necessarily represent the same contrast in exposure

NO₂ Entire pregnancy exposure - primary meta-analysis - SGA

NO₂ entire pregnancy exposure and SGA



Publication bias - entire pregnancy exposure

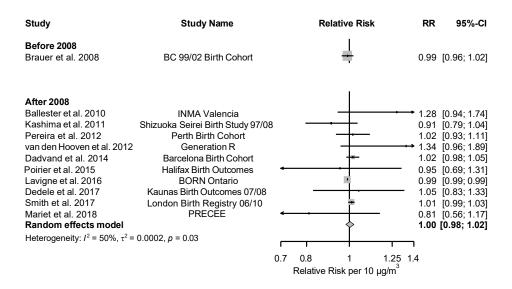


Footnote: The vertical lines in the funnel plots represent the pooled fixed and random effect estimates. The vertical dashed line in the middle of the funnel shows the fixed effect estimate. As the Panel applied a random-effects model, the funnel plot also presents the random-effects estimate with the dotted line.

Subgroup analysis – entire pregnancy exposure

By publication year

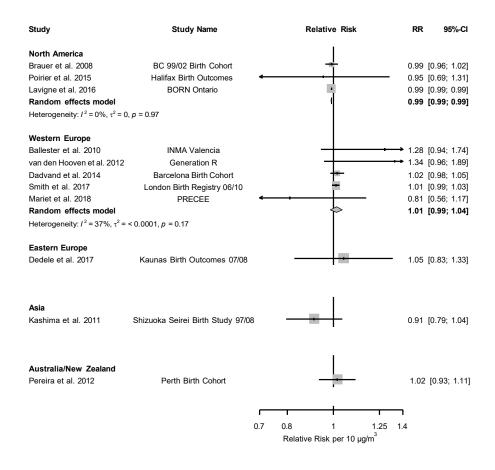
NO₂ - SGA by publication year



By study design – all cohort studies

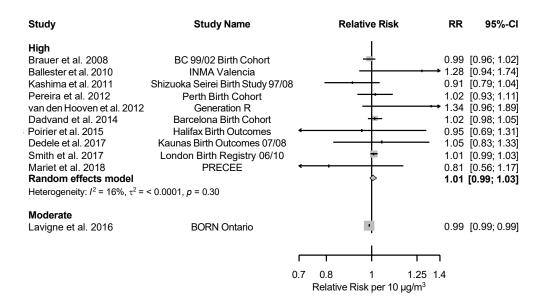
By region

NO₂ - SGA by region



By traffic specificity

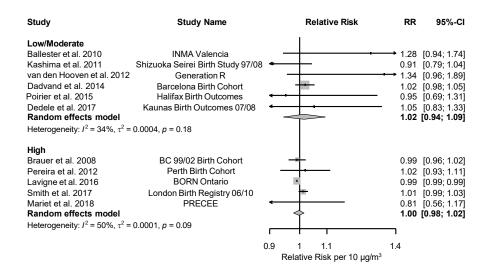
NO₂ - SGA by Traffic Specificity



By risk of bias

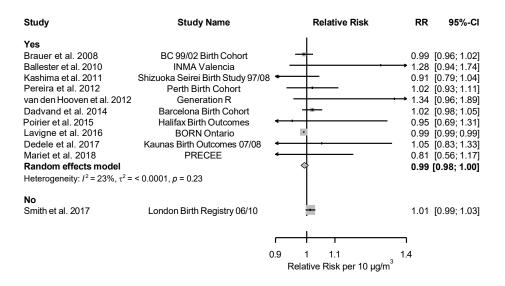
Plots not shown for risk of bias domains if all studies were rated low or moderate

 $\ensuremath{\mathsf{NO}}_2$ - SGA by Risk of bias assessment on confounding



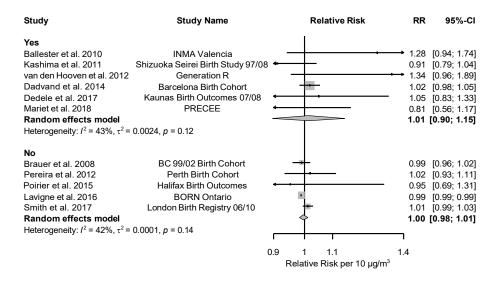
By smoking adjustment

NO₂ - SGA by smoking adjustment



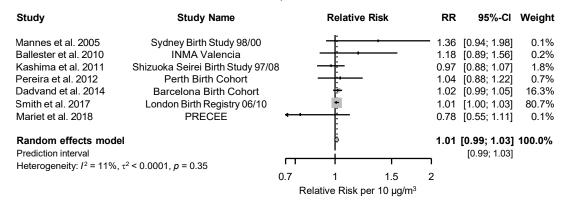
By BMI adjustment

NO₂ - SGA by BMI



NO₂ First trimester exposure - primary meta-analysis - SGA

NO₂ first trimester exposure and SGA

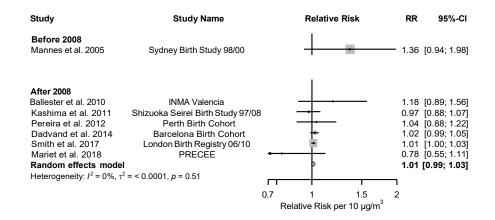


Subgroup analysis – first trimester exposure

By study design - all cohort studies

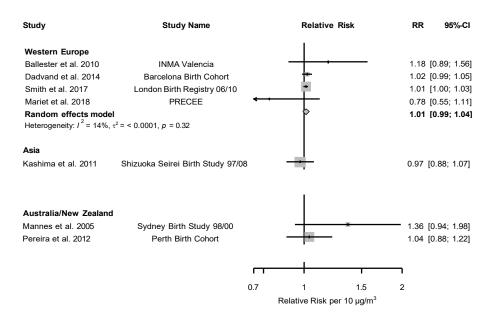
By publication year

 $\ensuremath{\mathsf{NO}}_2$ first trimester exposure and SGA by publication year



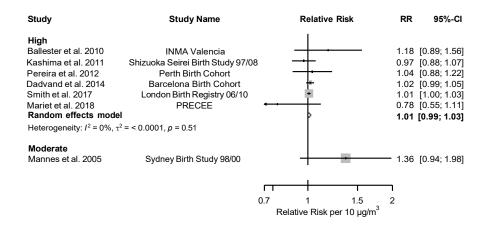
By region

NO₂-first trimester exposure and SGA by region



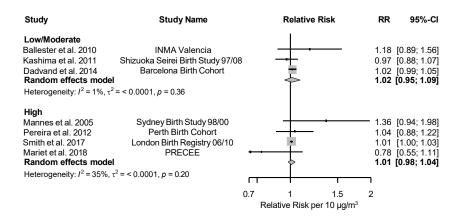
By traffic specificity

NO₂ first trimester - SGA by Traffic Specificity



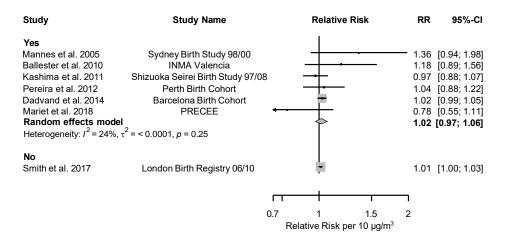
Plots not shown for risk of bias domains if all studies were rated low or moderate

 $\ensuremath{\mathsf{NO}}_2$ first trimester - SGA by Risk of bias assessment on confounding



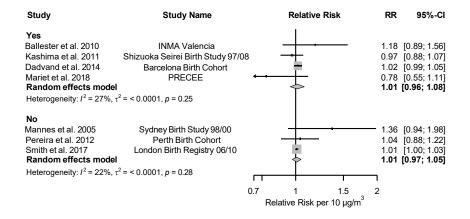
By smoking adjustment

NO₂ first trimester - SGA by smoking adjustment



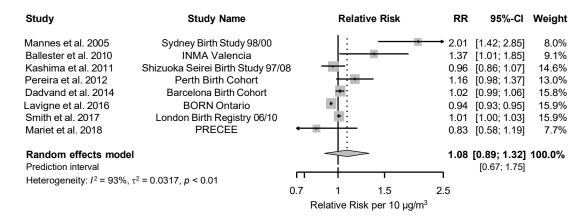
By BMI adjustment

$\ensuremath{\mathsf{NO}}_2$ - first trimester SGA by BMI



NO₂ Second trimester exposure - primary meta-analysis - SGA

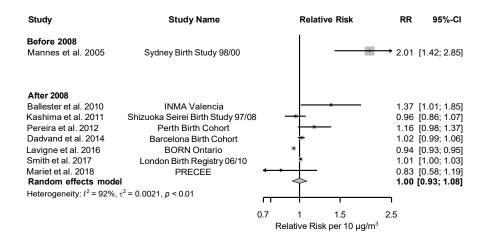
NO₂ second trimester exposure and SGA



Subgroup - second trimester exposure

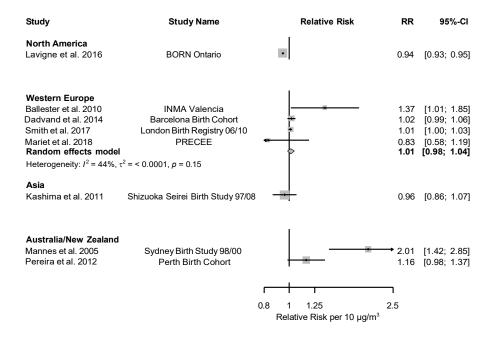
By publication year

 $\ensuremath{\mathsf{NO}}_2$ second trimester exposure and SGA by publication year



By region

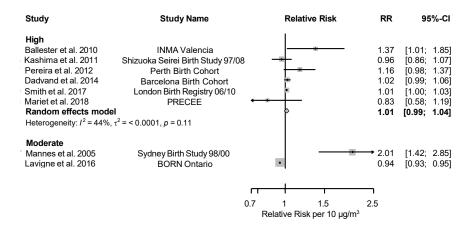
NO2 second trimester exposure and SGA by region



By study design – all cohort studies

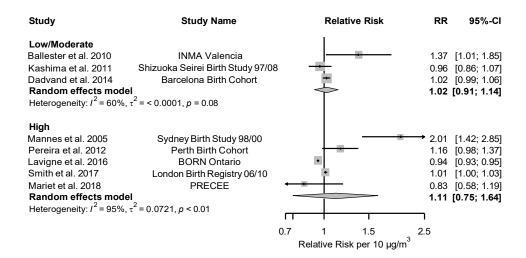
By traffic specificity

NO₂ second trimester - SGA by Traffic Specificity



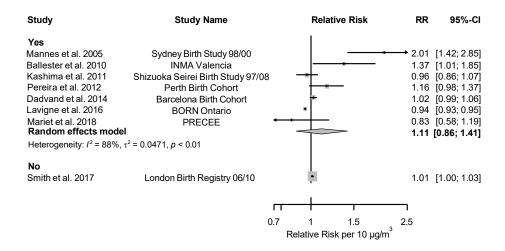
Plots not shown for risk of bias domains if all studies were rated low or moderate

NO2 second trimester - SGA by Risk of bias assessment on confounding



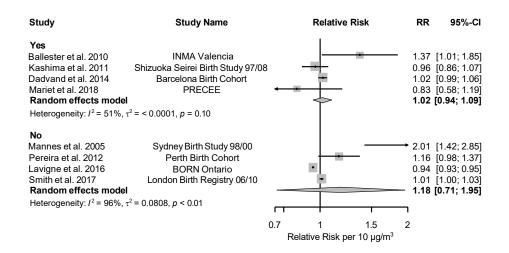
By smoking adjustment

NO2 second trimester - SGA by smoking adjustment



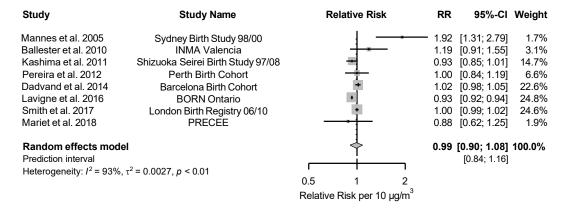
By BMI adjustment

NO_2 - second trimester SGA by BMI



NO₂ Third trimester exposure - primary meta-analysis - SGA

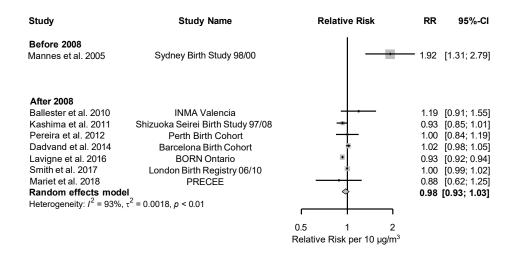
NO₂ third trimester exposure and SGA



Subgroup analysis – third trimester exposure

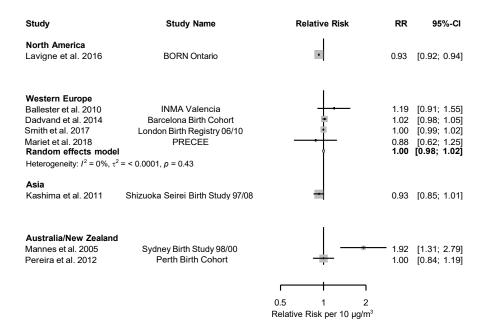
By publication year

NO₂ third trimester exposure and SGA by publication year



By region

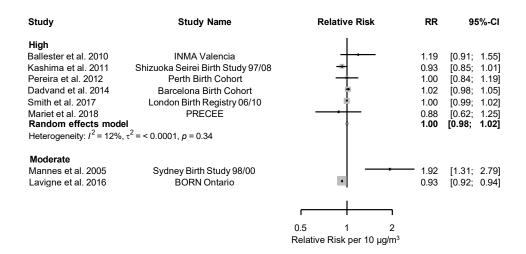
NO₂ third trimester exposure and SGA by region



By study design – all cohort studies

By traffic specificity

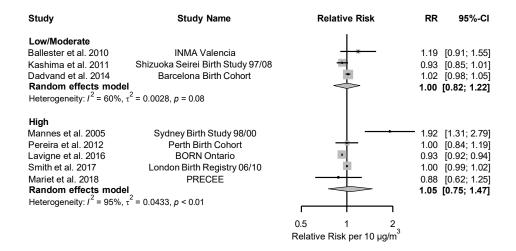
NO2 third trimester - SGA by Traffic Specificity



By risk of bias

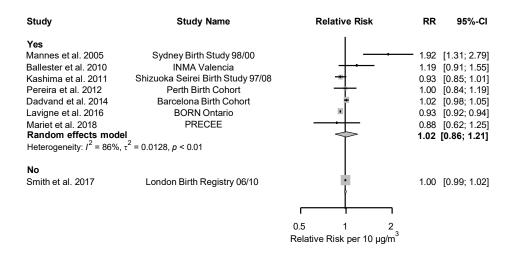
Plots not shown for risk of bias domains if all studies were rated low or moderate

NO2 second trimester - SGA by Risk of bias assessment on confounding



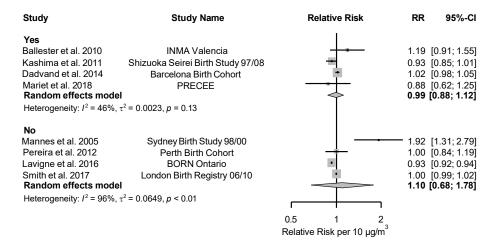
By smoking adjustment

NO₂ third trimester - SGA by smoking adjustment



By BMI adjustment

NO₂ - third trimester SGA by BMI



NO_x

Only 2 studies report effects for all exposure windows (Smith et al. 2017 and Dadvand et al. 2014); hence no meta-analysis.

EC Entire pregnancy exposure - primary meta-analysis - SGA

EC entire pregnancy exposure and SGA

Study	Study Name	pollutant	Relative Risk	R	R 95%-CI	Weight
Brauer et al. 2008 Dadvand et al. 2014 Kingsley et al. 2017	BC 99/02 Birth Cohort Barcelona Birth Cohort Rhode Island Birth Outcomes	PM2.5 abs PM2.5 abs BC	÷ +	1.0	01 [0.99; 1.03] 05 [0.97; 1.13] 03 [0.97; 1.83]	79.4% 19.2% 1.4%
Random effects mode Prediction interval Heterogeneity: $I^2 = 47\%$,	-		0.75 1 1 Relative Risk per 1 µg/n	1 .5	[0.92; 1.14] [0.68; 1.53]	

Subgroup analysis

All cohorts (2 in North America and 1 in Western Europe) adjusted for smoking but only Dadvand et al. 2014 adjusted for BMI. Hence only Dadvand et al. 2014 rated low for risk of bias confounding while the other 2 rated high. Dadvand et al. 2014 and Kingsley et al. 2017 rated moderate for risk of bias in exposure, whereas Brauer et al. 2008 rated low.

All rated high traffic specificity.

EC – only 2 studies reported trimester-specific exposure (Dadvand et al. 2014 and Kingsley et al. 2017); hence no meta-analysis.

PM₁₀ Entire pregnancy exposure - primary meta-analysis - SGA

PM₁₀ entire pregnancy exposure and SGA

Study	Study Name	Relative Risk	RR	95%-CI	Weight
van den Hooven et al. 2012 Dadvand et al. 2014 Winckelmans et al. 2015 Smith et al. 2017	Generation R Barcelona Birth Cohort Flanders Birth Study 99/09 London Birth Registry 06/10	- 	1.05 1.09	[0.91; 1.98] [0.84; 1.32] [1.06; 1.12] [0.97; 1.10]	1.2% 3.3% 67.0% 28.5%
Random effects model Prediction interval Heterogeneity: I^2 = 11%, τ^2 = 0.0005, p = 0.34		0.75 1 1.5 Relative Risk per 10 µg/m³	1.08	[1.01; 1.14] [0.95; 1.22]	100.0%

All cohort studies from Western Europe

Subgroup analysis – entire pregnancy exposure

By traffic specificity - all rated moderate

By risk of bias

van der Hooven et al. 2012 and Dadvand et al 2014 were low risk of bias for confounding, Smith et al. 2017 and Winckelmans et al. 2015 were rated high risk of bias for confounding.

By smoking adjustment

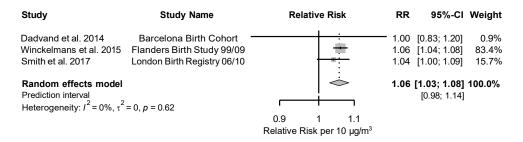
van der Hooven et al. 2012 and Dadvand et al 2014 adjusted for smoking, Smith et al. 2017 and Winckelmans et al. 2015 did not adjust for smoking.

By BMI adjustment

van der Hooven et al. 2012 and Dadvand et al 2014 adjusted for BMI, Smith et al. 2017 and Winckelmans et al. 2015 did not adjust for BMI.

PM₁₀ First trimester exposure - primary meta-analysis - SGA

PM₁₀ First trimester pregnancy exposure and SGA



PM₁₀ Second trimester exposure - primary meta-analysis - SGA

PM₁₀ Second trimester pregnancy exposure and SGA

Study	Study Name	Rela	ative Risk		RR	95%-CI	Weight
Dadvand et al. 2014	Barcelona Birth Cohort	-	<u> </u>	-	1.05	[0.86; 1.30]	6.9%
Winckelmans et al. 2015	Flanders Birth Study 99/09		+		1.07	[1.05; 1.10]	50.0%
Smith et al. 2017	London Birth Registry 06/10		T		1.00	[0.96; 1.04]	43.2%
Random effects model			⇔		1.04	[0.94; 1.15]	100.0%
Prediction interval			-			[0.58; 1.87]	
Heterogeneity: $I^2 = 76\%$, τ^2	2 = 0.0016, ρ = 0.02		1				
3 ,		0.75	1	1.5			
		Relative F	Risk per 10) µg/m³			

PM₁₀ Third trimester exposure - primary meta-analysis - SGA

PM₁₀ Third trimester pregnancy exposure and SGA

Study	Study Name	Relative Risk	RR	95%-CI	Weight
Dadvand et al. 2014 Winckelmans et al. 2015 Smith et al. 2017	Barcelona Birth Cohort Flanders Birth Study 99/09 London Birth Registry 06/10	-	1.04	[0.86; 1.25] [1.02; 1.06] [0.94; 1.02]	6.5% 52.1% 41.3%
Random effects model Prediction interval Heterogeneity: I^2 = 70%, τ^2 = 0.0012, p = 0.04		0.75 1 1.5 Relative Risk per 10 µg/m ³	1.01	[0.93; 1.11] [0.61; 1.69]	100.0%

All were Western European cohorts that rated moderate for traffic specificity.

Only Dadvand et al. 2014 adjusted for smoking and BMI.

Dadvand et al. 2014 rated low in risk of bias for confounding and the other 2 high. Winckelmans et al. 2015 rated low for risk of bias in exposure and the other two studies moderate risk of bias.

PM_{2.5} Entire pregnancy exposure - primary meta-analysis - SGA

PM_{2.5} entire pregnancy exposure and SGA

Study	Study Name	Relative Risk	RR	95%-CI	Weight
Brauer et al. 2008 Dadvand et al. 2014 Kingsley et al. 2017 Smith et al. 2017	BC 99/02 Birth Cohort Barcelona Birth Cohort Rhode Island Birth Outcomes London Birth Registry 06/10	*	1.12 - 1.19 1.07	[1.03; 1.19] [0.96; 1.30] [0.96; 1.47] [1.00; 1.14]	38.4% 9.2% 4.7% 47.8%
Prediction interval Heterogeneity: $I^2 = 0\%$, τ	$p^2 = 0, p = 0.76$	0.8 1 1.25 Relative Risk per 5 μg/m³		[1.03; 1.16]	

Subgroup analysis – entire pregnancy exposure

By region

Brauer et al. 2008 and Kingsley et al. 2017 from North America, Dadvand et al. 2013 and Smith et al. 2017 from Western Europe.

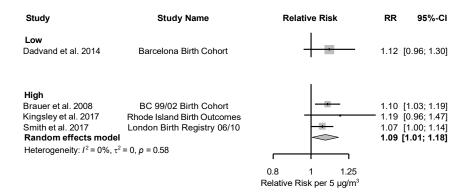
By study design – all cohort studies

By traffic specificity - all rated moderate

By risk of bias

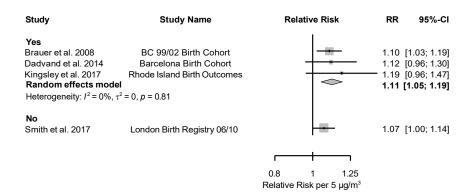
Plots not shown for risk of bias domains if all studies were rated low or moderate

 $\ensuremath{\mathsf{PM}}_{2.5}\,\ensuremath{\mathsf{SGA}}$ by Risk of bias assessment on confounding



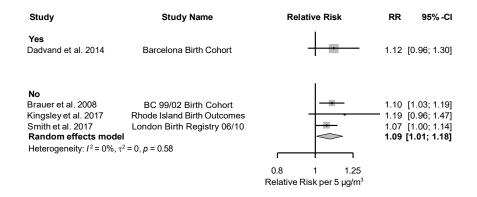
By smoking adjustment

 $\ensuremath{\mathsf{PM}}_{2.5}$ entire pregnancy - SGA by smoking adjustment



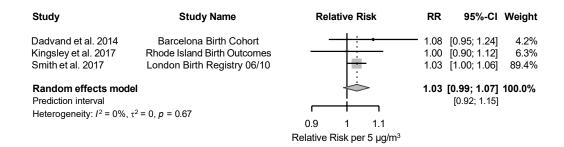
By BMI adjustment

PM_{2.5} entire pregnancy SGA by BMI



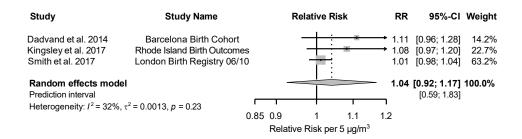
PM_{2.5} First trimester exposure - primary meta-analysis - SGA

PM_{2.5}- First trimester exposure and SGA



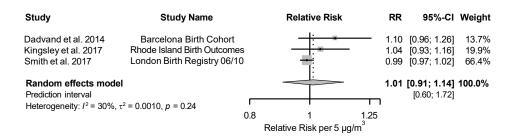
PM_{2.5} Second trimester exposure - primary meta-analysis - SGA

PM_{2.5} Second trimester exposure and SGA



PM_{2.5} Third trimester exposure - primary meta-analysis - SGA

PM_{2.5} Third trimester exposure and SGA



2 Western European and 1 North American cohort. All rated moderate in traffic specificity.

Dadvand et al. 2014 adjusted for smoking and BMI. Smith et al. 2017 did not adjust for smoking.

Dadvand et al. 2014 rated low in risk of bias for confounding and the other 2 rated high risk of bias in confounding. All rated moderate in risk of bias for exposure.

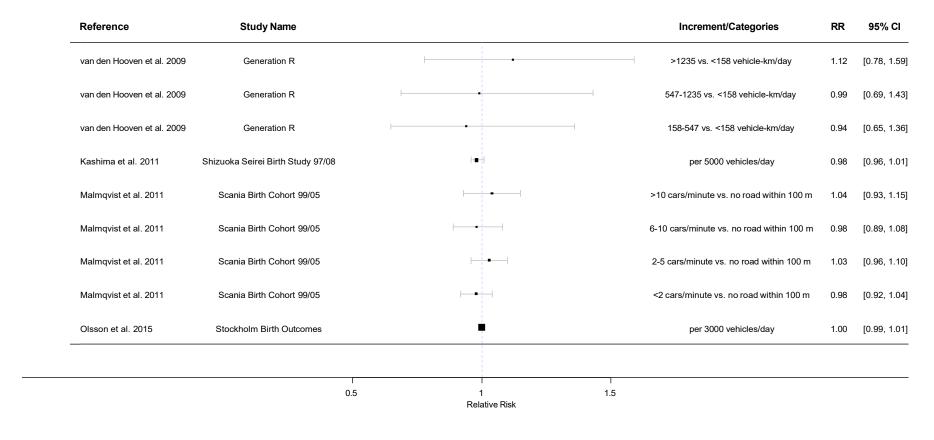
Distance measures

Traffic Distance measures - SGA

Reference	Study Name		Categories	RR	95% CI
Brauer et al. 2008	BC 99/02 Birth Cohort		<150 m to highway or <50 m to major road vs. higher	0.99	[0.92, 1.06]
Genereux et al. 2008	Montreal Birth Outcome Study	<u> </u>	<200 vs. >200 m	1.06	[0.96, 1.17]
van den Hooven et al. 2009	Generation R	-	<50 vs. >200 m	1.14	[0.77, 1.68]
van den Hooven et al. 2009	Generation R	-	50-100 vs. >200 m	1.12	[0.78, 1.62]
van den Hooven et al. 2009	Generation R	<u> </u>	100-150 vs. >200 m	1.01	[0.69, 1.48]
van den Hooven et al. 2009	Generation R	<u> </u>	150-200 vs. >200 m	1.00	[0.67, 1.49]
Hannam et al. 2013	NWPSU	⊢	<100 vs. >100 m	1.02	[0.92, 1.12]
Miranda et al. 2013	North Carolina Birth Registry 04/08	H	<250 vs. 250-500 m	1.01	[0.98, 1.05]
Miranda et al. 2013	North Carolina Birth Registry 04/08	<u> </u>	<250 vs. >500 m	1.01	[0.99, 1.04]
Sathyanarayana et al. 2013	Puget Sound Birth Registry		<50 vs. > 50 m to highway	1.11	[1.00, 1.23]
Sathyanarayana et al. 2013	Puget Sound Birth Registry	•	< 50 vs. >50 m to major road	1.01	[0.98, 1.04]
Gehring et al. 2014	BC 99/02 Birth Cohort		<50 vs. >50 m	1.10	[0.97, 1.26]
Wesselink et al. 2017	Cape Cod Family Health	-	<100 vs. >200 m	0.91	[0.63, 1.31]
Wesselink et al. 2017	Cape Cod Family Health	-	100-199 vs. >200 m	0.81	[0.55, 1.19]
		0.5 1 1.5			
		Relative Risk			

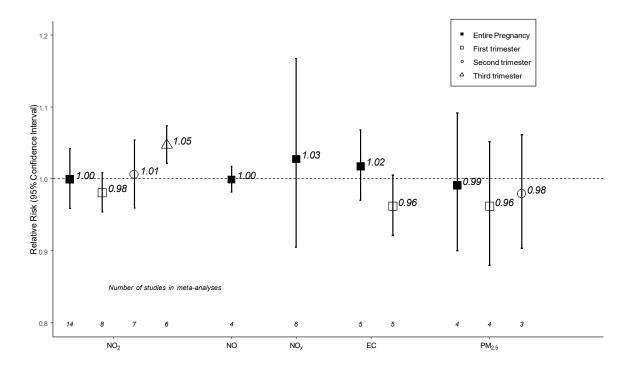
Density measures

Traffic Density measures - SGA



8.4 Preterm birth (PTB)

Summary of meta-analysis



Footnote: The following increments were used: $10 \, \mu g/m^3$ for NO_2 , $10 \, \mu g/m^3$ for NO_3 , $20 \, \mu g/m^3$ for NO_3 , $1 \, \mu g/m^3$ for EC and $10 \, \mu g/m^3$ for $10 \, \mu g/m^3$ for PM_{2.5}. Effect estimates cannot be directly compared across the different traffic-related pollutants because the selected increments do not necessarily represent the same contrast in exposure.

1.25 1.4

0.8 1 1.25 Relative Risk per 10 µg/m³

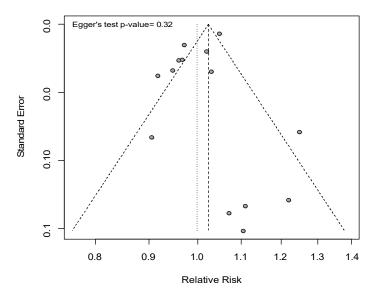
NO₂ Entire pregnancy exposure - primary meta-analysis - PTB

Study Study Name Relative Risk RR 95%-CI Weight Maroziene et al. 2002 Kaunas Birth Outcomes 98 1.25 [1.07; 1.46] 3.6% Wilhelm et al. 2003 LA County Birth Registry 94/96 0.97 [0.92; 1.02] 10.8% Gehring et al. 2011 PIAMA 1 07 [0.82: 1.41] 14% Wilhelm et al. 2011 LA County Birth Registry 04/06 0.97 [0.94; 1.00] 12.9% Wu et al. 2011 South Coast Births 97/06 LA 0.92 8.5% [0.85; 0.99] Wu et al. 2011 South Coast Births 97/06 OC 0.95 [0.89; 1.01] 9.3% van den Hooven et al. 2012 Generation R 1.10 [0.82; 1.49] 1.2% Gehring et al. 2014 BC 99/02 Birth Cohort [0.98; 1.06] 12.0% 1.02 Poirier et al. 2015 Halifax Birth Outcomes 0.91 [0.77: 1.06] 3.4% Estarlich et al. 2016 INMA 1.11 [0.85; 1.44] 1.5% Lavigne et al. 2016 **BORN Ontario** 1 05 [1.04: 1.06] 13.9% Dedele et al. 2017 Kaunas Birth Outcomes 07/08 1.22 [0.95; 1.57] 1.6% Giorgis-Allemand et al. 2017 **ESCAPE** 0.96 [0.91; 1.01] 10.7% Ji et al. 2019 Shanghai PTB Study 1.03 [0.96; 1.10] 9.1% Random effects model 1.00 [0.96; 1.04] 100.0% Prediction interval [0.90; 1.11] Heterogeneity: $I^2 = 79\%$, $\tau^2 = 0.0021$, p < 0.01

0.7 0.8

NO₂ entire pregnancy exposure and Pre-term birth

Publication bias - entire pregnancy exposure



Footnote: The vertical lines in the funnel plots represent the pooled fixed and random effect estimates. The vertical dashed line in the middle of the funnel shows the fixed effect estimate. As the Panel applied a random-effects model, the funnel plot also presents the random-effects estimate with the dotted line.

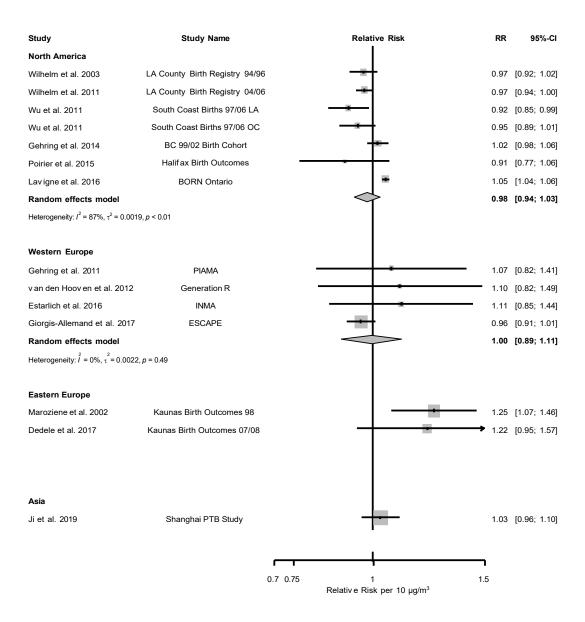
Subgroup analysis – entire pregnancy exposure

By publication year

 $\ensuremath{\mathsf{NO}}_2$ - Pre-term birth by publication year

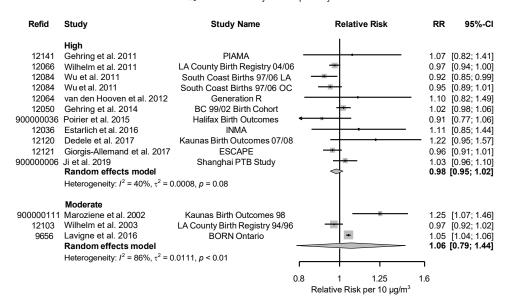
Study	Study Name	Relative Risk	RR	95%-CI
Before 2008 Maroziene et al. 2002 Wilhelm et al. 2003	Kaunas Birth Outcomes 98 LA County Birth Registry 94/96			[1.07; 1.46] [0.92; 1.02]
After 2008 Gehring et al. 2011 Wilhelm et al. 2011 Wu et al. 2011 Wu et al. 2011 van den Hooven et al. 2012 Gehring et al. 2014 Poirier et al. 2015 Estarlich et al. 2016 Lavigne et al. 2017 Giorgis-Allemand et al. 2017 Ji et al. 2019 Random effects model Heterogeneity: 12 = 789%, x2 = 0	PIAMA LA County Birth Registry 04/06 South Coast Births 97/06 LA South Coast Births 97/06 OC Generation R BC 99/02 Birth Cohort Halifax Birth Outcomes INMA BORN Ontario Kaunas Birth Outcomes 07/08 ESCAPE Shanghai PTB Study	*	0.97 0.92 0.95 1.10 1.02 0.91 1.11 1.05 1.22 0.96 1.03	[0.82; 1.41] [0.94; 1.00] [0.85; 0.99] [0.89; 1.01] [0.82; 1.49] [0.98; 1.06] [0.77; 1.06] [0.85; 1.44] [1.04; 1.06] [0.95; 1.57] [0.91; 1.01] [0.96; 1.10]
Heterogeneity: $I^2 = 78\%$, $\tau^2 = 0$	0.0017, p < 0.01		\neg	
	0.5	•	2	
		Relative Risk per 10 µg/m³		

By region



By traffic specificity

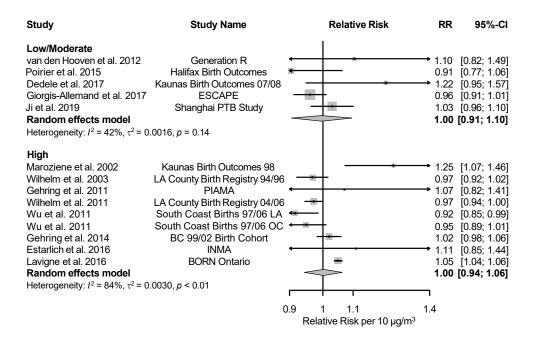
NO₂ - Pre-term birth by Traffic Specificity



By risk of bias

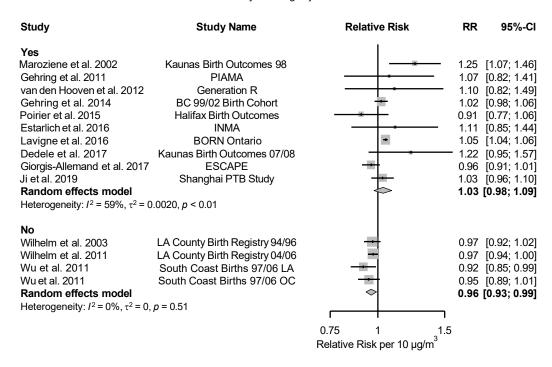
Plots not shown for risk of bias domains if all studies were rated low or moderate

NO₂ - Pre-term birth by Risk of bias assessment on confounding



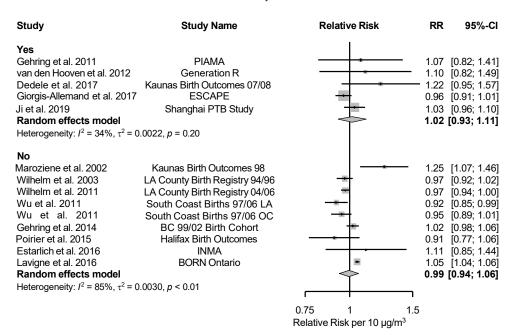
By smoking adjustment

NO₂ - Pre-term birth by smoking adjustment



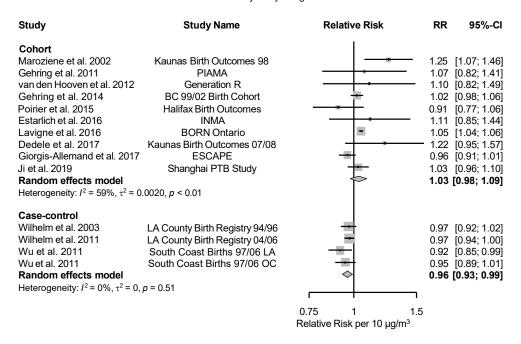
By BMI adjustment

NO₂ - Pre-term birth by BMI



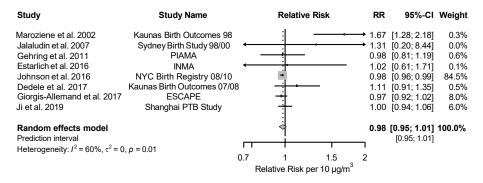
By study design

NO₂ - Pre-term birth by study design



NO₂ First trimester exposure - primary meta-analysis - PTB

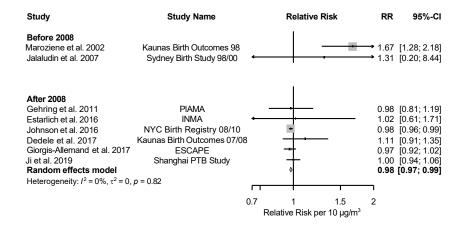
NO₂ first trimester exposure and Pre-term birth



Subgroup analysis - first trimester exposure

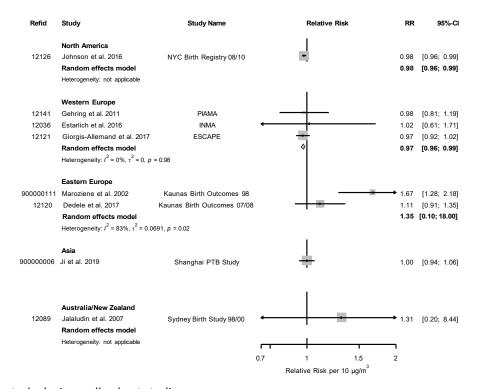
By publication year

NO₂ first trimester exposure and Pre-term birth by publication year



By region

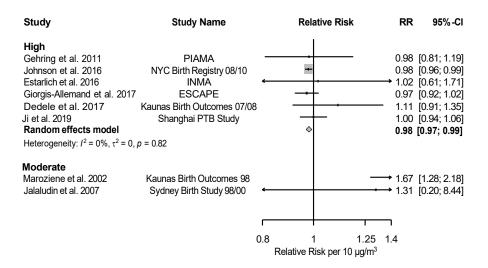




By study design – all cohort studies

By traffic specificity

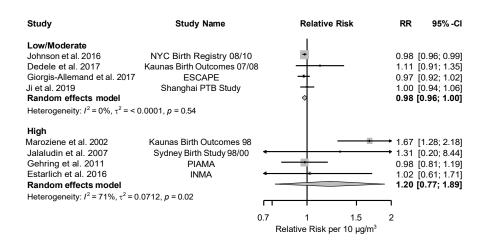
NO₂ first trimester - Pre-term birth by Traffic Specificity



By risk of bias

Plots not shown for risk of bias domains if all studies were rated low or moderate

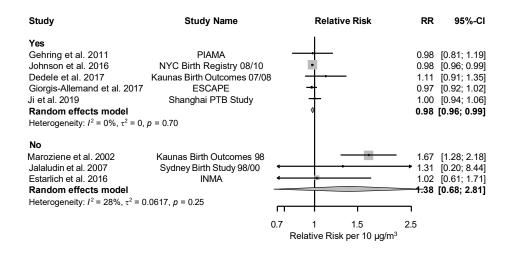
NO21rst trimester - Pre-term birth by Risk of bias assessment on confounding



By smoking adjustment - all studies adjusted for smoking

By BMI adjustment

NO₂ 1rt trimester Pre-term birth by BMI



NO₂ Second trimester exposure - primary meta-analysis - PTB

Study Name Relative Risk 95%-CI Weight Study Maroziene et al. 2002 Kaunas Birth Outcomes 98 1.13 [0.91; 1.41] Estarlich et al. 2016 INMA 1.06 [0.86; 1.31] 2.9% Johnson et al. 2016 NYC Birth Registry 08/10 0.97 [0.95; 0.99] 26.6% Lavigne et al. 2016 **BORN Ontario** 1.04 [1.03; 1.05] 27.5% Dedele et al. 2017 Kaunas Birth Outcomes 07/08 1.15 [0.96; 1.38] 3.7% Giorgis-Allemand et al. 2017 **ESCAPE** 0.96 [0.92; 1.01] 19.9% Ji et al. 2019 Shanghai PTB Study 1.01 [0.95; 1.07] 16.8% Random effects model 1.01 [0.96; 1.05] 100.0% Prediction interval [0.90; 1.12] Heterogeneity: $I^2 = 88\%$, $\tau^2 = 0.0013$, p < 0.01

0.8

1.25

Relative Risk per 10 µg/m³

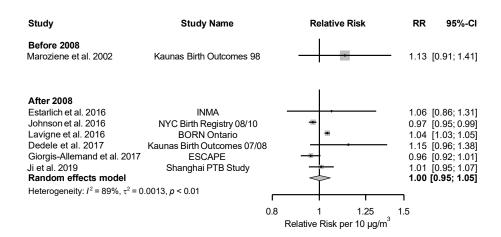
1.5

NO₂ second trimester exposure and Pre-term birth

Subgroup – second trimester exposure

By publication year

NO2 second trimester exposure and Pre-term birth by publication year



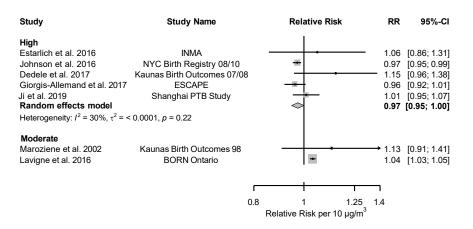
By region

Lavigne et al. 2016 and Johnson et al. 2016 from North America; Estarlich et al. 2016 and Giorgis-Allemand et al. 2017 from Western Europe; Maroziene et al. 2002 and Dedele et al. 2017 from Eastern Europe and Ji et al. 2019 from Asia.

By study design – all cohort studies

By traffic specificity

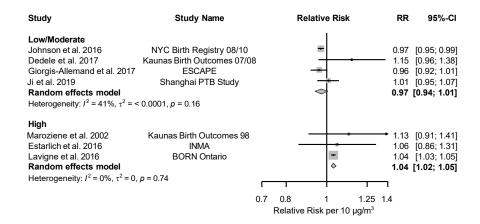
NO₂ second trimester - Pre-term birth by Traffic Specificity



By risk of bias

Plots not shown for risk of bias domains if all studies were rated low or moderate

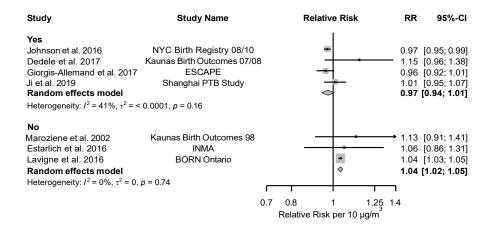
 $\ensuremath{\mathsf{NO}}_2$ second trimester - Pre-term birth by Risk of bias assessment on confounding



By smoking adjustment - all adjusted for smoking

By BMI adjustment

NO₂ second trimester Pre-term birth by BMI



NO₂ Third trimester exposure - primary meta-analysis - PTB

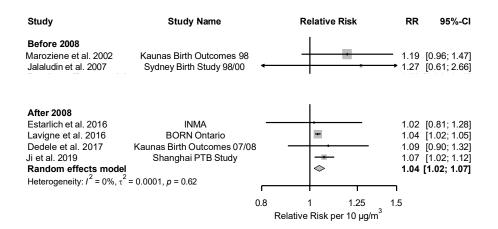
NO₂ third trimester exposure and Pre-term birth Study **Study Name** Relative Risk RR 95%-CI Weight Maroziene et al. 2002 Kaunas Birth Outcomes 98 1.19 [0.96; 1.47] Sydney Birth Study 98/00 Jalaludin et al. 2007 1.27 [0.61; 2.66] 0.1% [0.81; 1.28] Estarlich et al. 2016 INMA 1.02 1.4% **BORN Ontario** Lavigne et al. 2016 70.6% 1.04 [1.02; 1.05] Dedele et al. 2017 Kaunas Birth Outcomes 07/08 1.09 [0.90; 1.32] 2.0% Ji et al. 2019 Shanghai PTB Study 1.07 [1.02; 1.12] 24.3% Random effects model 1.05 [1.02; 1.08] 100.0% Prediction interval [1.00; 1.10] Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0.0002$, p = 0.610.8 1.25 1.5

Relative Risk per 10 µg/m³

Subgroup analysis – third trimester exposure

By publication year

NO₂ third trimester exposure and Pre-term birth by publication year



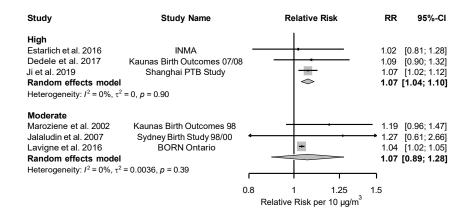
By study design – all cohort studies

By region

Lavigne et al. 2016 from North America; Estarlich et al. 2016 from Western Europe; Maroziene et al. 2002 and Dedele et al. 2017 from Eastern Europe, Ji et al. 2019 from Asia and Jalaludin et al. 2007 from Australia.

By traffic specificity

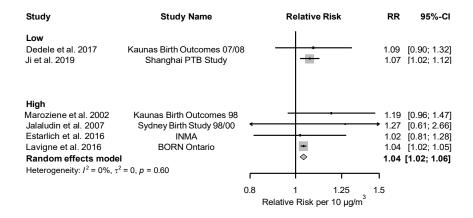
NO₂ third trimester - Pre-term birth by Traffic Specificity



By risk of bias

Plots not shown for risk of bias domains if all studies were rated low or moderate

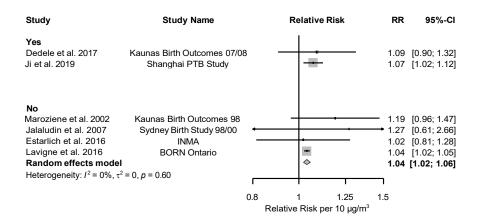
NO2 third trimester - Pre-term birth by Risk of bias assessment on confounding



By smoking adjustment - all adjusted for smoking

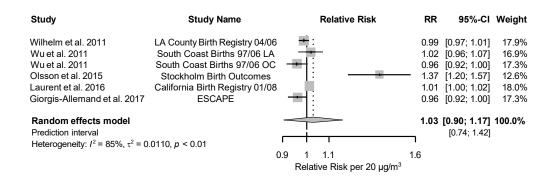
By BMI adjustment

 NO_2 third trimester Pre-term birth by BMI



NO_x Entire pregnancy exposure - primary meta-analysis - PTB

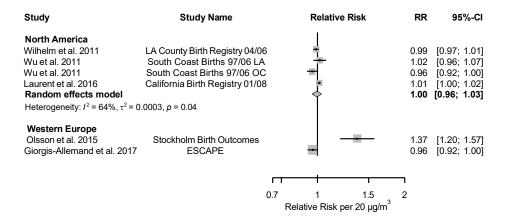
NO_x entire pregnancy exposure and Pre-term birth



Subgroup analysis – entire pregnancy exposure

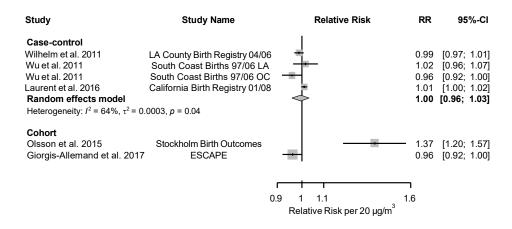
By region

NO_x - Pre-term birth by region



By study design

NO_x - Pre-term birth by study design

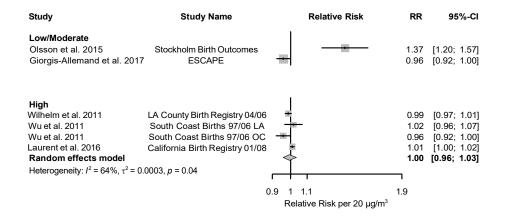


By traffic specificity - all high traffic specificity

By risk of bias

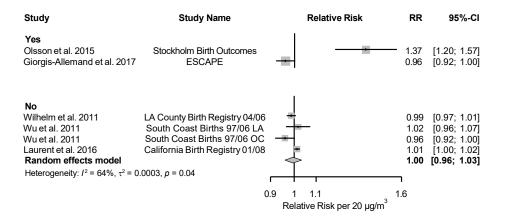
Plots not shown for risk of bias domains if all studies were rated low or moderate

 $\ensuremath{\mathsf{NO}_{\mathsf{x}}}\xspace$ - Pre-term birth by Risk of bias assessment on confounding



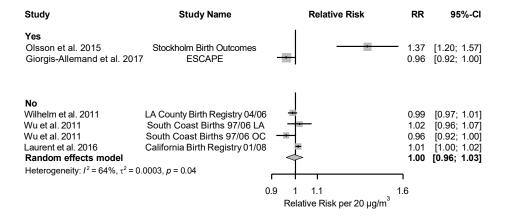
By smoking adjustment

NO_x - Pre-term birth by smoking adjustment



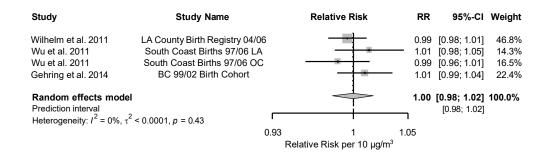
By BMI adjustment

NO_x - Pre-term birth by BMI



NO Entire pregnancy exposure - primary meta-analysis - PTB

NO entire pregnancy exposure and Pre-term birth

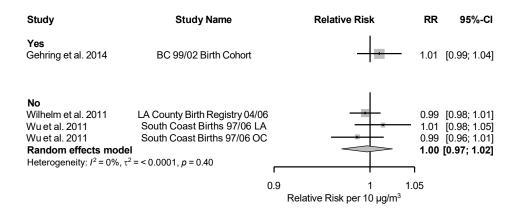


By traffic specificity - all high traffic specificity

By risk of bias - all high risk of bias for confounding and low or moderate for other categories.

By smoking adjustment

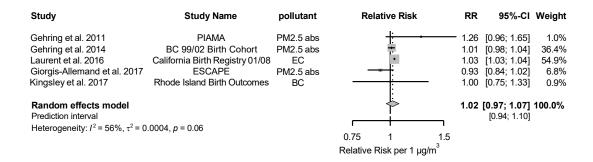
NO - Pre-term birth by smoking adjustment



By BMI adjustment - no studies adjusted for BMI

EC Entire pregnancy exposure - primary meta-analysis - PTB

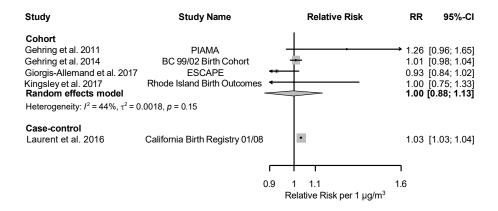
EC entire pregnancy exposure and Pre-term birth



Subgroup analysis – entire pregnancy exposure

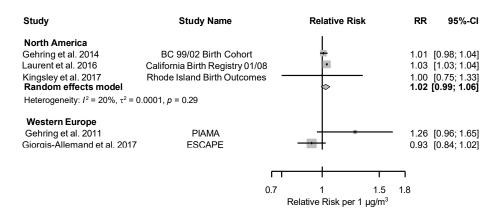
By study design

EC - Pre-term birth by study design



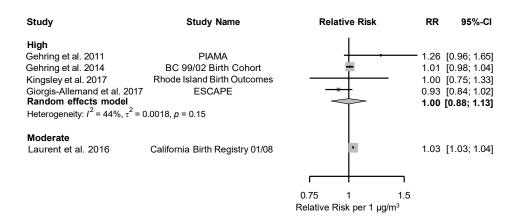
By region

EC - Pre-term birth by region



By traffic specificity

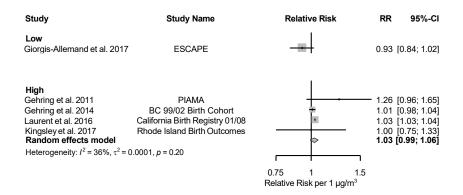
EC - Pre-term birth by Traffic Specificity



By risk of bias

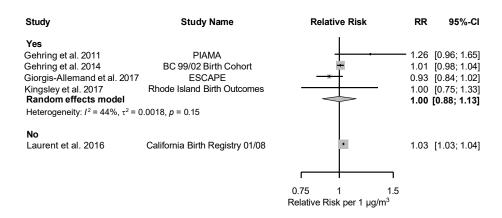
Plots not shown for risk of bias domains if all studies were rated low or moderate

EC - Pre-term birth by Risk of bias assessment on confounding



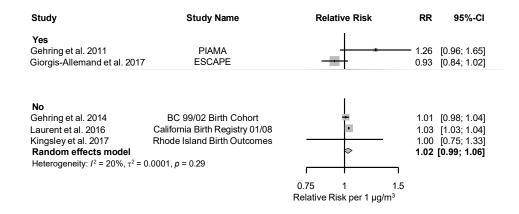
By smoking adjustment

EC - Pre-term birth by smoking adjustment



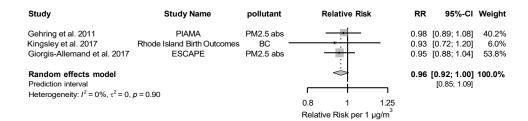
By BMI adjustment

EC - Pre-term birth by BMI



EC First trimester exposure - primary meta-analysis - PTB

EC First trimester pregnancy exposure and Pre-term birth



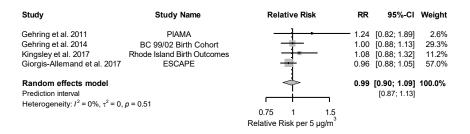
Subgroup analyses

All high traffic specificity and all three studies adjusted for smoking. Only Giorgis-Allemand et al. 2017 adjusted for BMI.

Gehring et al. 2011 and Kingsley et al. 2017 were rated high risk of bias for confounding, Giorgis-Allemand et al. 2017 was rated low.

PM_{2.5} Entire pregnancy exposure - primary meta-analysis - PTB

PM_{2.5} entire pregnancy exposure and Pre-term birth



Subgroup analysis - entire pregnancy exposure

By region

Gehring et al. 2014 and Kingsley et al. 2017 from North America, Gehring et al. 2011 and Giorgis-Allemand et al. 2017 from Western Europe.

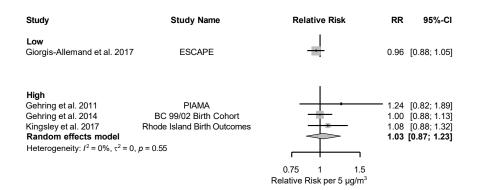
By study design - all cohort studies

By traffic specificity – all rated moderate

By risk of bias

Plots not shown for risk of bias domains if all studies were rated low or moderate

PM_{2.5} Pre-term birth by Risk of bias assessment on confounding



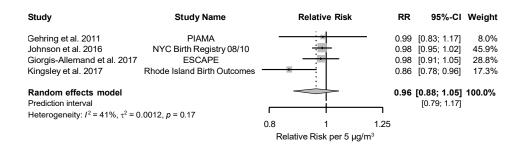
By smoking adjustment – all studies adjusted for smoking

By BMI adjustment

Gehring et al. 2011 and Giorgis-Allemand et al. 2017 adjusted for BMI, Gehring et al. 2014 and Kingsley et al. 2017 did not adjust for BMI.

PM_{2.5} First trimester exposure – primary meta-analysis - PTB

PM_{2.5}- First trimester exposure and Pre-term birth



By region

Johnson et al. 2016 and Kingsley et al. 2017 from North America, Gehring et al. 2011 and Giorgis-Allemand et al. 2017 from Western Europe.

By study design - all cohort studies

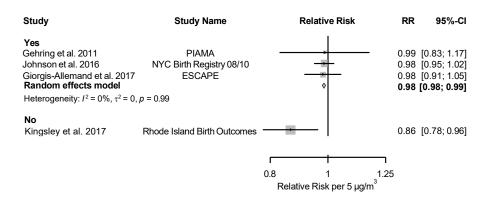
By traffic specificity – all rated moderate

By risk of bias

Giorgis-Allemand et al. 2017 and Johnson et al. 2016 were low/moderate risk of bias for confounding, Gehring et al. 2011 and Kingsley et al. 2017 were rated high risk of bias.

By BMI adjustment

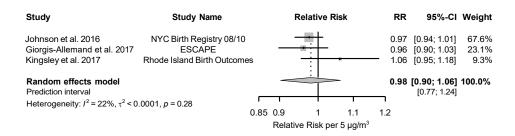
PM_{2.5} first trimester Pre-term birth by BMI



By smoking adjustment – all studies adjusted for smoking

PM_{2.5} Second trimester exposure - primary meta-analysis - PTB

PM_{2.5} Second trimester exposure and Pre-term birth



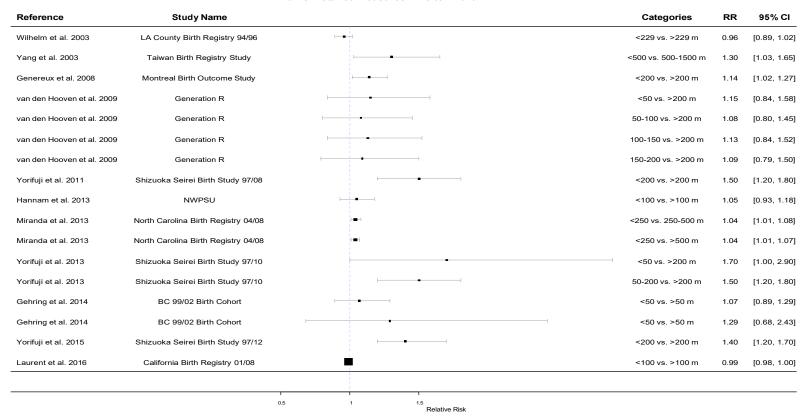
All North American cohort studies.

All rated moderate traffic specificity and risk of bias for exposure assessment, all adjusted for smoking, only Kingsley et al. 2017 did not adjust for BMI.

Kingsley et al. 2017 was rated high risk of bias for confounding; Johnson et al. 2016 was rated moderate and Giorgis-Allemand et al. 2017 was rated low.

Distance measures

Traffic Distance measures - Pre-term birth



Density measures

Traffic Density measures - Pre-term birth

