# 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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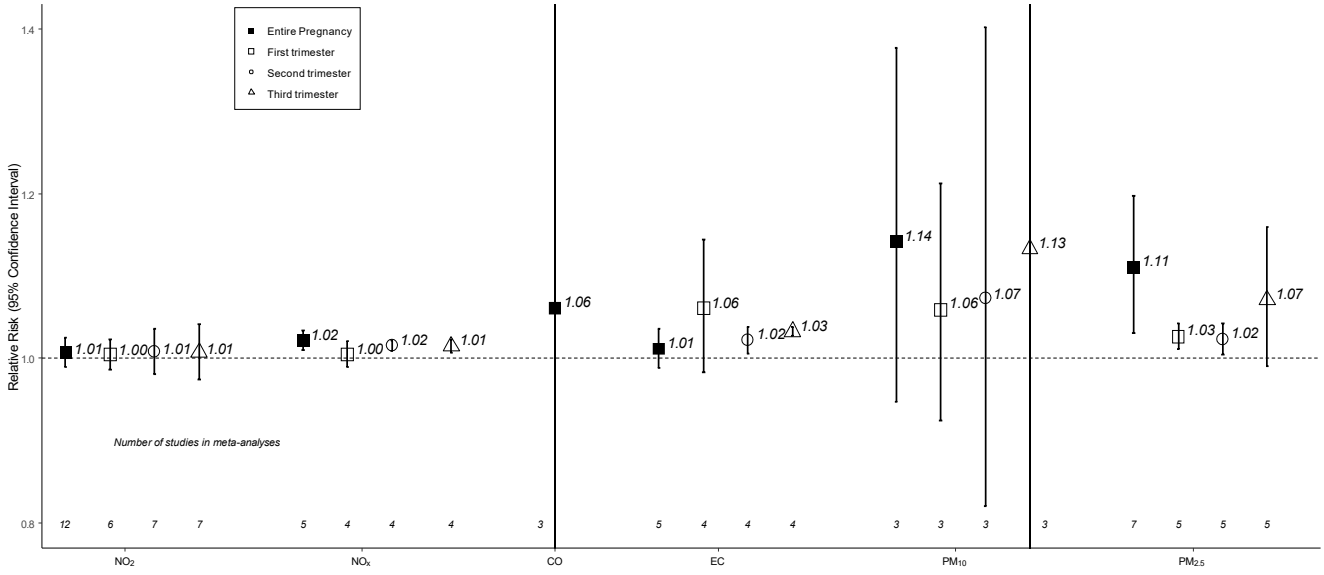
# Chapter 8: Traffic-Related Air Pollution and Birth Outcomes

## Additional Materials: All Analyses

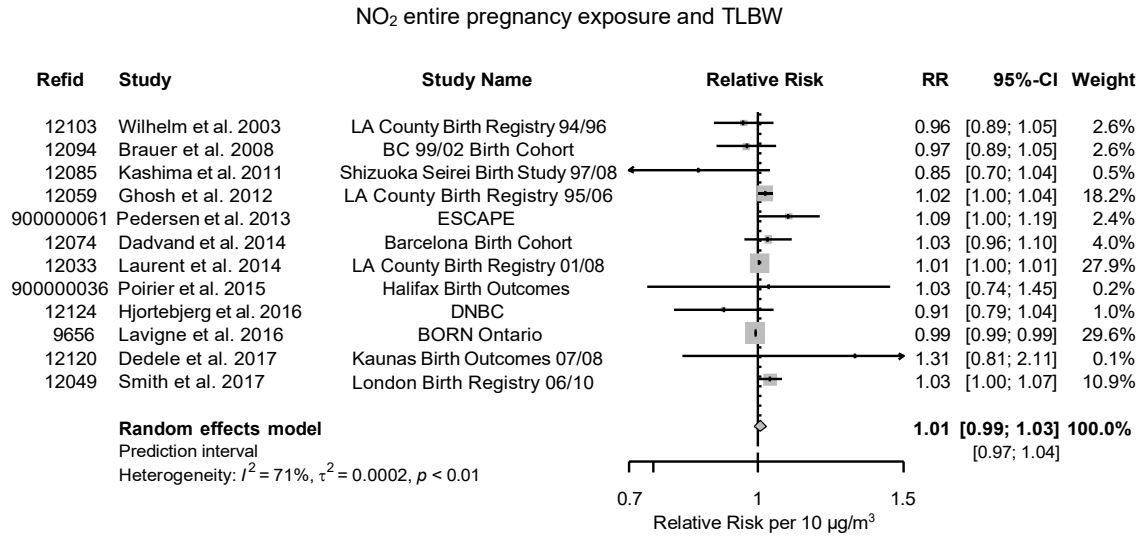
## 8.1 Term low birth weight (TLBW)

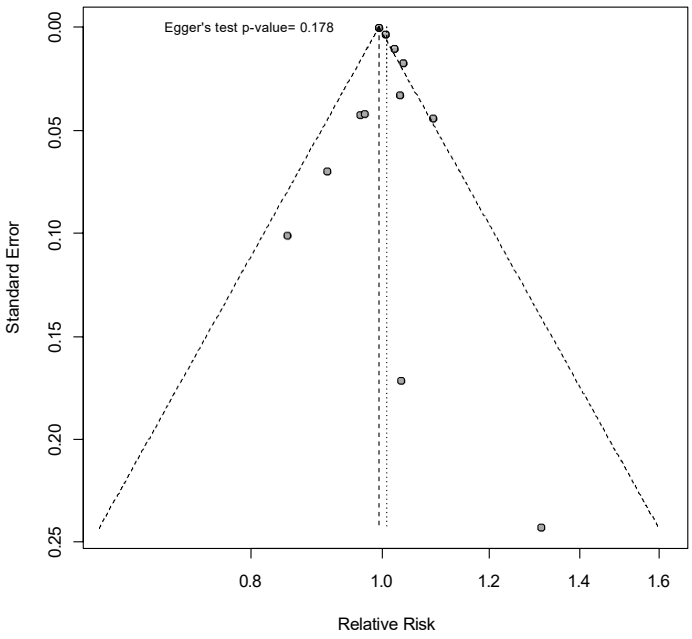
Summary of meta-analysis




Footnote: The following increments were used: 10 µg/m$^3$ for $NO_2$, 20 µg/m$^3$ for $NO_x$, 1 mg/m$^3$, 1 µg/m$^3$ for EC, 10 µg/m$^3$ for $PM_{2.5}$ and 5 µg/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.

**$NO_2$- Entire pregnancy exposure - primary meta-analysis - TLBW**

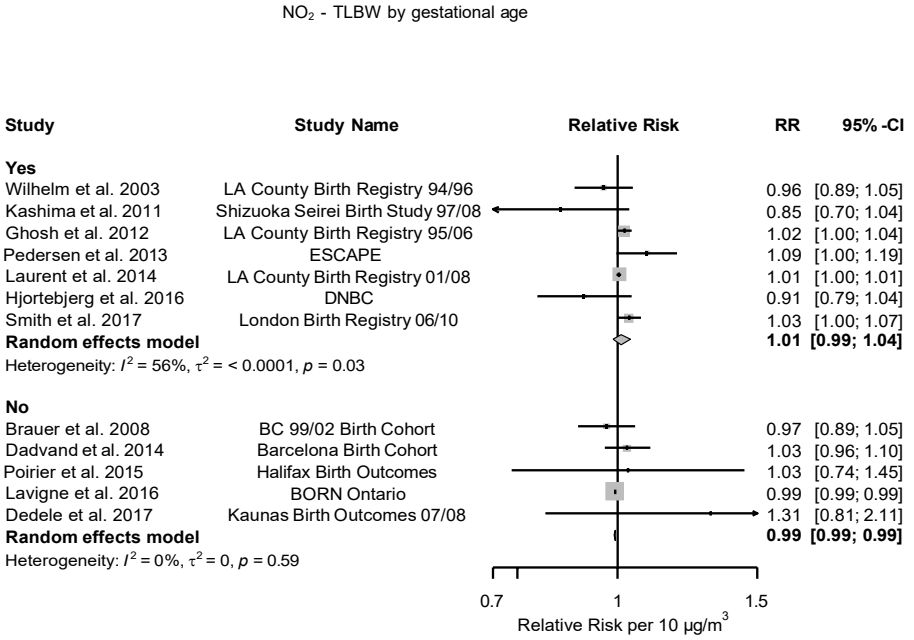


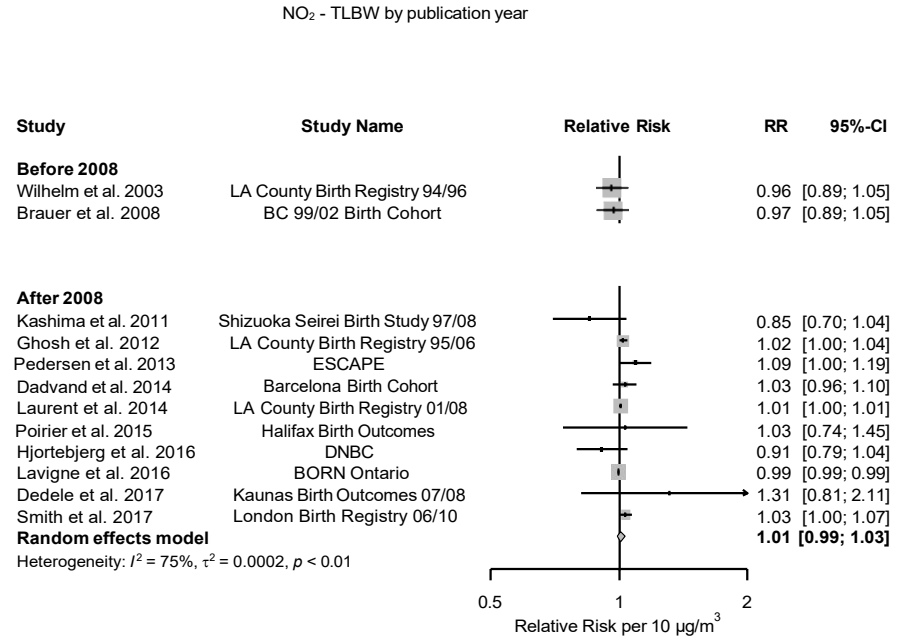

Footnote: The vertical lines in the funnel plots represent the pooled fixed and random effect estimates. The vertical dashed line in the middle of the funnel shows the fixed effect estimate. As the Panel applied a random-effects model, the funnel plot also presents the random-effects estimate with the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

Subgroup analysis – entire pregnancy exposure

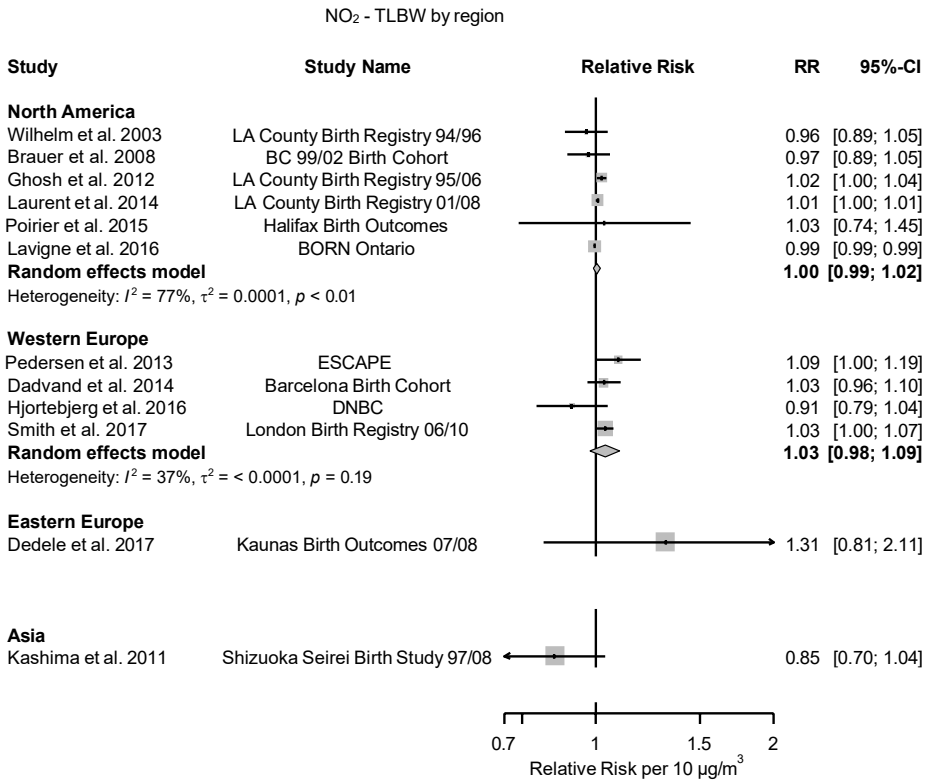
By gestational age adjustment



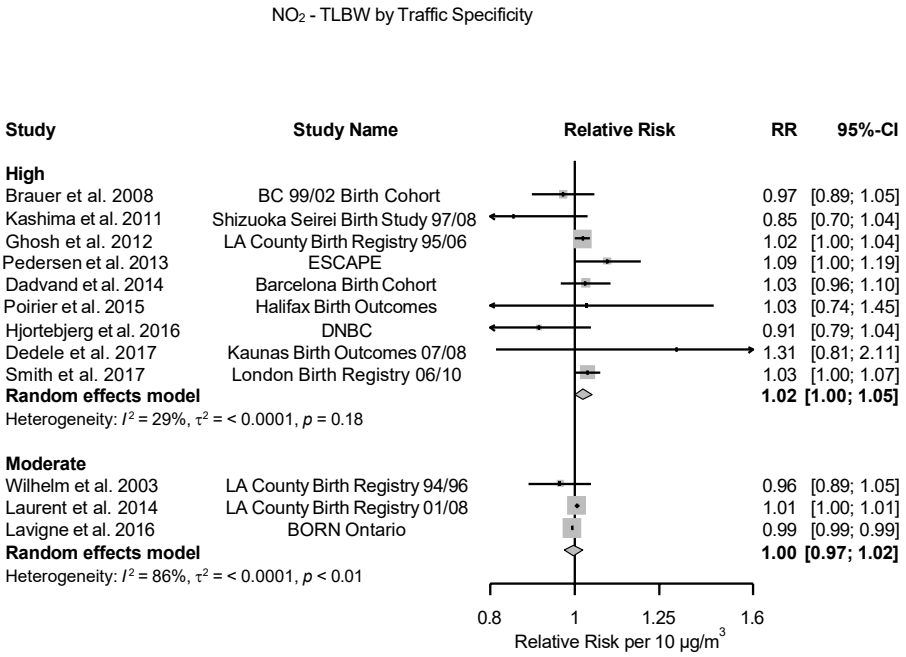

By publication year



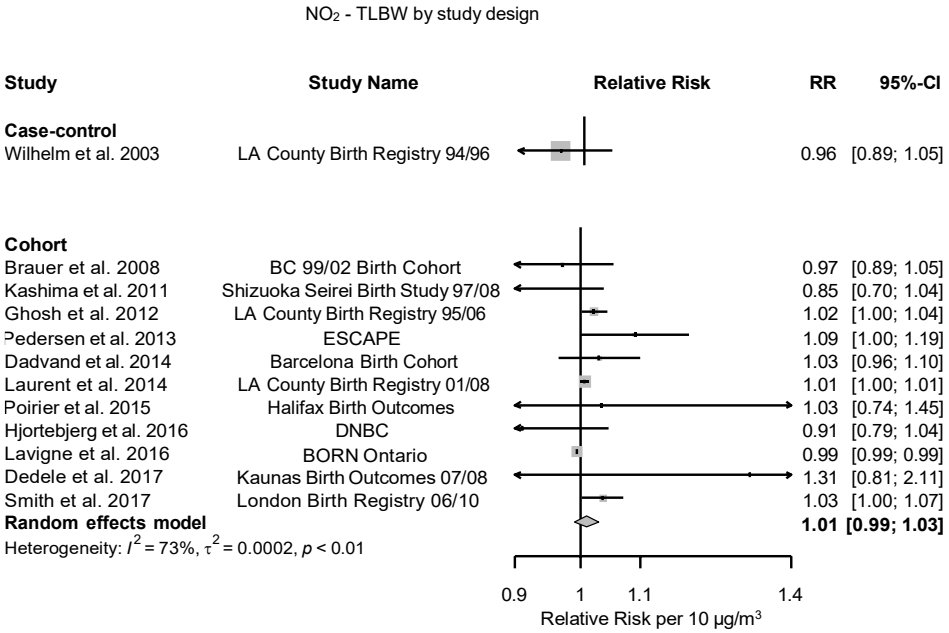
By region




By traffic specificity

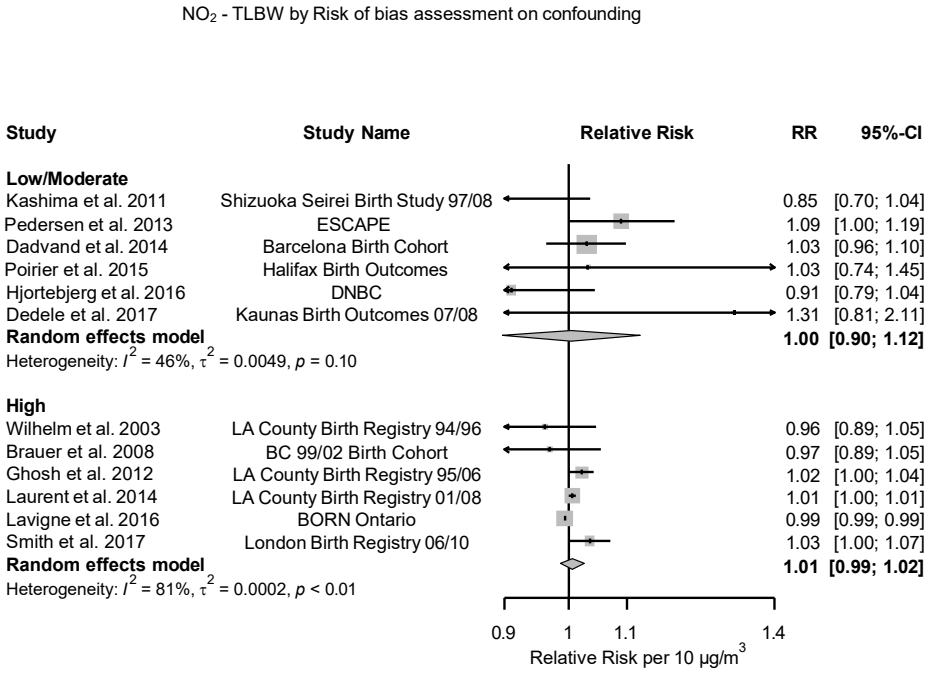


By study design

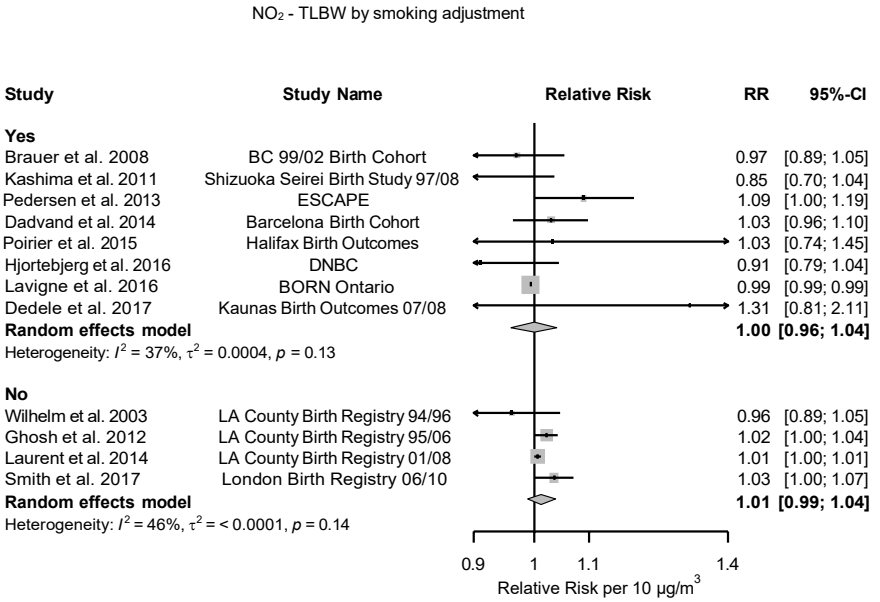



By risk of bias

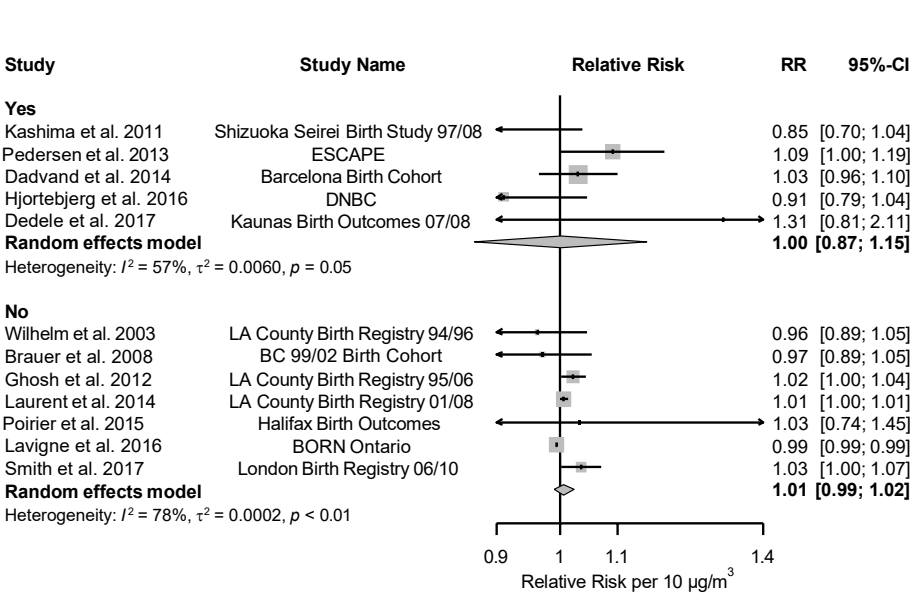
Plots not shown for risk of bias domains if all studies were rated low or moderate



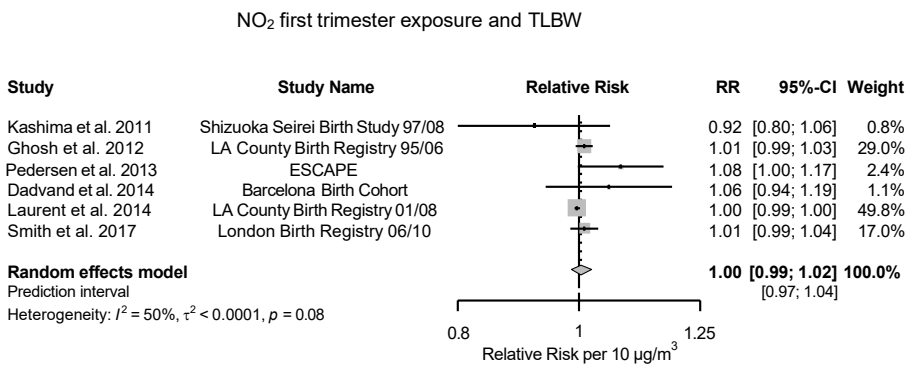
By smoking adjustment




By BMI adjustment

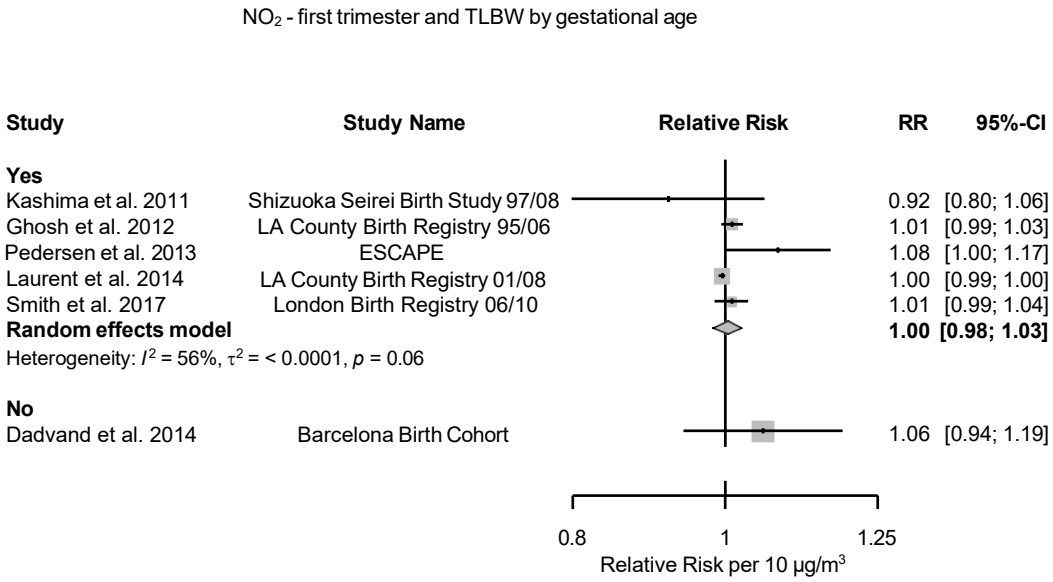


**$NO_2$ First trimester exposure - primary meta-analysis - TLBW**

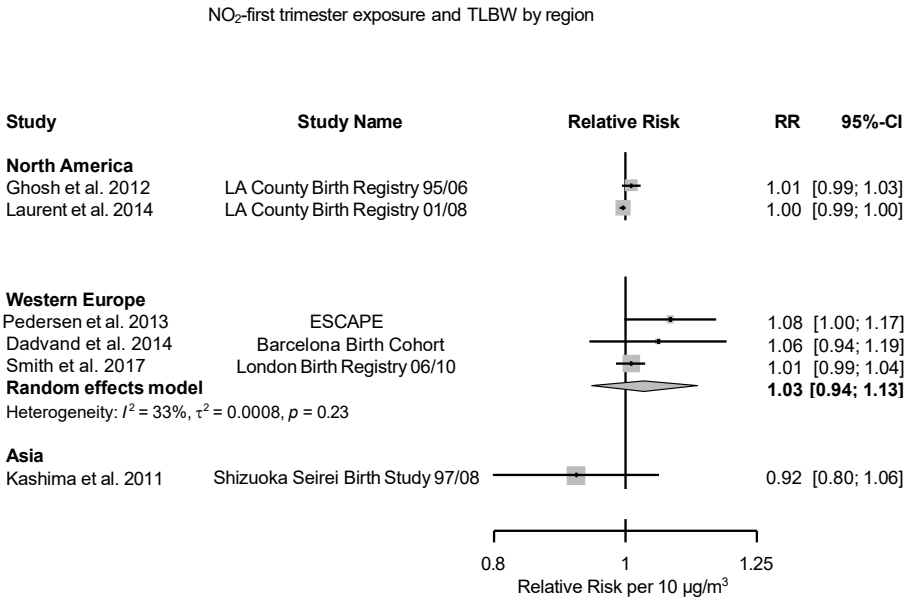



Subgroup analysis

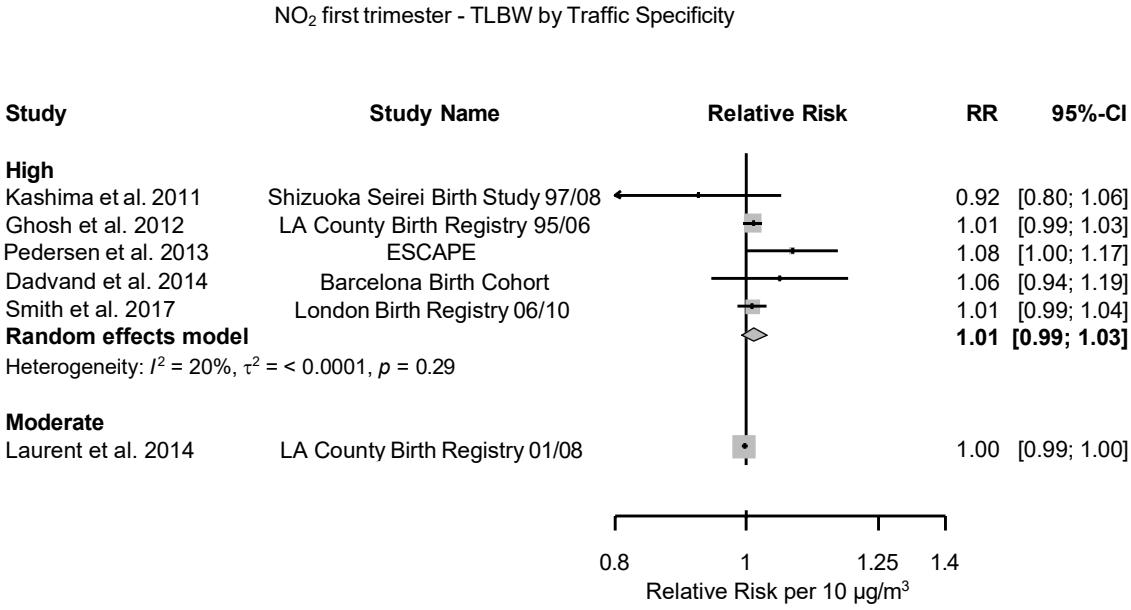
By gestational age adjustment



By region



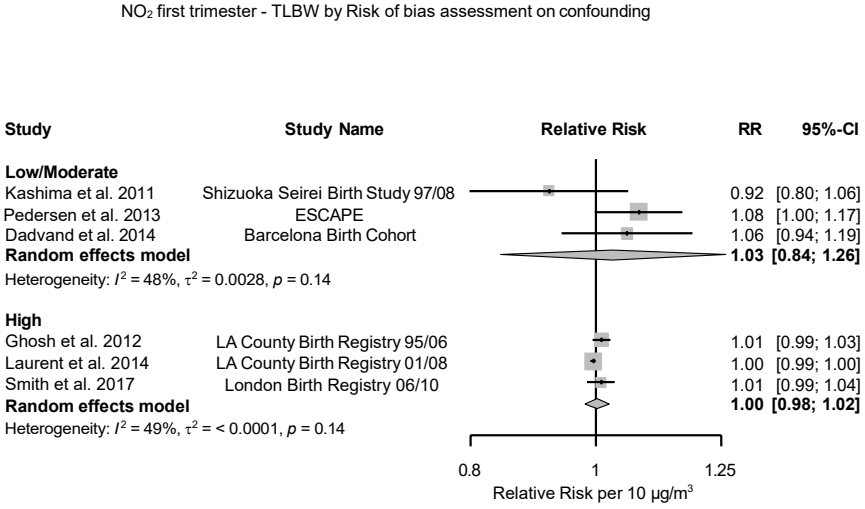

By traffic specificity



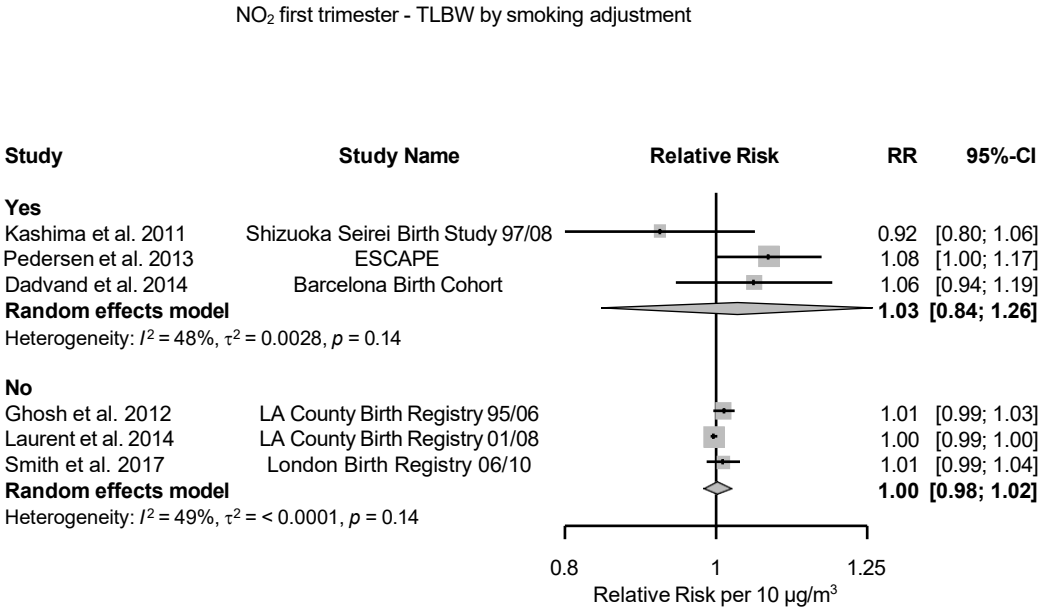

By study design- all cohort studies

By risk of bias

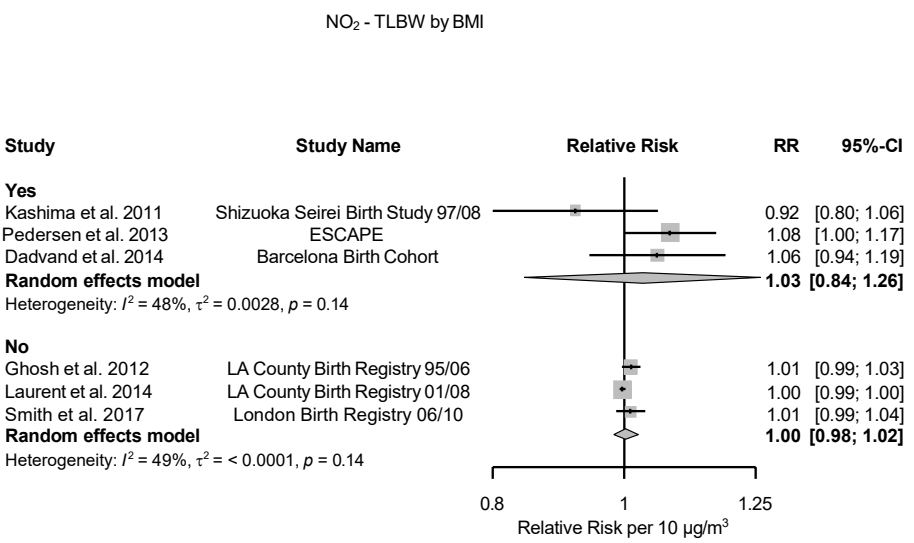
Plots not shown for risk of bias domains if all studies were rated low or moderate



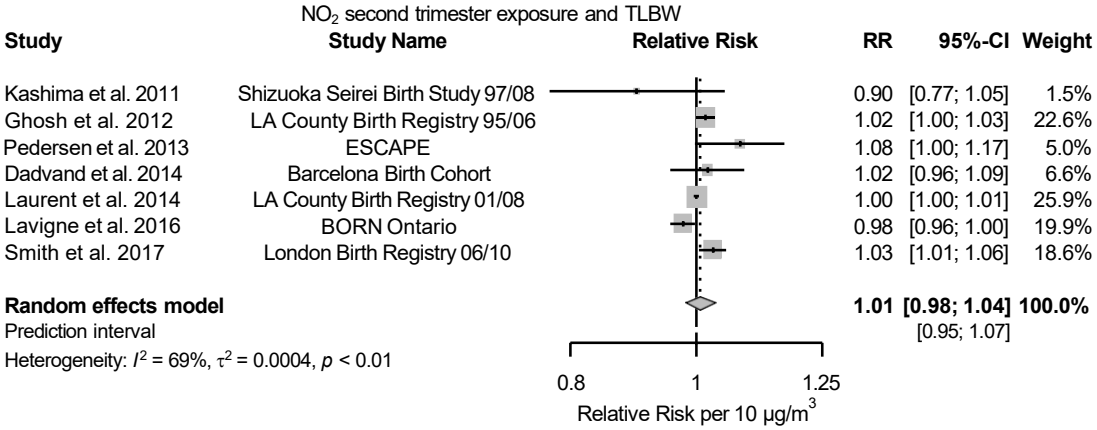
By smoking adjustment




By BMI adjustment

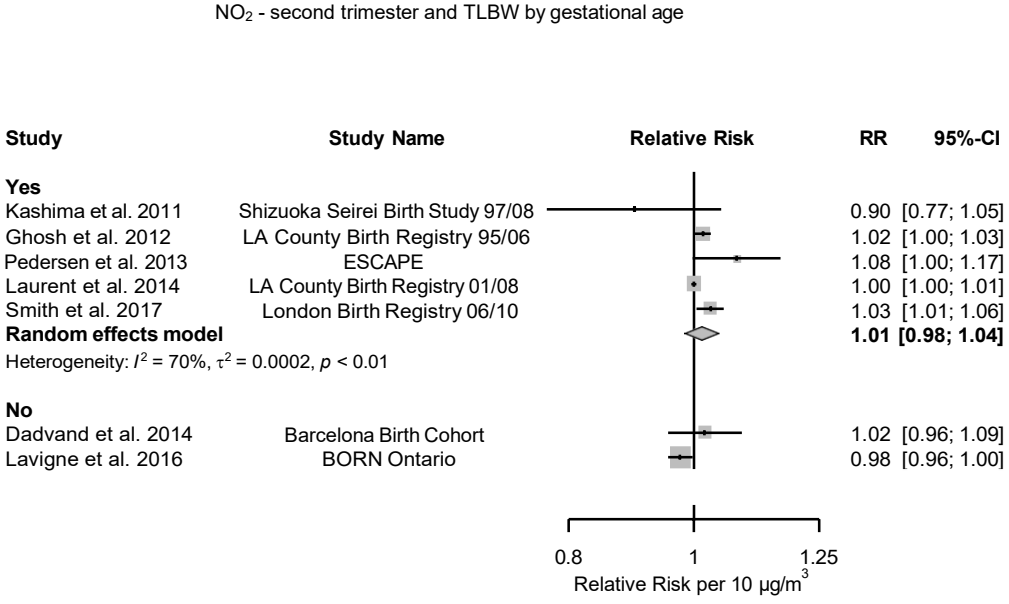


**$NO_2$ Second trimester exposure - primary meta-analysis - TLBW**



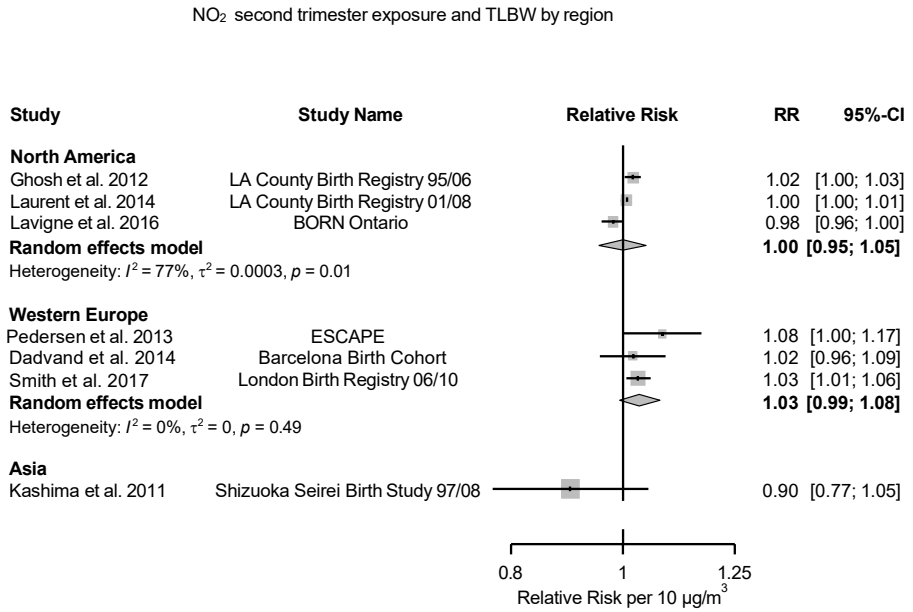

Subgroup analysis

By gestational age adjustment

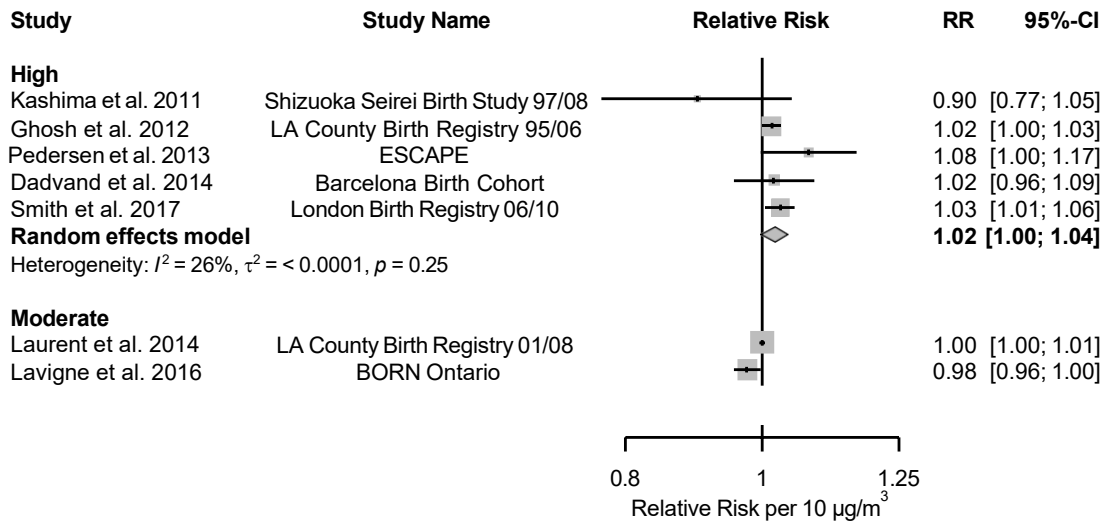



By study design - all cohort studies

By region

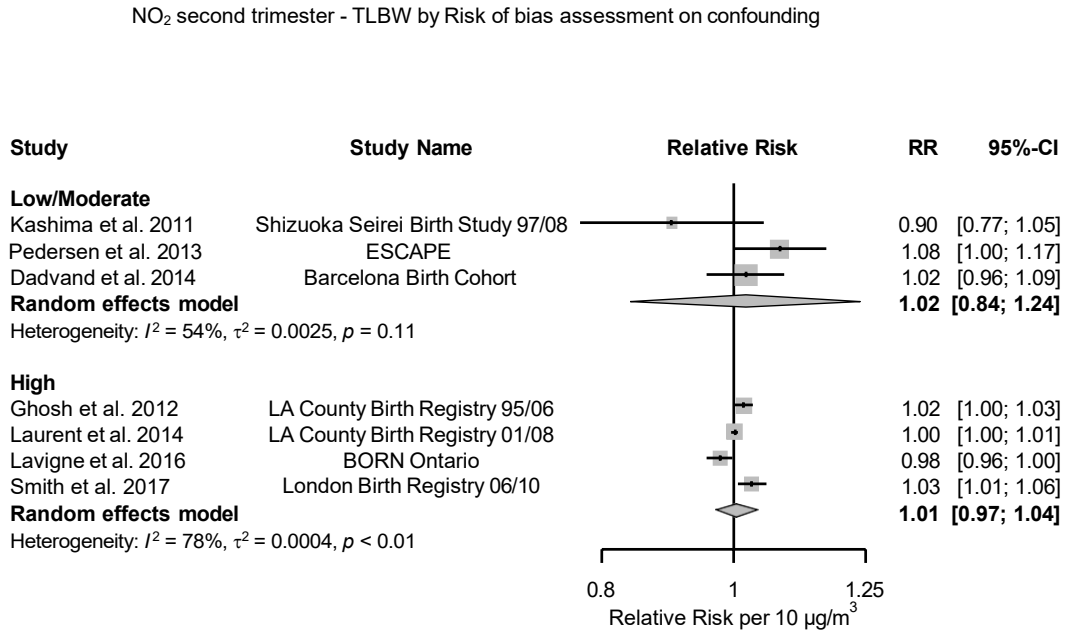



By traffic specificity

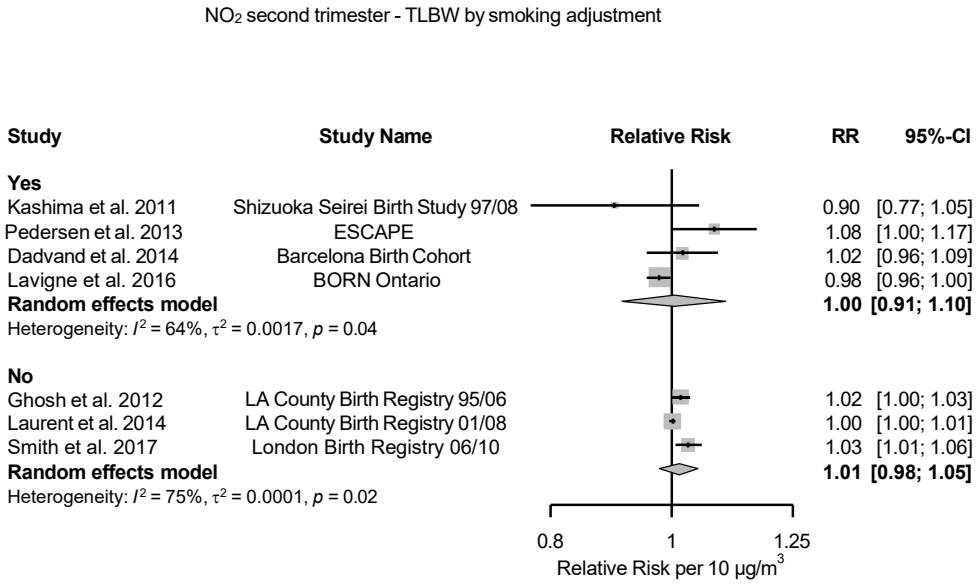


By risk of bias

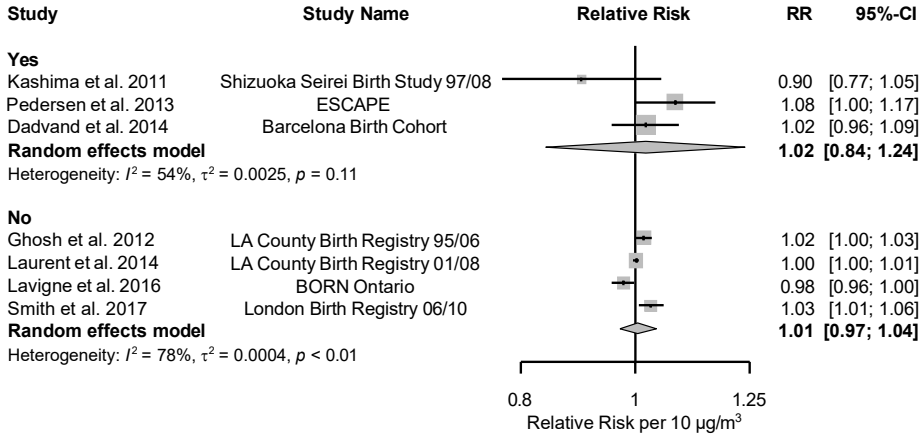
Plots not shown for risk of bias domains if all studies were rated low or moderate



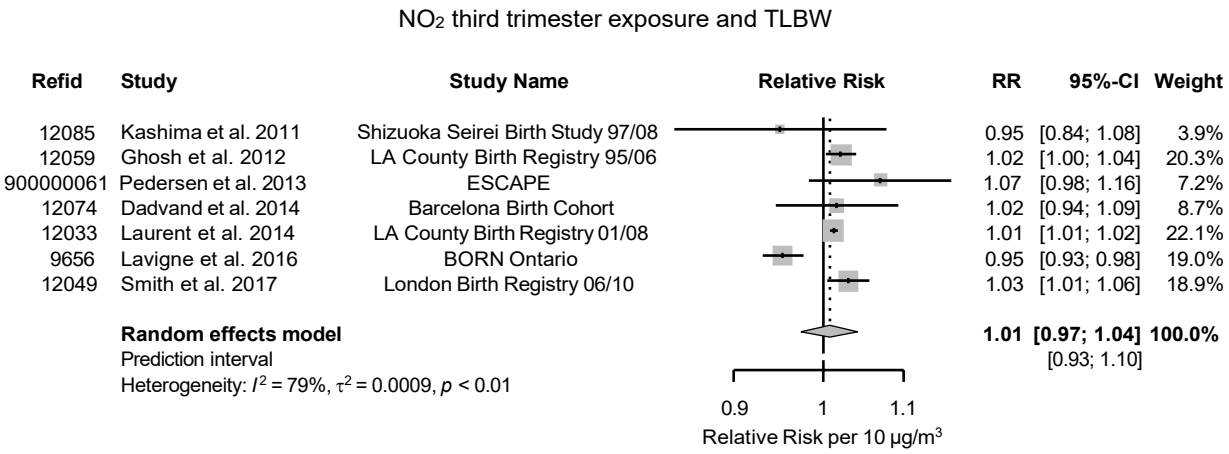
By smoking adjustment




By BMI adjustment

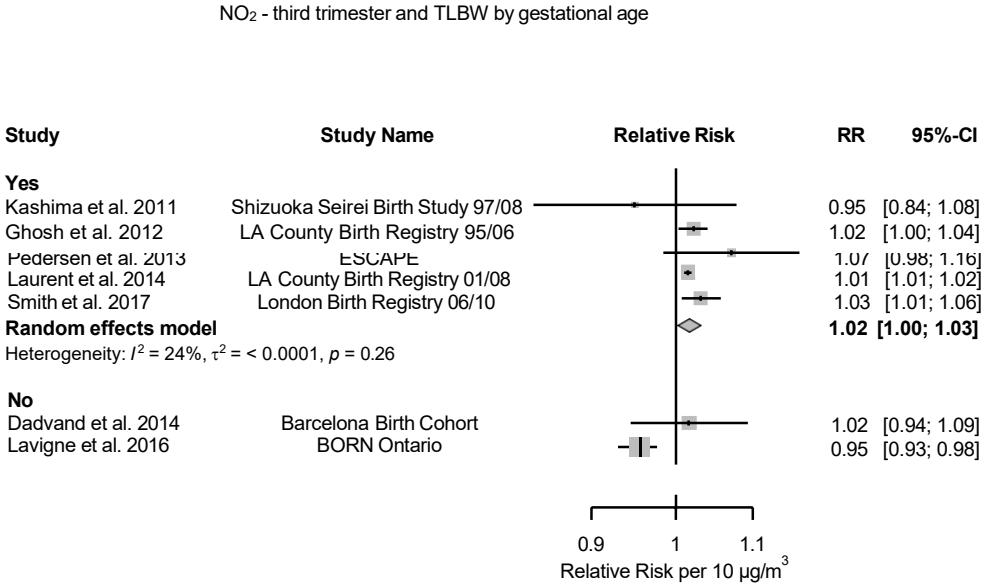


**$NO_2$ Third trimester exposure - primary meta-analysis - TLBW**



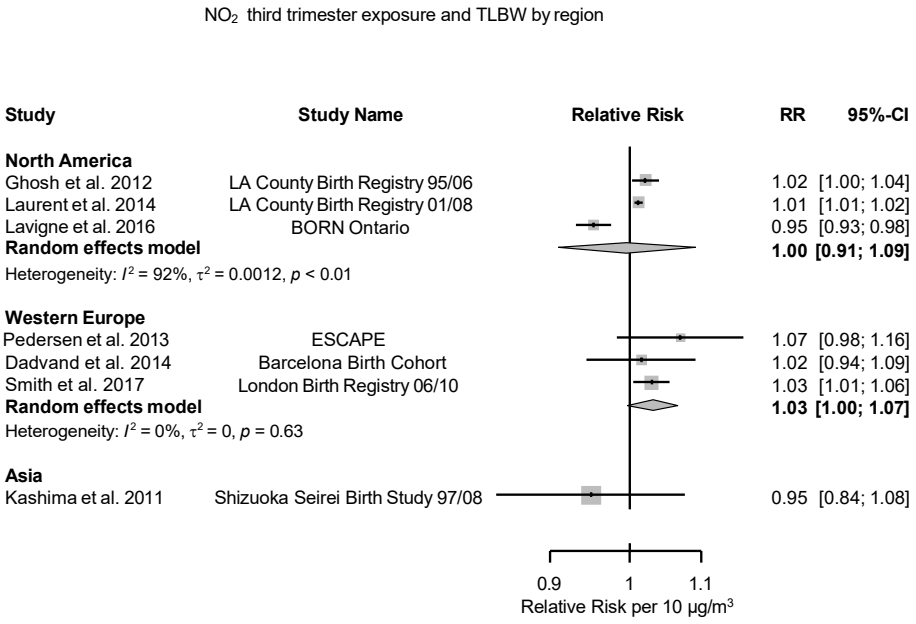

Subgroup analysis – third trimester exposure

By gestational age adjustment

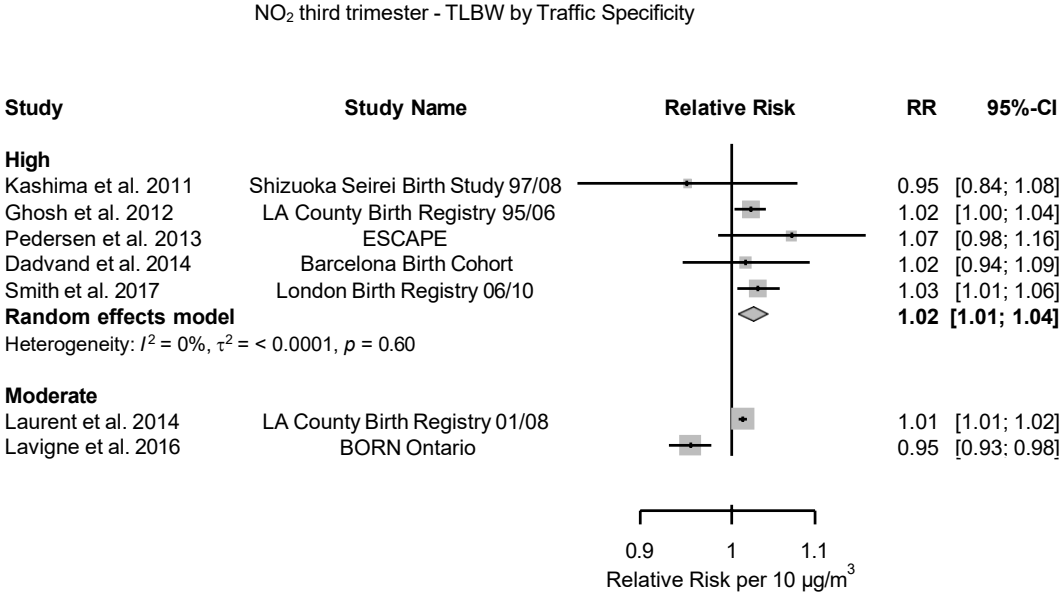



By study design - all cohort studies

By region

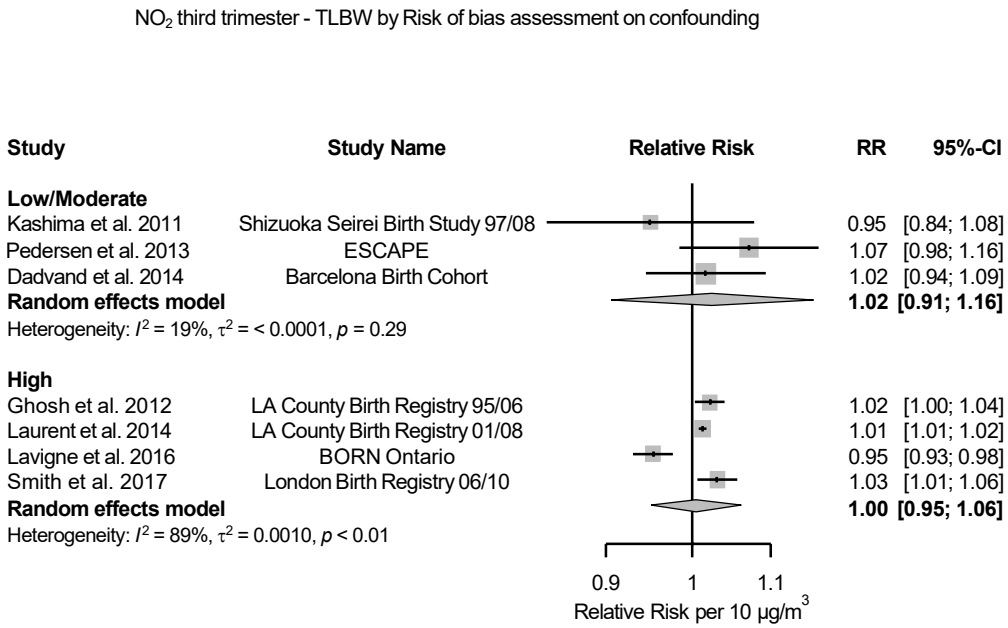



By traffic specificity

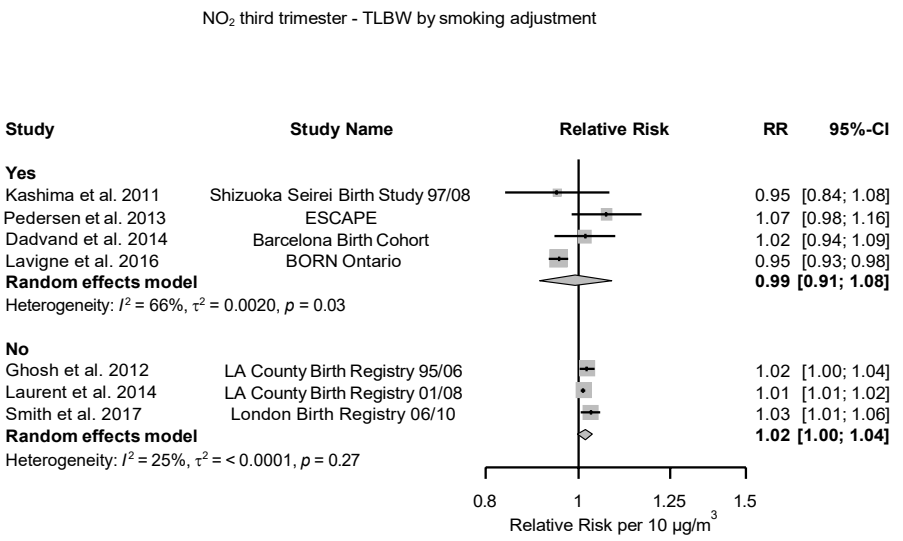


By risk of bias

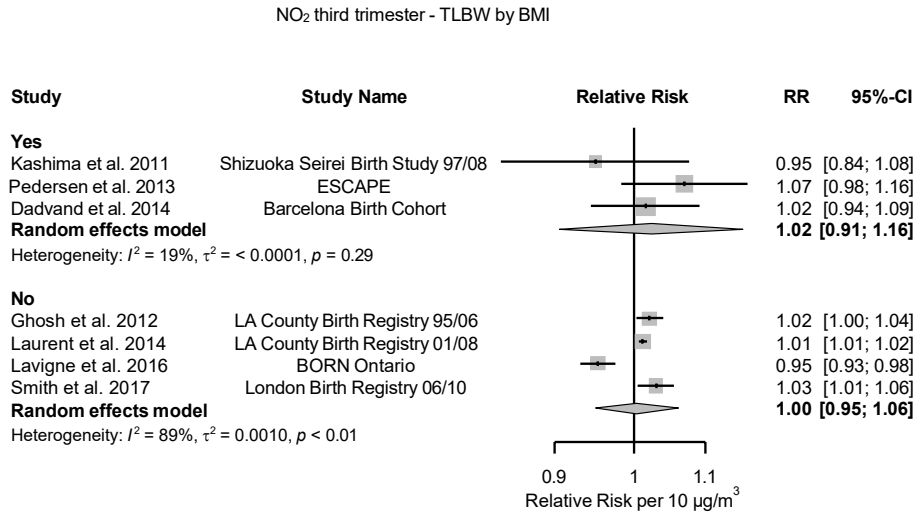
Plots not shown for risk of bias domains if all studies were rated low or moderate



By smoking adjustment

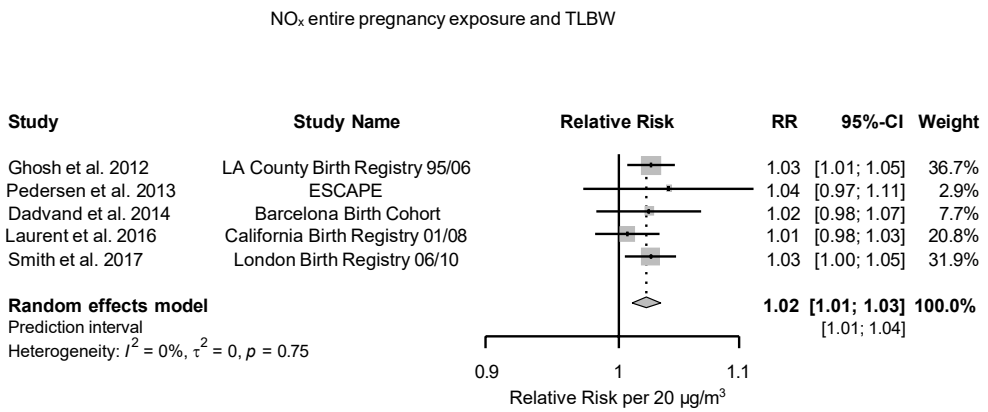



By BMI adjustment



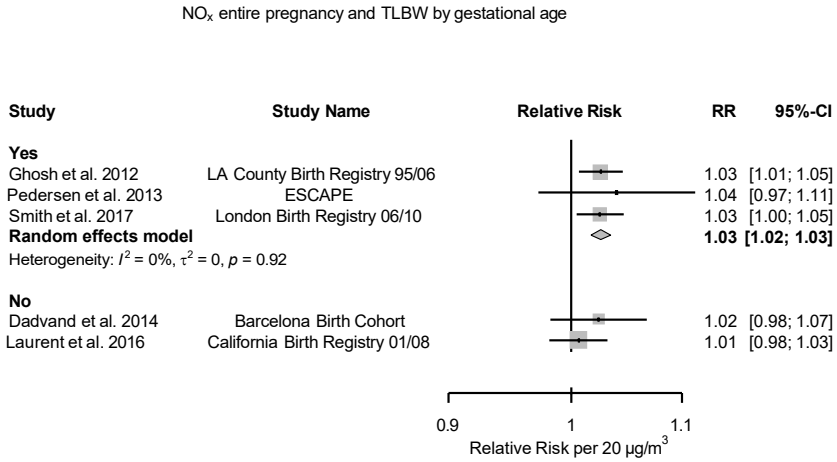

NO - entire pregnancy only 2 independent cohorts for TLBW (Brauer et al. 2008, Gosh et al. 2012); hence no meta-analysis.

**$NO_x$ Entire pregnancy exposure - primary meta-analysis - TLBW**

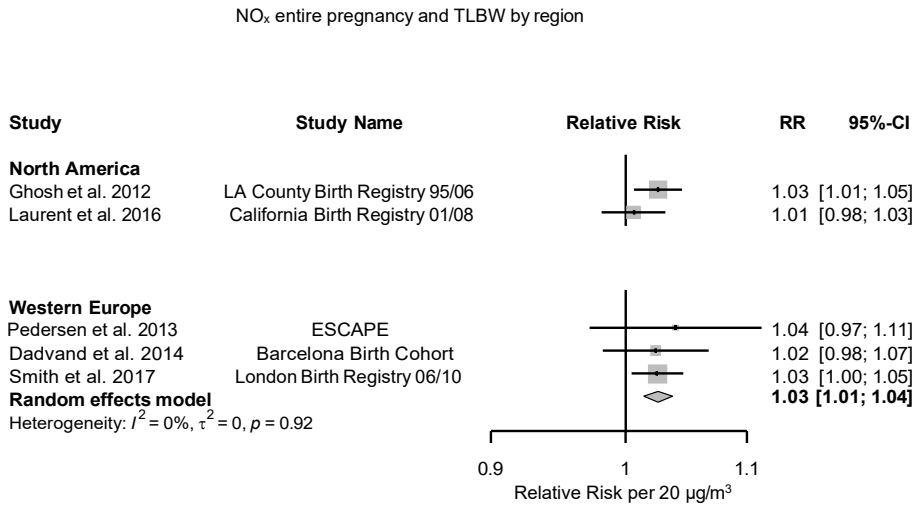



Subgroup analysis – entire pregnancy exposure

By gestational age adjustment



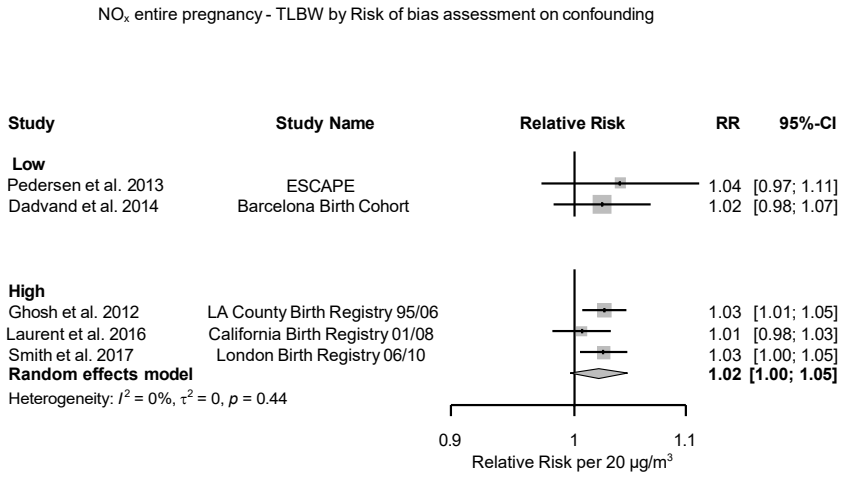
By region



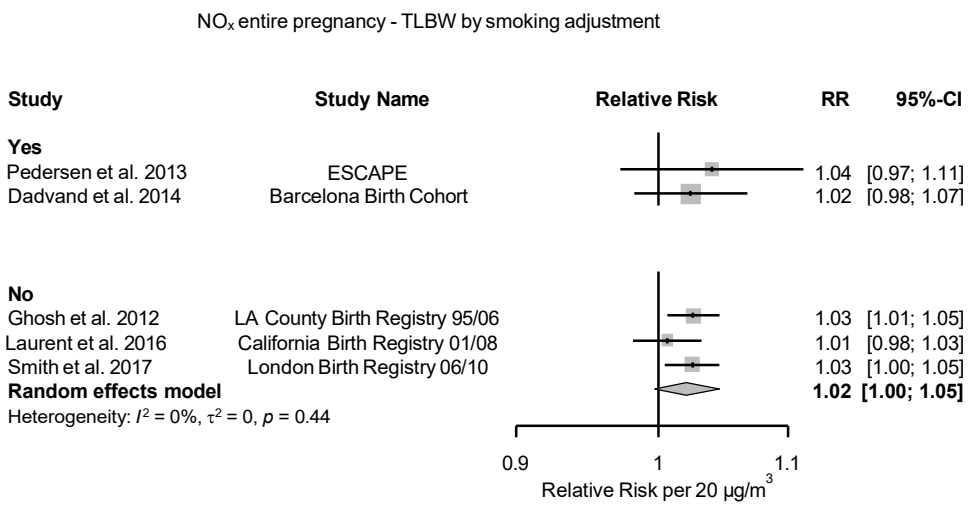

By traffic specificity - all rated high

By risk of bias

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

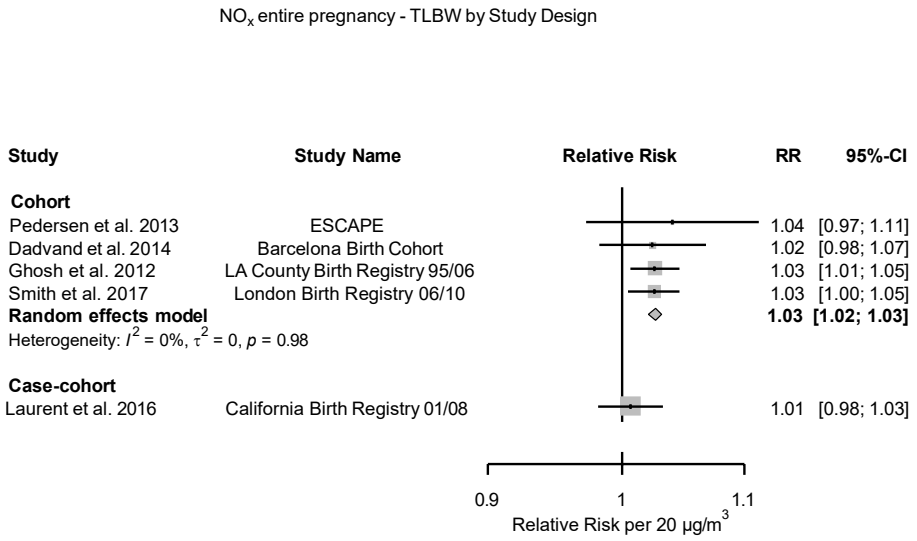


By smoking adjustment




By BMI adjustment

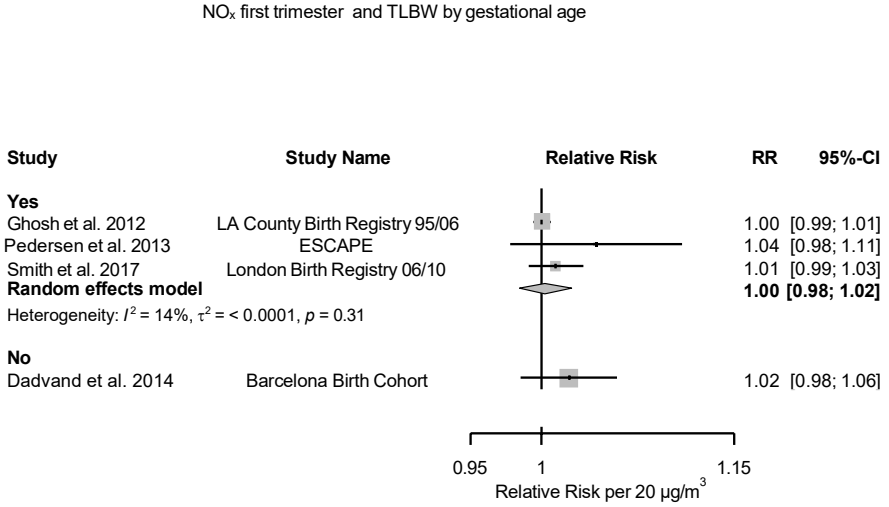
By study design



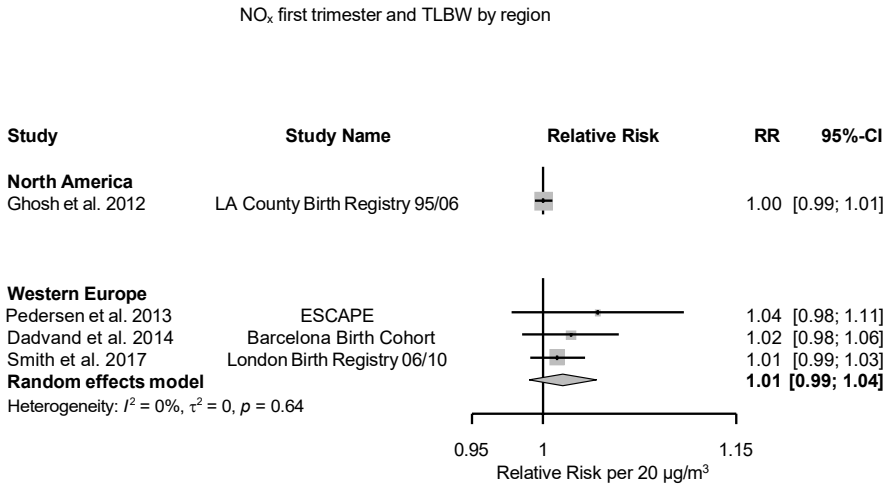
**$NO_x$ First trimester exposure - primary meta-analysis - TLBW**


Subgroup analysis – first trimester exposure

By gestational age adjustment



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.

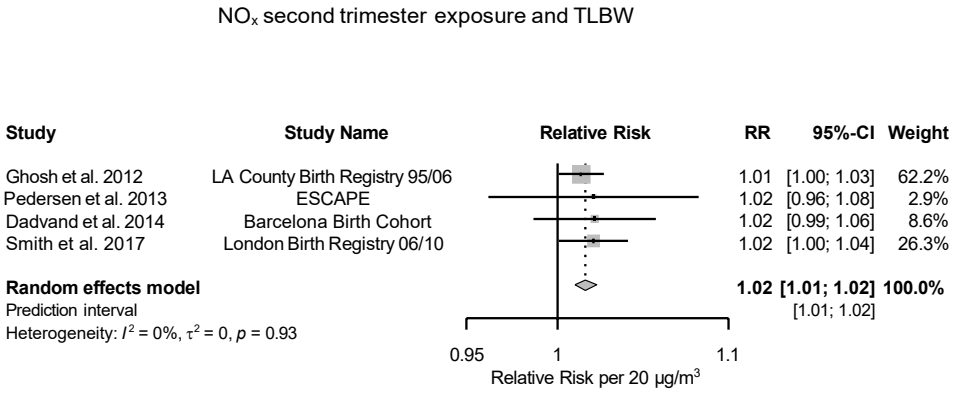
By smoking adjustment

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

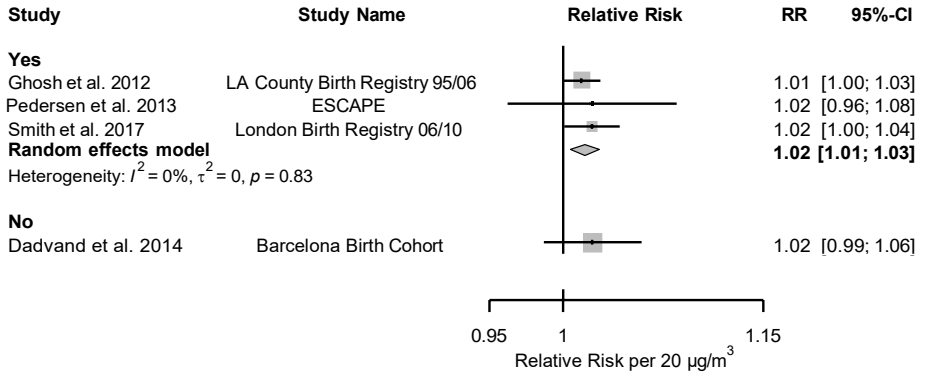
Dadvand et al. 2014 and Pedersen et al. 2013 adjusted for BMI, Ghosh et al. 2012 and Smith et al. 2017 did not adjust for BMI.

**$NO_x$ Second trimester exposure - primary meta-analysis - TLBW**

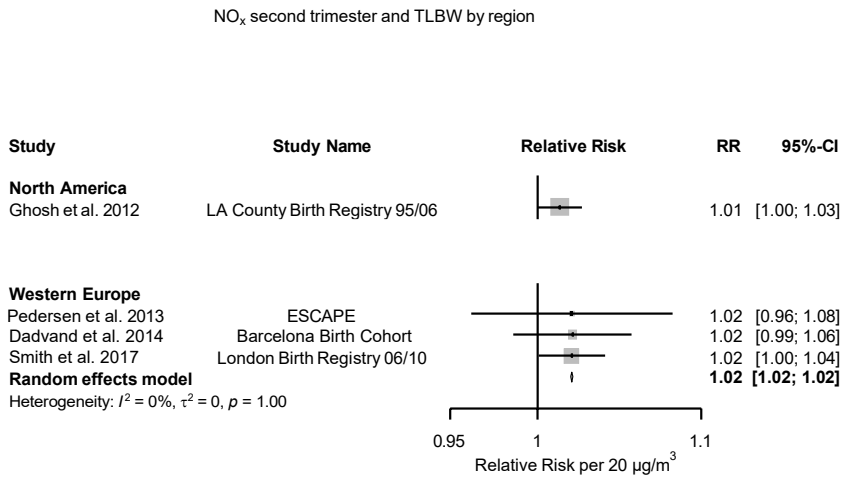



Subgroup analysis – second trimester exposure

By gestational age adjustment



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

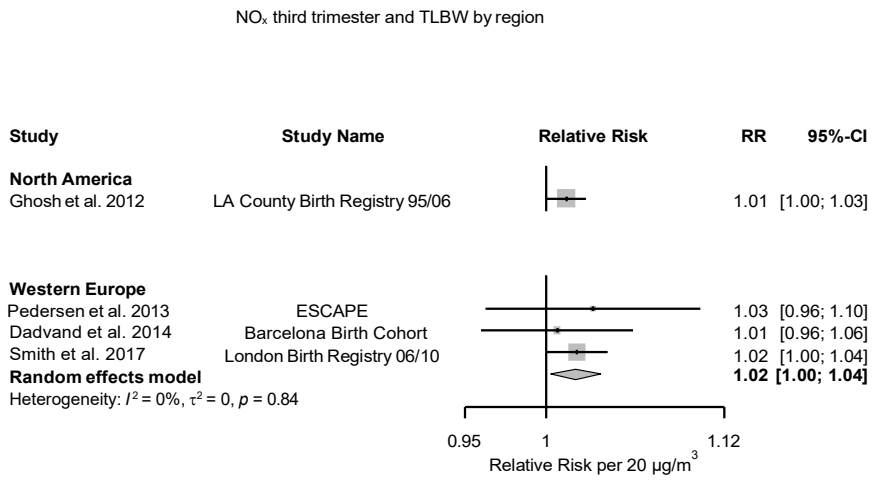
Dadvand et al. 2014 and Pedersen et al. 2013 adjusted for BMI, Ghosh et al. 2012 and Smith et al. 2017 did not adjust for BMI.

**$NO_x$ Third trimester exposure - primary meta-analysis - TLBW**


Subgroup analysis – third trimester exposure

By gestational age adjustment

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

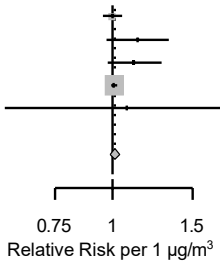
Dadvand et al. 2014 and Pedersen et al. 2013 adjusted for smoking, Ghosh et al. 2012 and Smith et al. 2017 did not adjust for smoking.

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 | RR | 95%-CI | Weight |
|---|---|---|---|---|---|
| Brauer et al. 2008 | BC 99/02 Birth Cohort | PM2.5 abs | 1.00 | [0.95; 1.05] | 10.2% |
| Pedersen et al. 2013 | ESCAPE | PM2.5 abs | 1.14 | [0.97; 1.33] | 1.0% |
| Dadvand et al. 2014 | Barcelona Birth Cohort | PM2.5 abs | 1.12 | [0.98; 1.28] | 1.3% |
| Laurent et al. 2016 | California Birth Registry 01/08 | EC | 1.01 | [0.99; 1.03] | 87.4% |
| Kingsley et al. 2017 | Rhode Island Birth Outcomes | BC | 1.08 | [0.58; 1.98] | 0.1% |
| **Random effects model** | | | **1.01** | **[0.99; 1.04]** | **100.0%** |
| Prediction interval | | | | [0.98; 1.04] | |

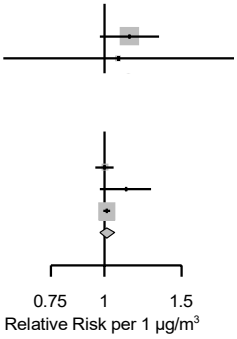
Heterogeneity: $I^2$ = 12%, $\tau^2$ = 0, $p$ = 0.34



Subgroup meta-analysis

By gestational age adjustment

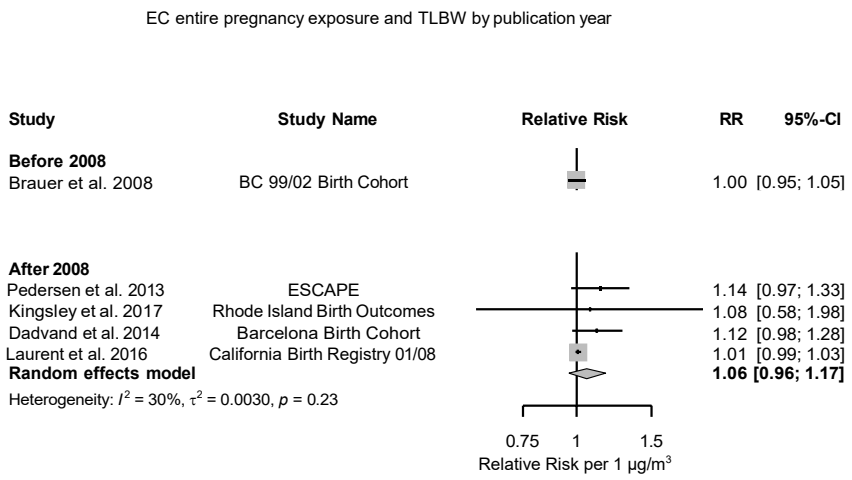
EC entire pregnancy exposure and TLBW by gestational age



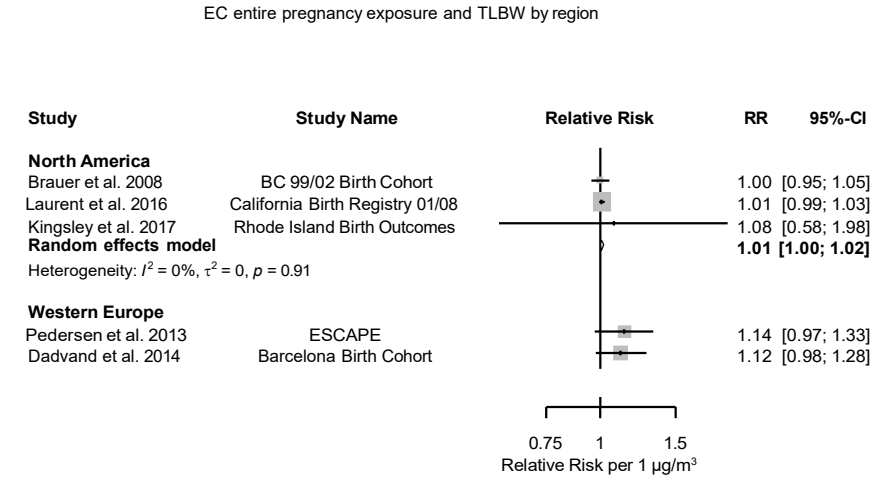
| Study | Study Name | RR | 95%-CI |
|---|---|---|---|
| **Yes** | | | |
| Pedersen et al. 2013 | ESCAPE | 1.14 | [0.97; 1.33] |
| Kingsley et al. 2017 | Rhode Island Birth Outcomes | 1.08 | [0.58; 1.98] |
| **No** | | | |
| Brauer et al. 2008 | BC 99/02 Birth Cohort | 1.00 | [0.95; 1.05] |
| Dadvand et al. 2014 | Barcelona Birth Cohort | 1.12 | [0.98; 1.28] |
| Laurent et al. 2016 | California Birth Registry 01/08 | 1.01 | [0.99; 1.03] |
| **Random effects model** | | **1.01** | **[0.97; 1.05]** |

Heterogeneity: $I^2$ = 14%, $\tau^2$ = < 0.0001, $p$ = 0.31

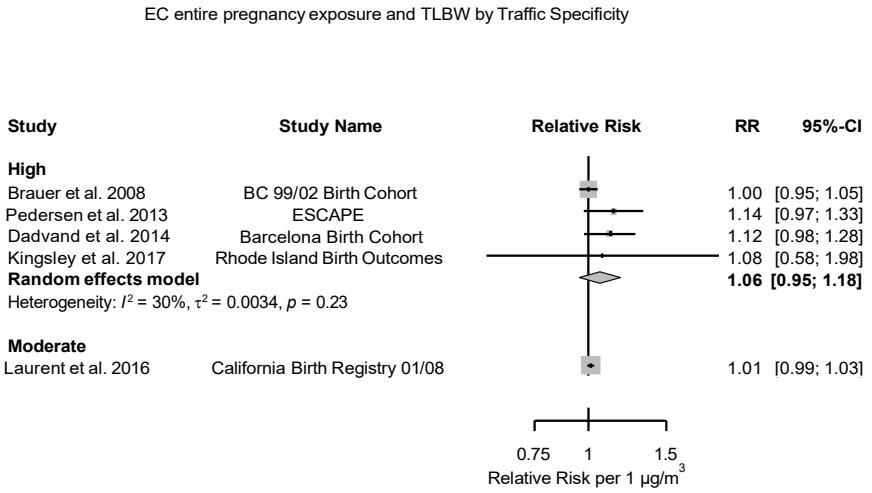
By publication year




By region

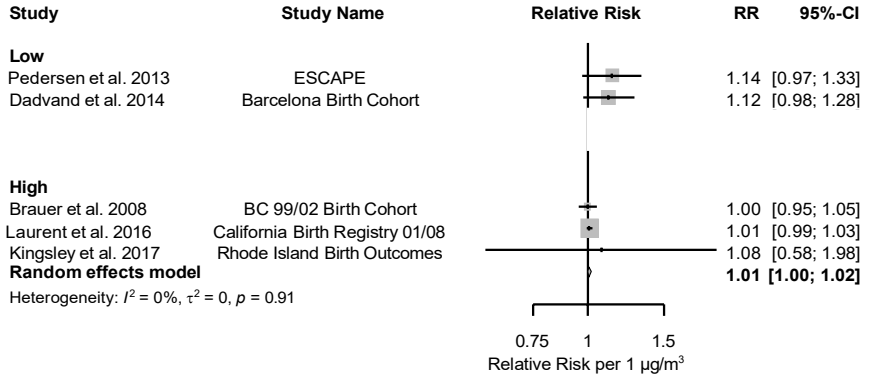


By traffic specificity

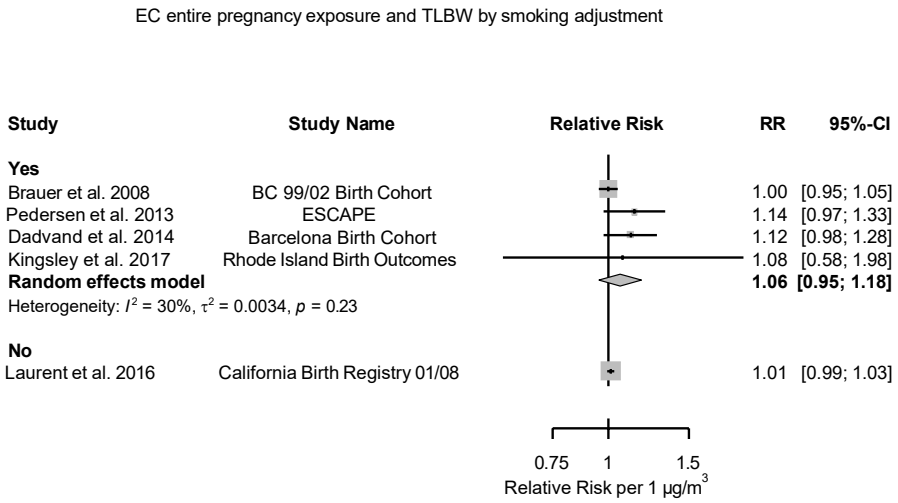



By risk of bias

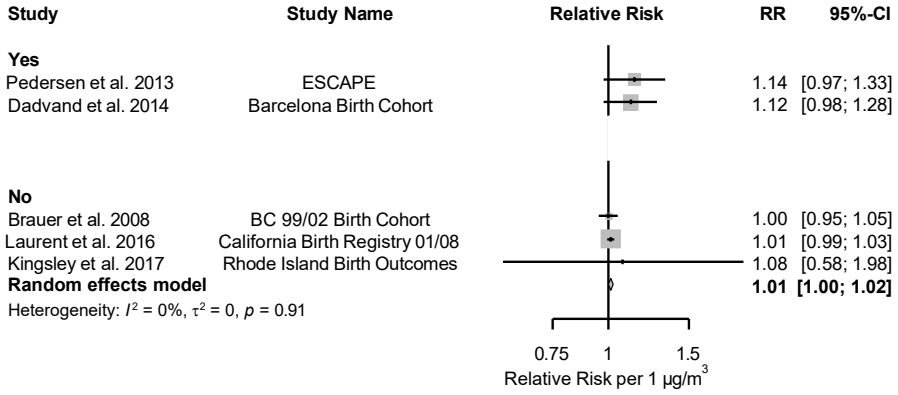
Plots not shown for risk of bias domains if all studies were rated low or moderate



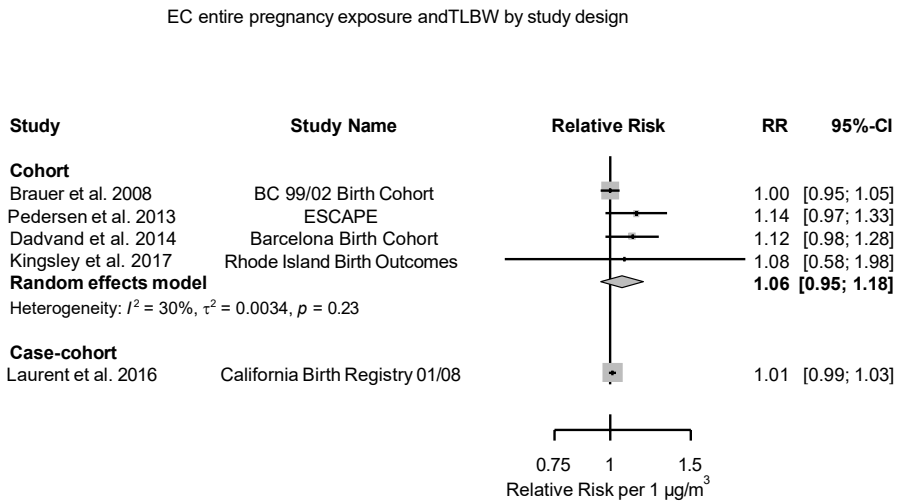
By smoking adjustment



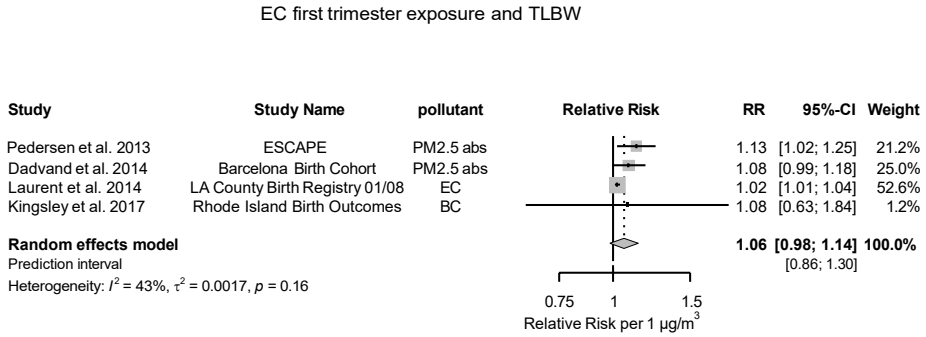

By BMI adjustment



By study design

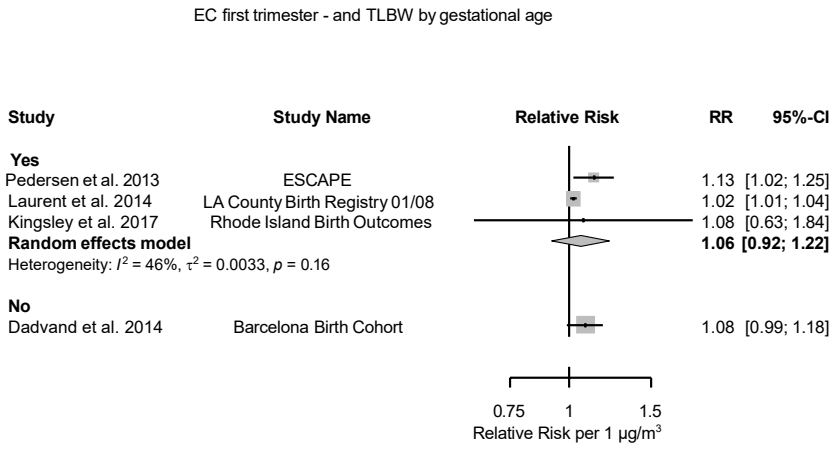


**EC First trimester exposure - primary meta-analysis - TLBW**




Subgroup meta-analysis

By gestational age adjustment

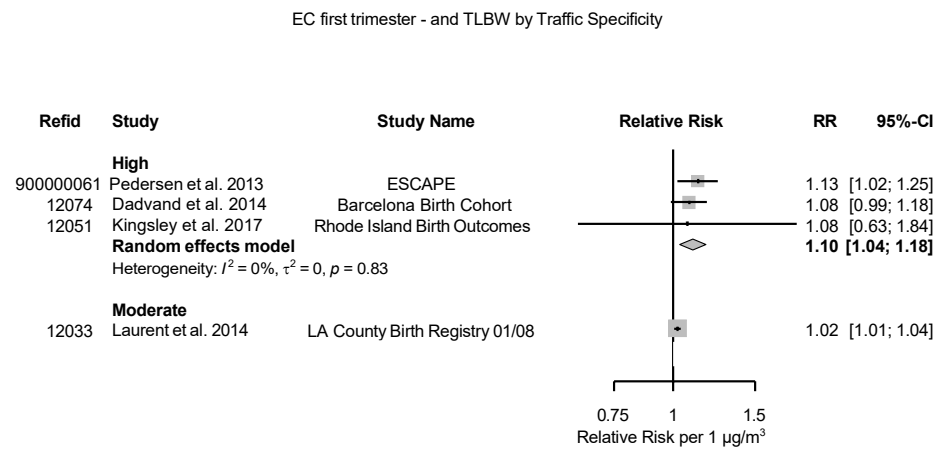



By region

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

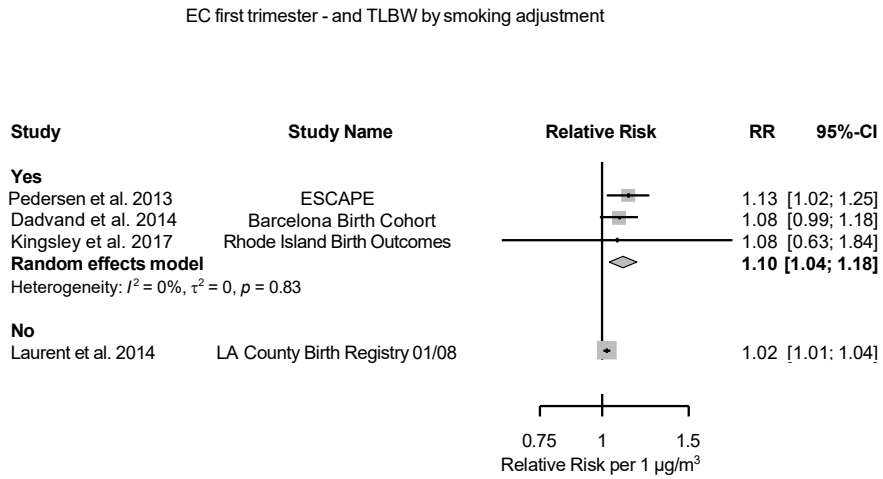
By traffic specificity




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.

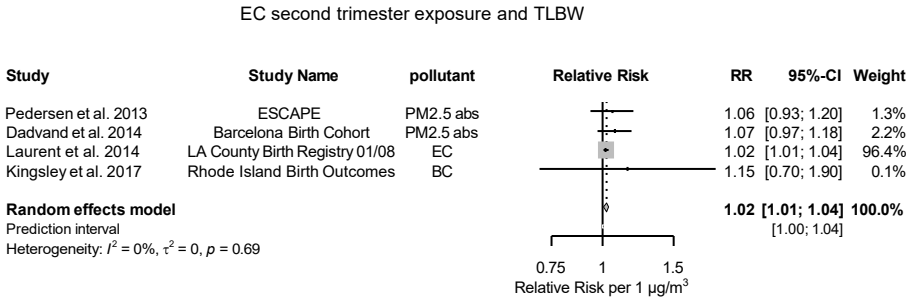
By smoking adjustment




By BMI adjustment

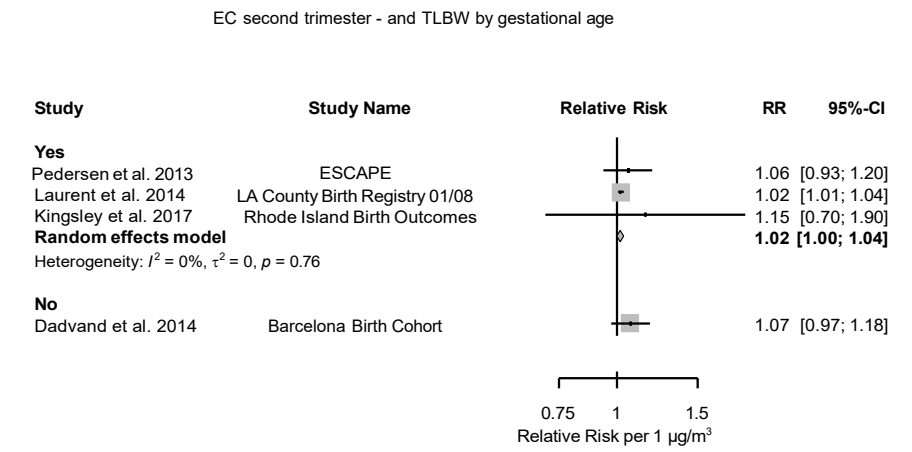
Dadvand et al. 2014 and Pedersen et al. 2013 adjusted for BMI, Laurent et al. 2014 and Kingsley et al. 2017 did not adjust for BMI.

**EC Second trimester exposure - primary meta-analysis - TLBW**




Subgroup meta-analysis

By gestational age adjustment

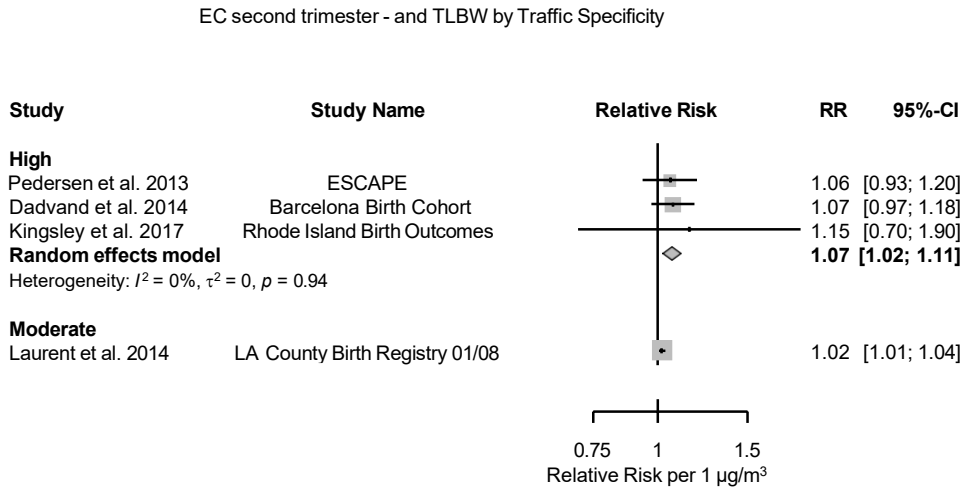



By region

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

By study design - all cohort studies

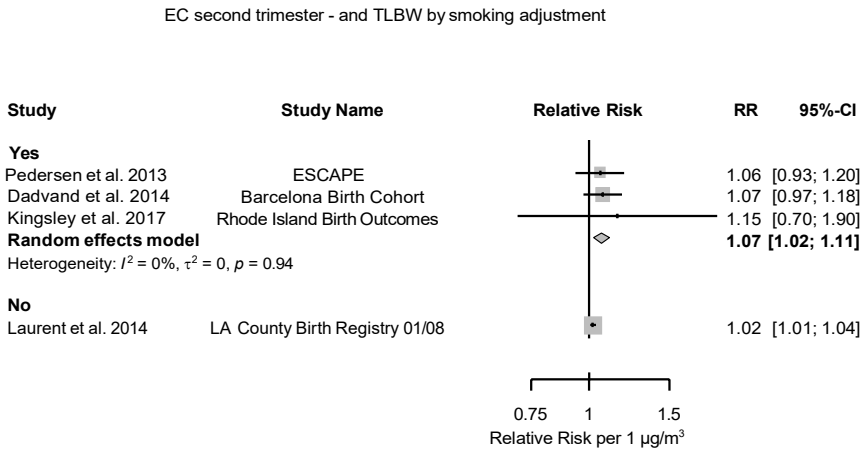
By traffic specificity




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.

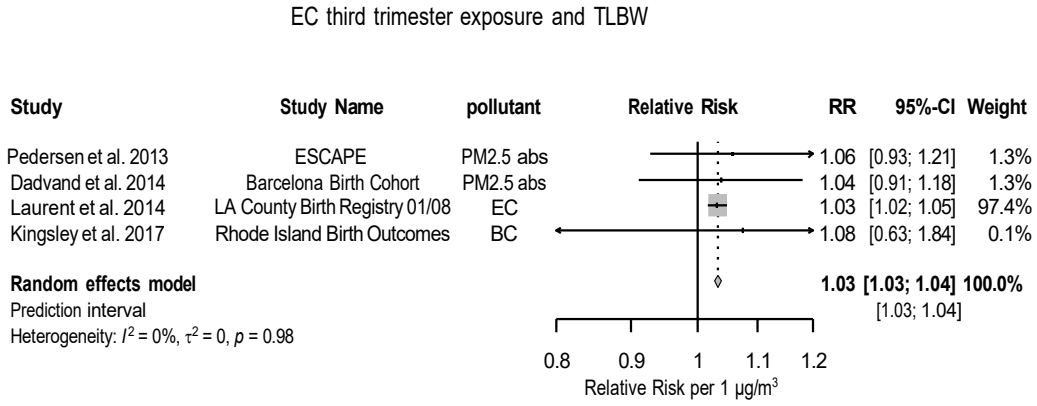
By smoking adjustment




BMI adjustment

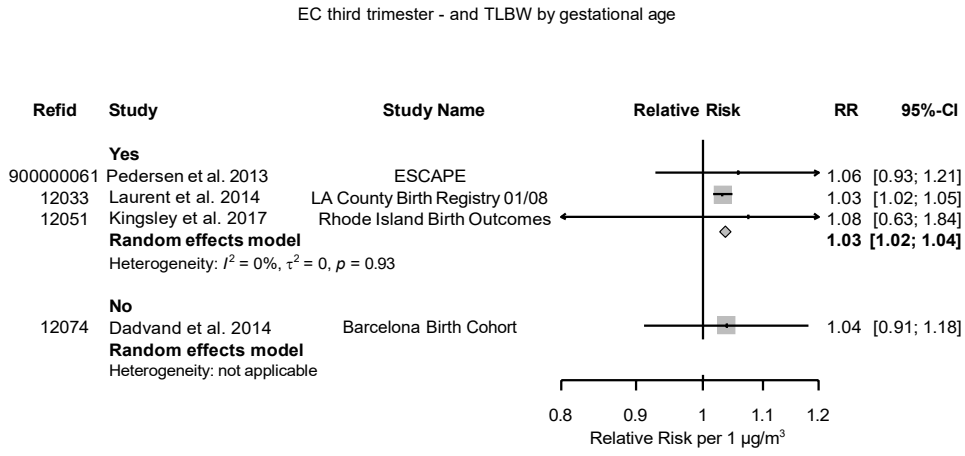
Dadvand et al. 2014 and Pedersen et al. 2013 adjusted for BMI, Laurent et al. 2014 and Kingsley et al. did not adjust for BMI.

**EC Third trimester exposure - primary meta-analysis - TLBW**




Subgroup meta-analysis

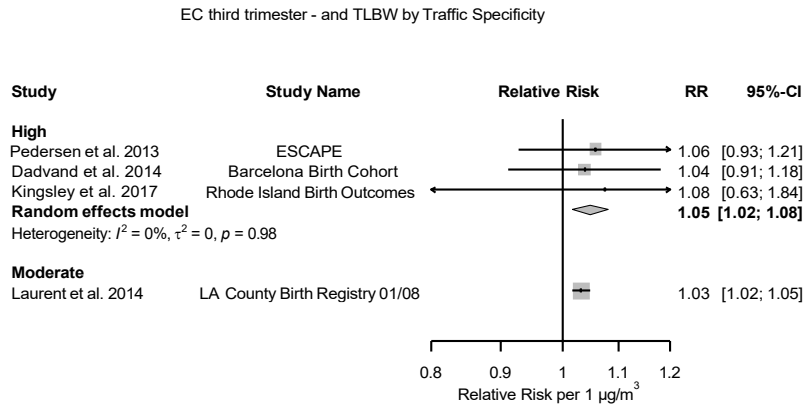
By gestational age adjustment



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

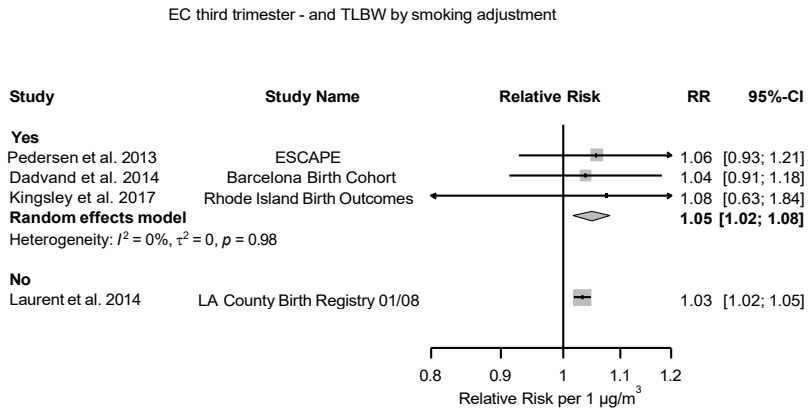



By study design - all cohort studies

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.

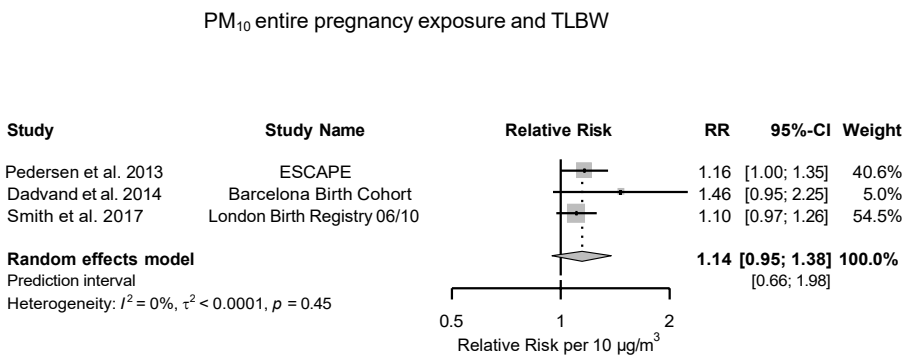
By smoking adjustment




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.

**$PM_{10}$ Entire pregnancy exposure – primary meta-analysis - TLBW**




Subgroup analysis

All Western European cohort studies.

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

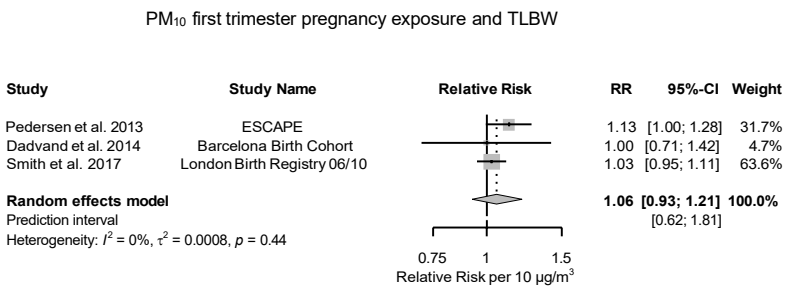
By traffic specificity: all rated moderate.

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.

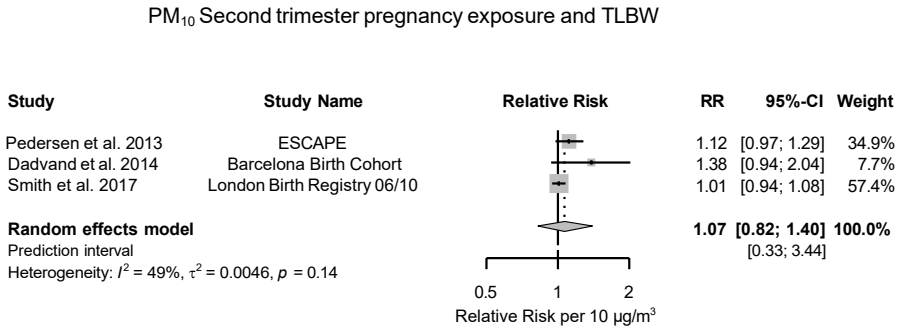
By smoking adjustment: Smith et al. 2017 did not adjust for smoking.

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

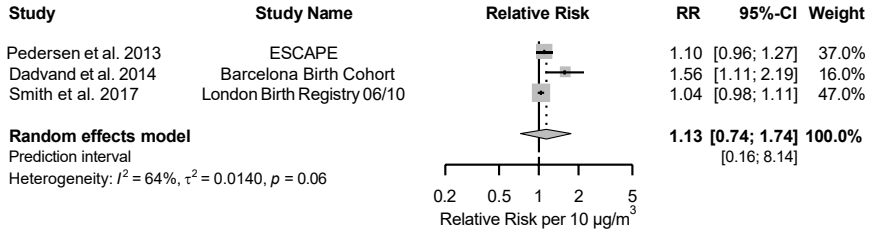
## $PM_{10}$ First trimester exposure - primary meta-analysis - TLBW




## $PM_{10}$ Second trimester exposure - primary meta-analysis - TLBW

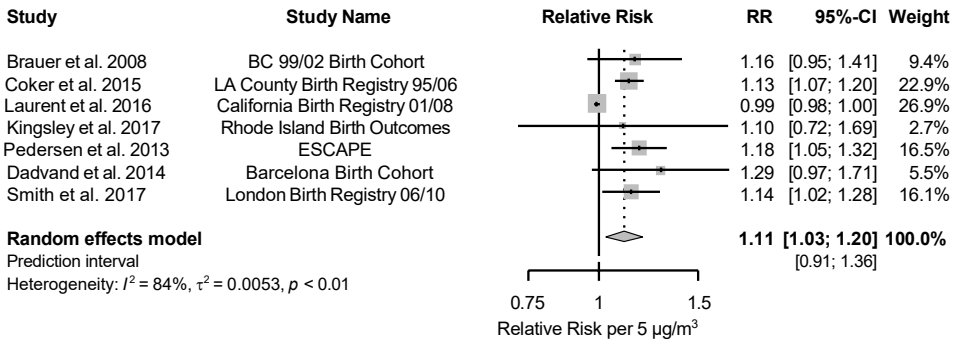



## $PM_{10}$ Third trimester exposure - primary meta-analysis - TLBW



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

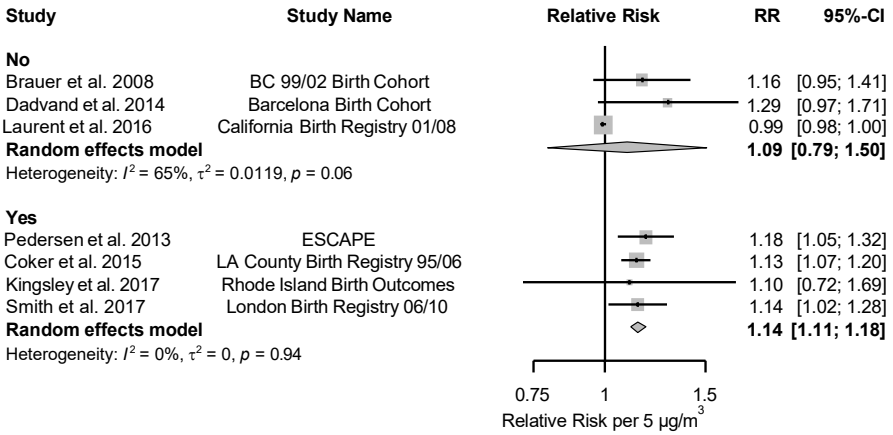
$PM_{2.5}$ entire pregnancy exposure and TLBW



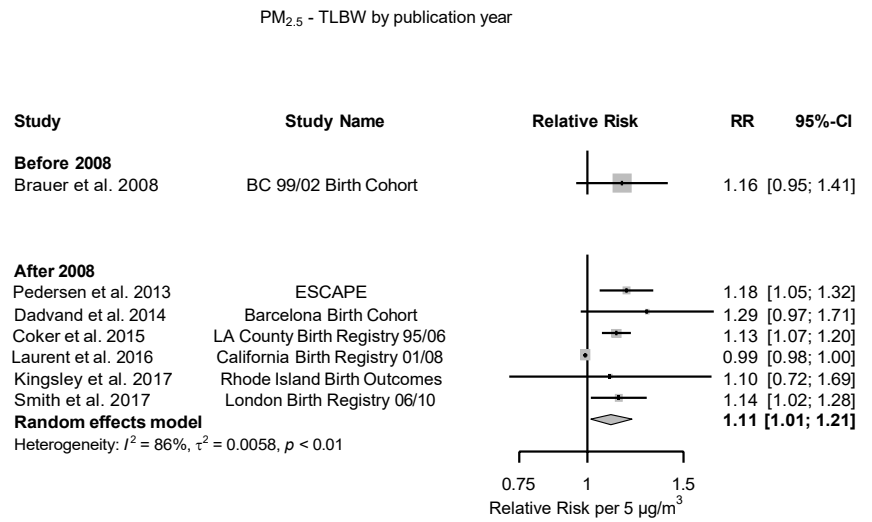

Subgroup meta-analysis

By gestational age adjustment

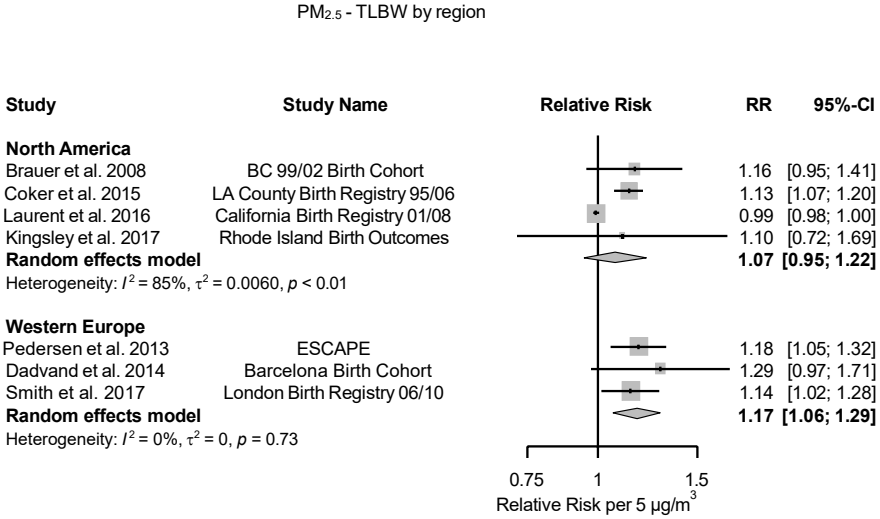
$PM_{2.5}$ - TLBW by gestational age



By publication year



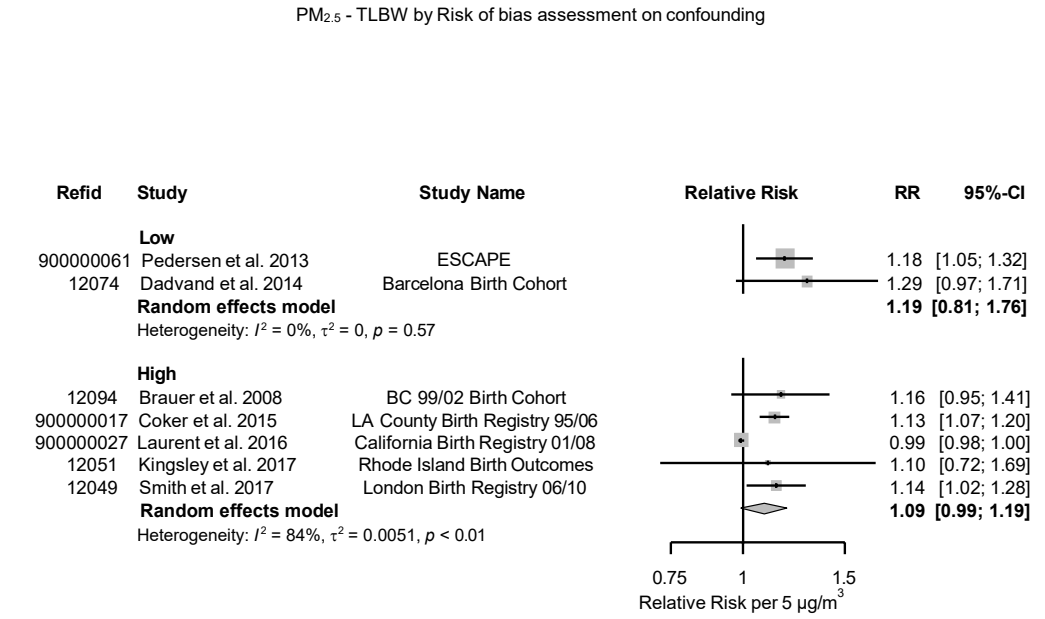

By region

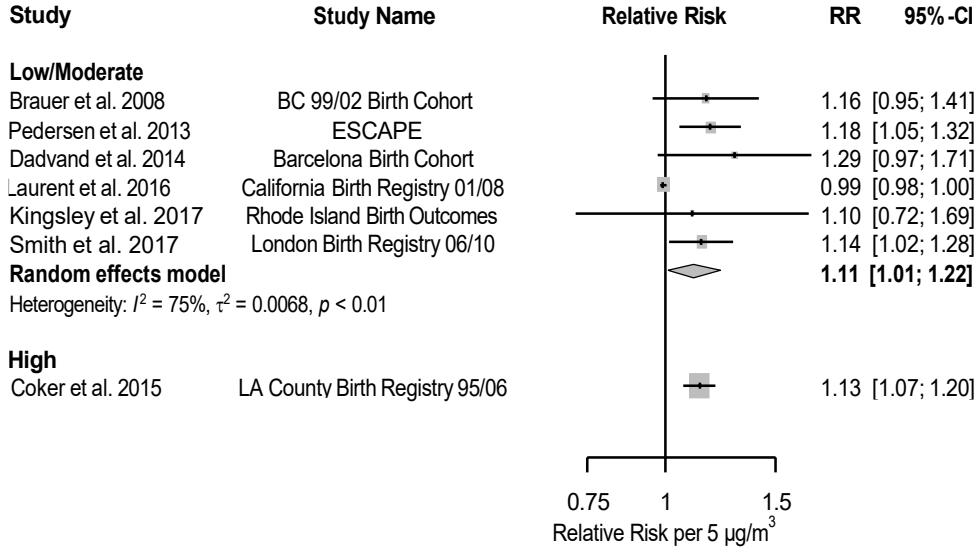



By traffic specificity – all rated moderate

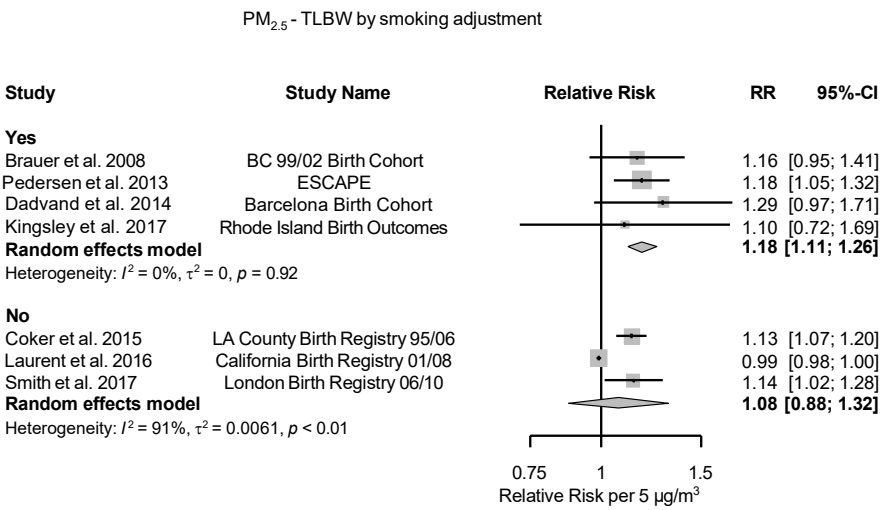
By risk of bias

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

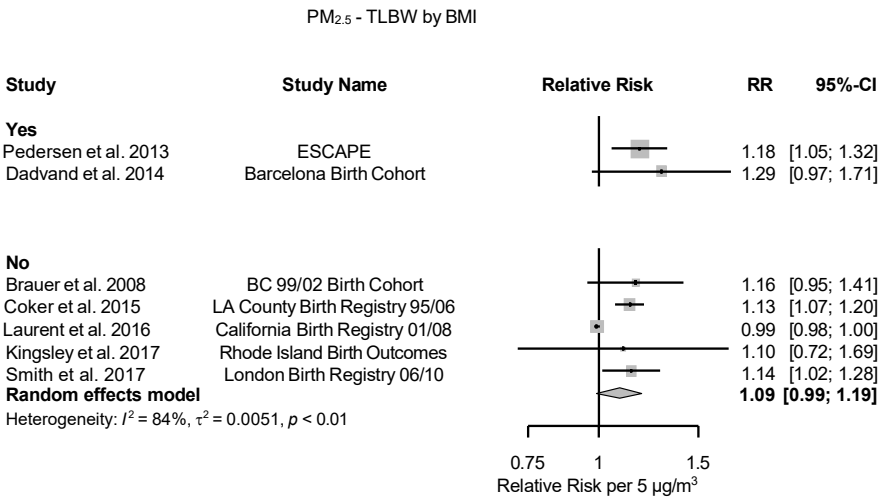


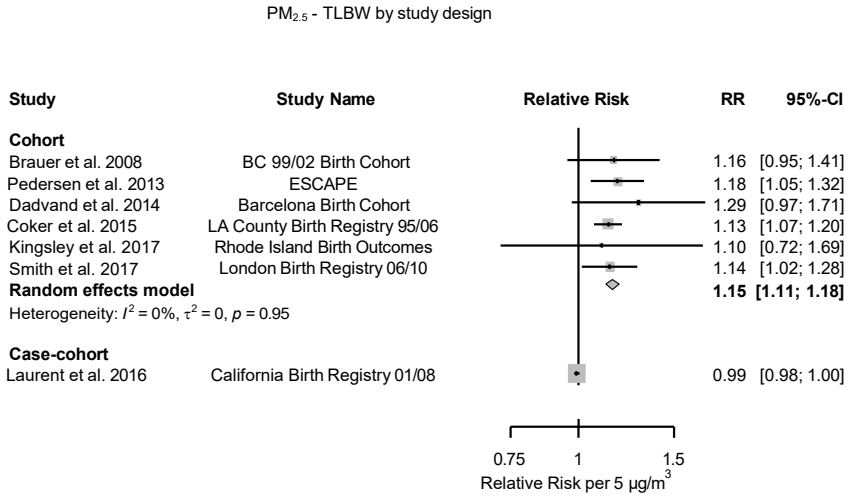
By smoking adjustment



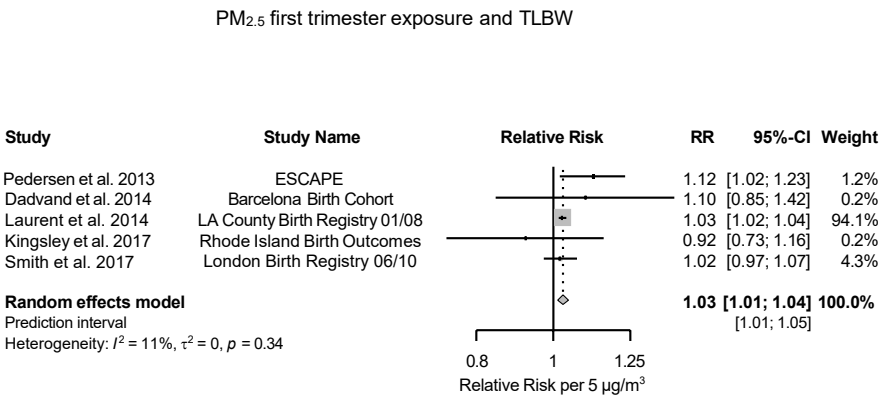

By BMI adjustment



By study design

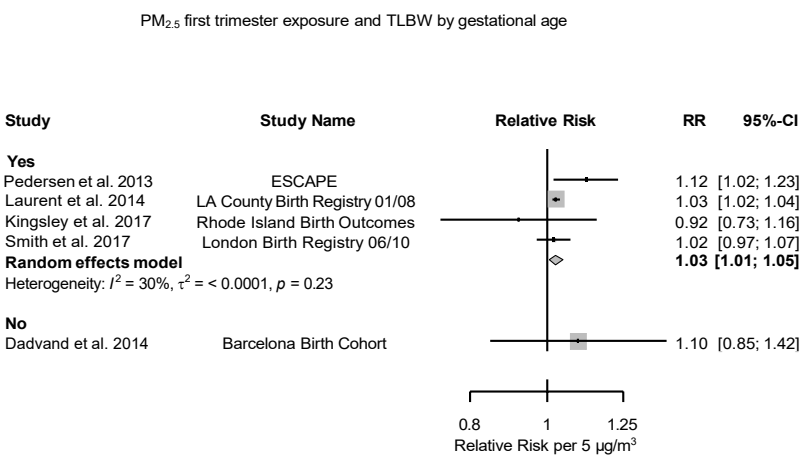


## $PM_{2.5}$ First trimester exposure – primary meta-analysis - TLBW

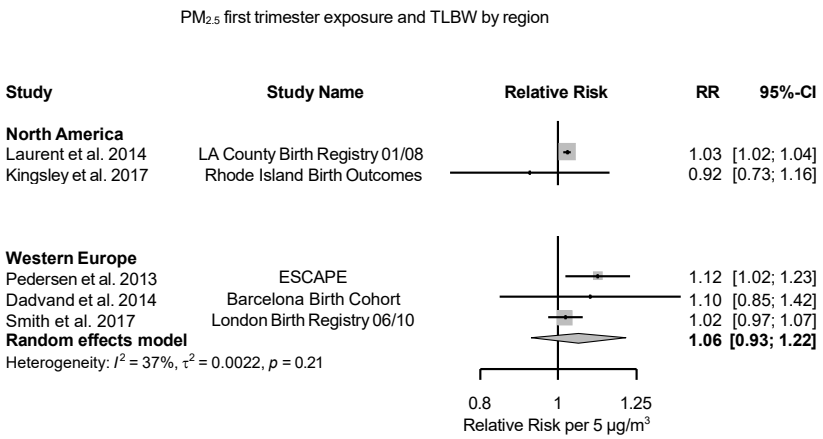



Subgroup meta-analysis

By gestational age adjustment



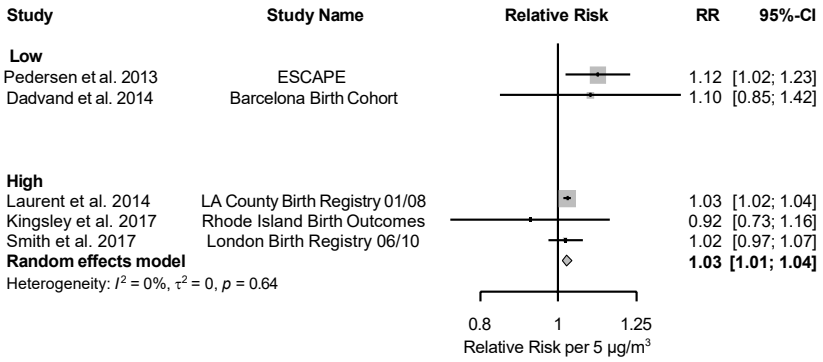
By region



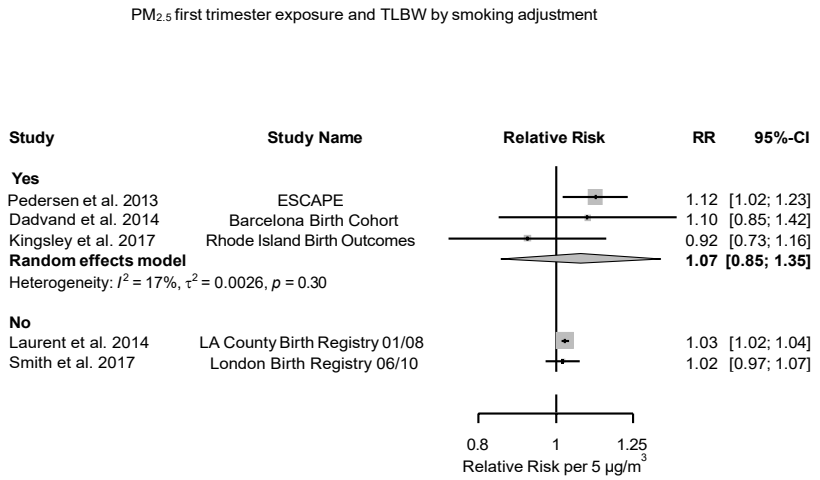

By traffic specificity - all rated moderate

By risk of bias

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



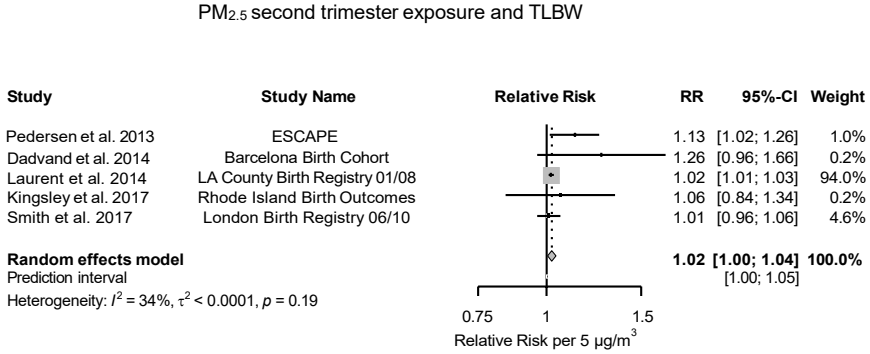
By smoking adjustment




By BMI adjustment

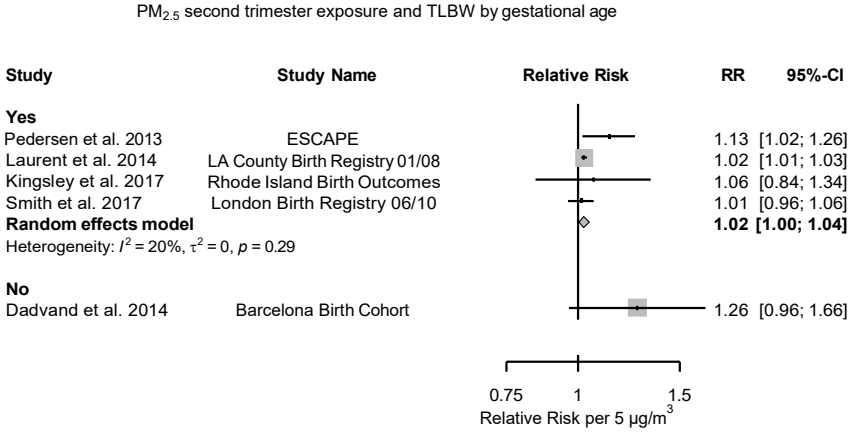

By study design - all cohort studies

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

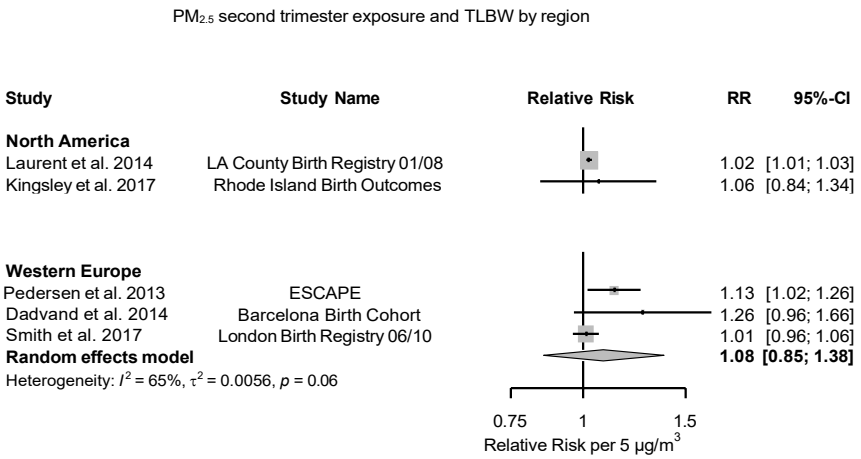



Subgroup meta-analysis

By gestational age adjustment



By region

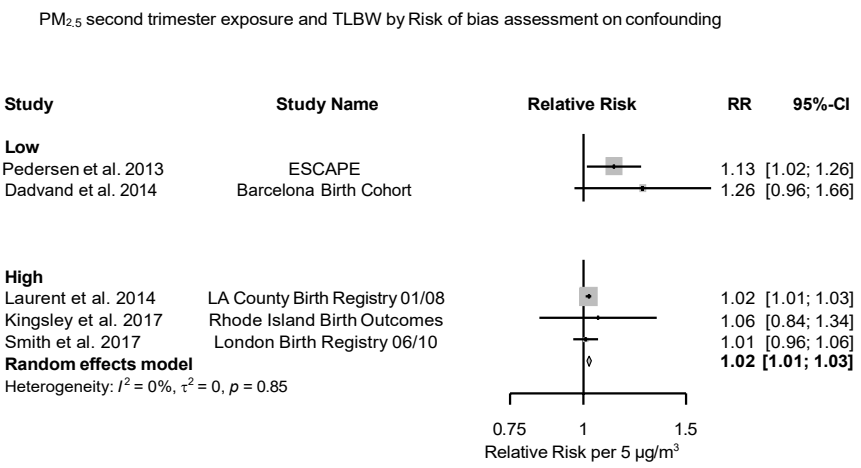



By traffic specificity - all rated moderate

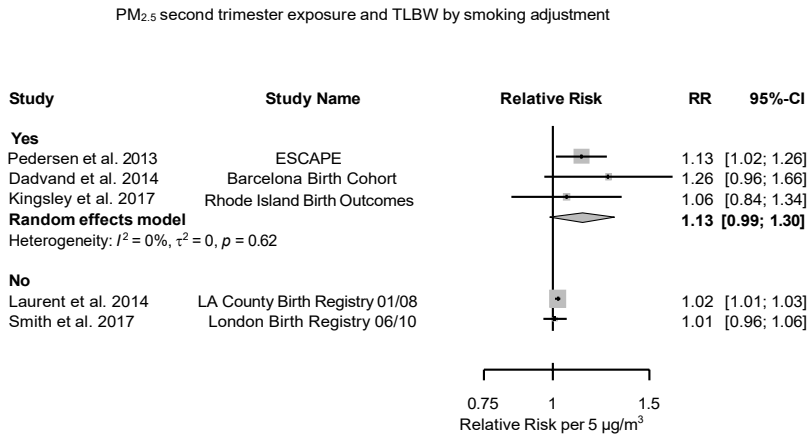
By study design - all cohort studies

By risk of bias

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



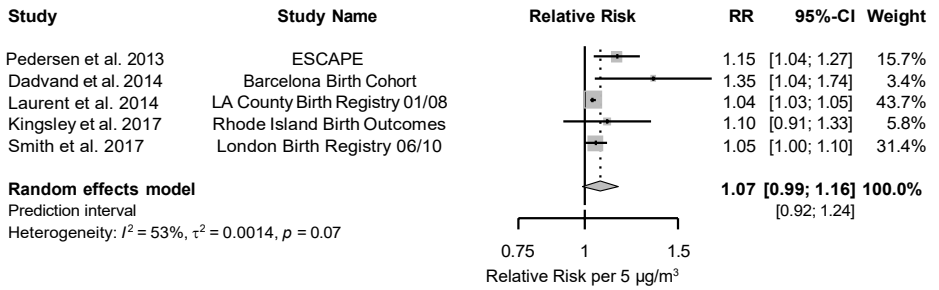
## By smoking adjustment




## By BMI adjustment

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

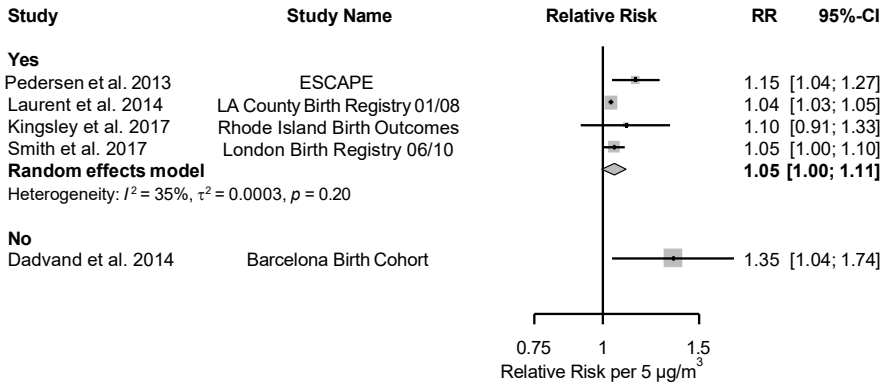
$PM_{2.5}$ third trimester exposure and TLBW



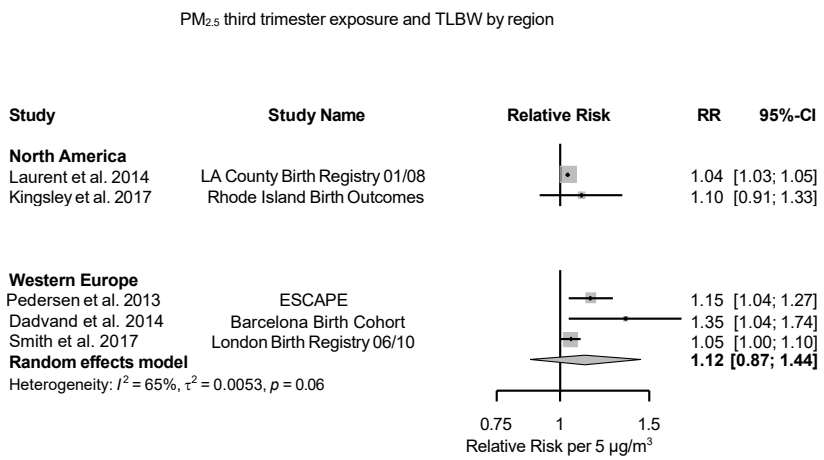

Subgroup meta-analysis

By gestational age adjustment

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



By region

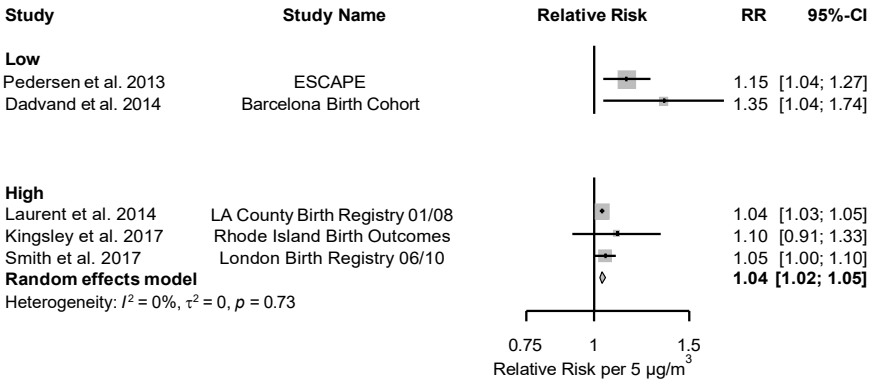



By traffic specificity - all rated moderate

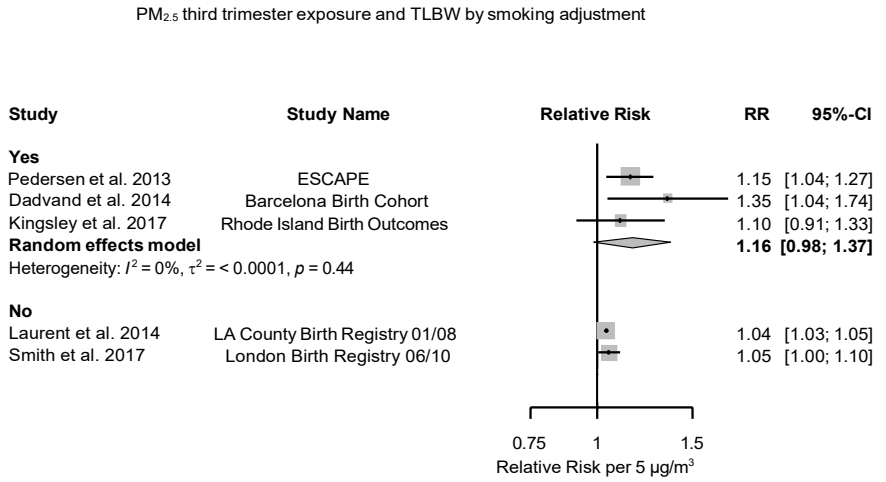
By study design- all cohort studies

By risk of bias

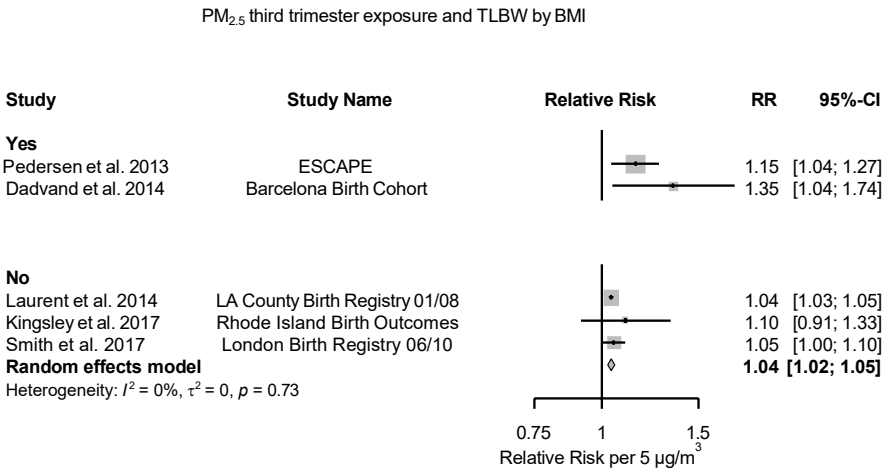
Plots not shown for risk of bias domains if all studies were rated low or moderate



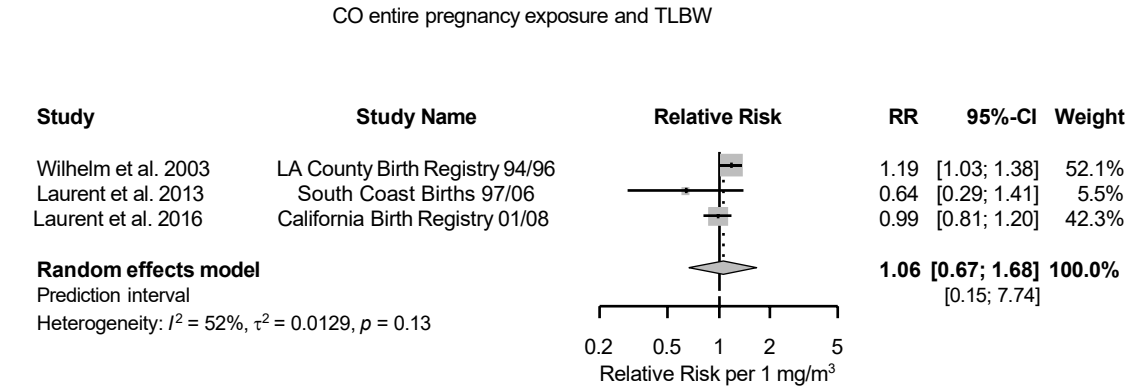
By smoking adjustment




By BMI adjustment



**CO Entire pregnancy exposure – primary meta-analysis - TLBW**




Subgroup analysis

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

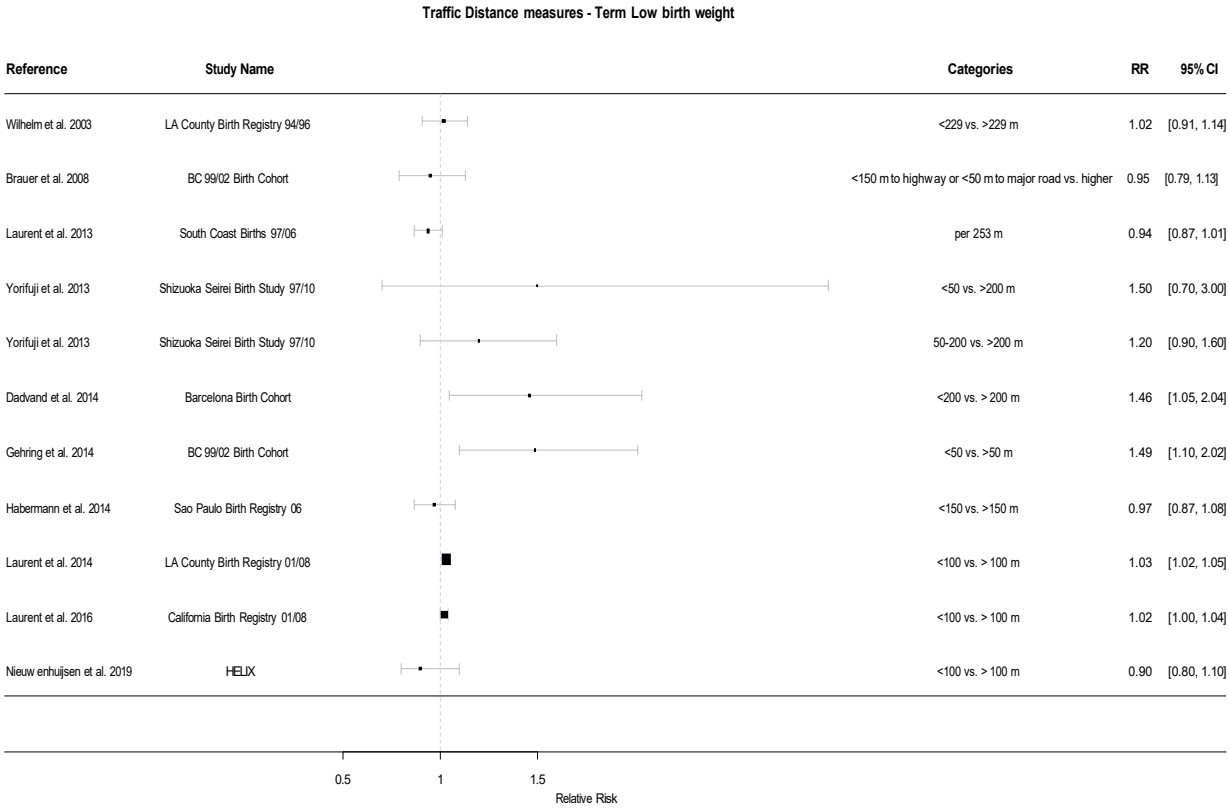
All three studies did not adjust for smoking and BMI.

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

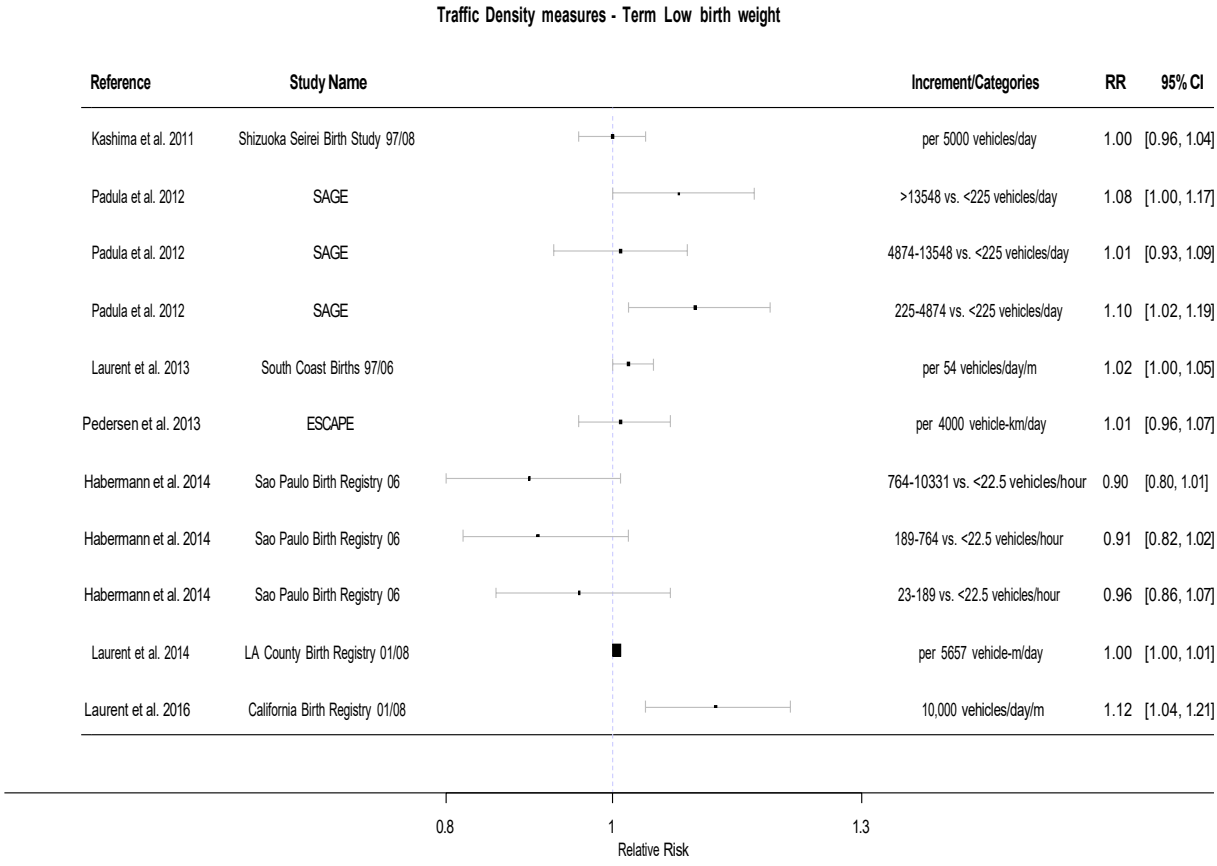
Risk of bias: all three studies rated low for domains, except for exposure where all rated moderate and for confounding where all rated high risk of bias.

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

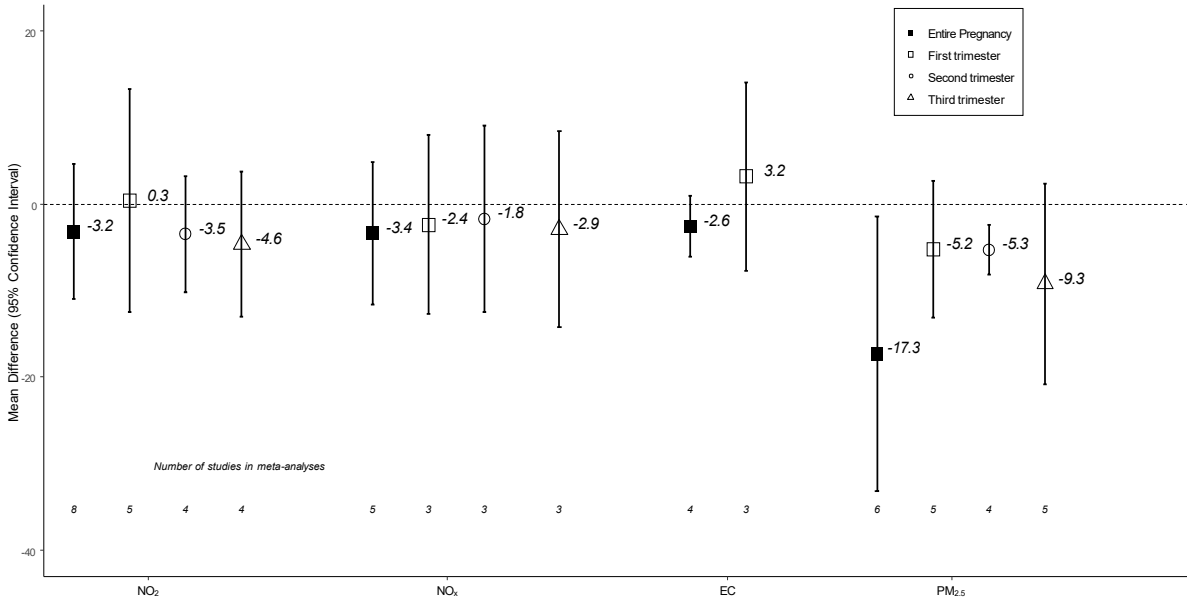


Density measures



## 8.2 Term birth weight (TBW)

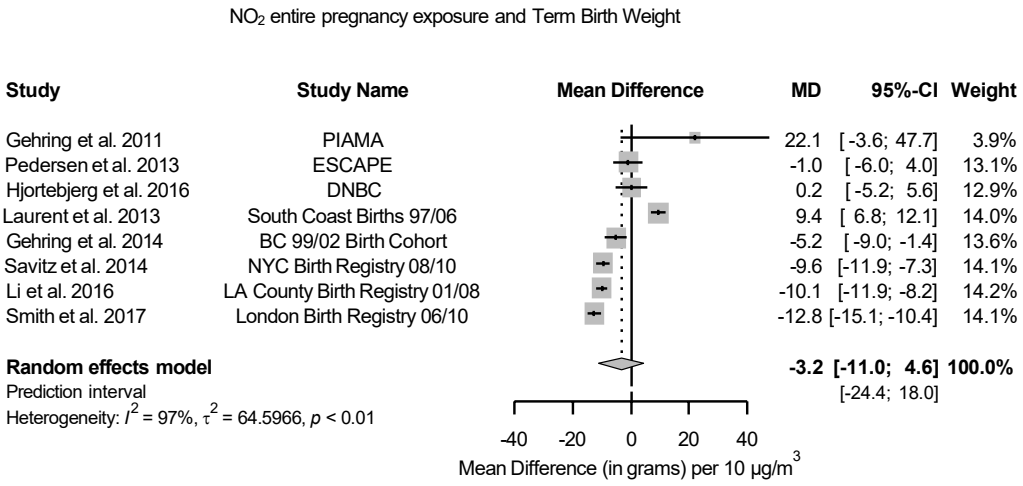
Summary of meta-analysis




Footnote: The following increments were used: 10 µg/m$^3$ for $NO_2$, 20 µg/m$^3$ for $NO_x$, 1 µg/m$^3$ for EC, 5 µg/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.

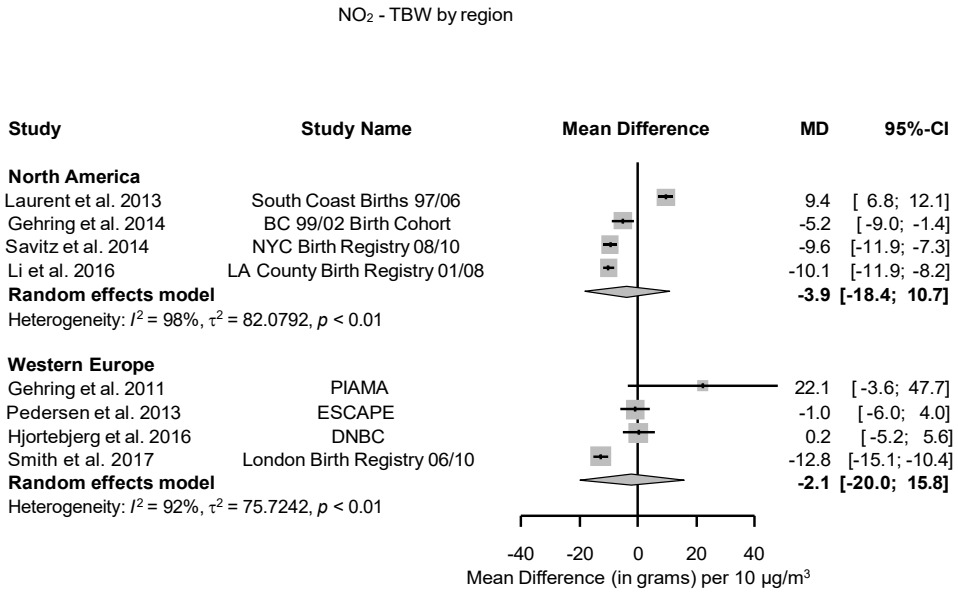
By gestational age - all term birth weight studies adjusted for gestational age

**$NO_2$ Entire pregnancy exposure - primary meta-analysis - TBW**




Subgroup analysis – entire pregnancy exposure

By region



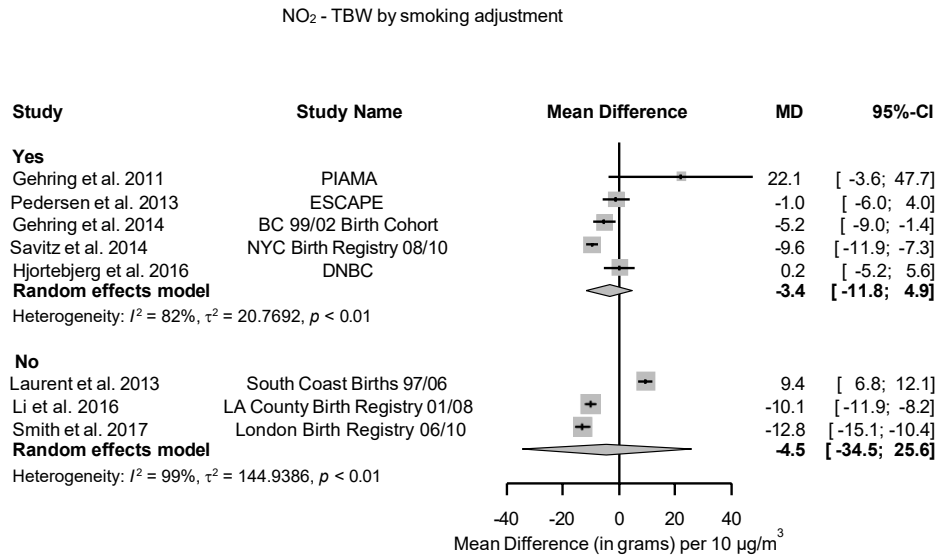

By traffic specificity – all high

By study design – all cohort studies

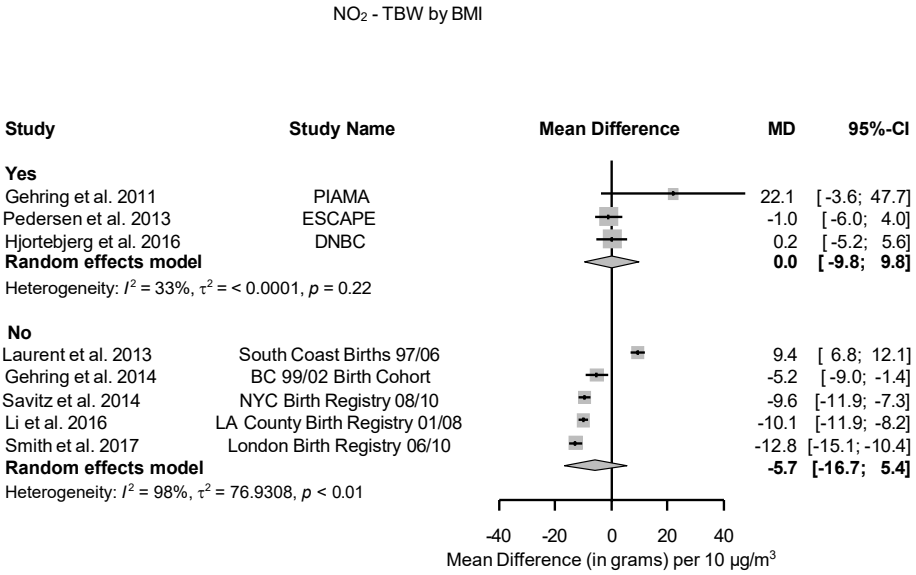
By risk of bias

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

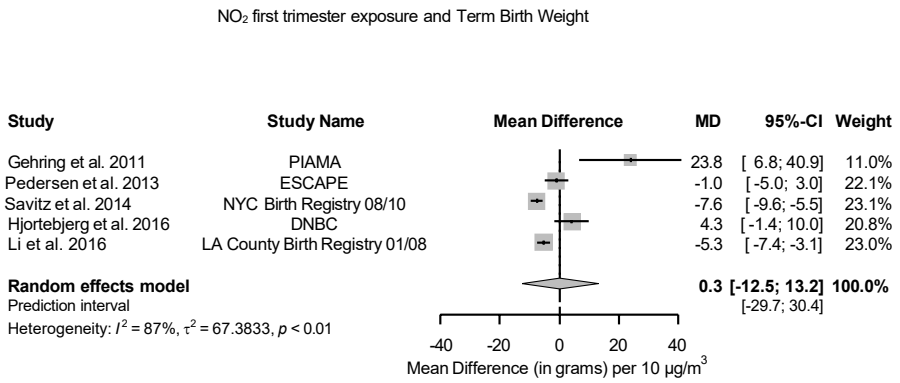
By smoking adjustment




By BMI adjustment

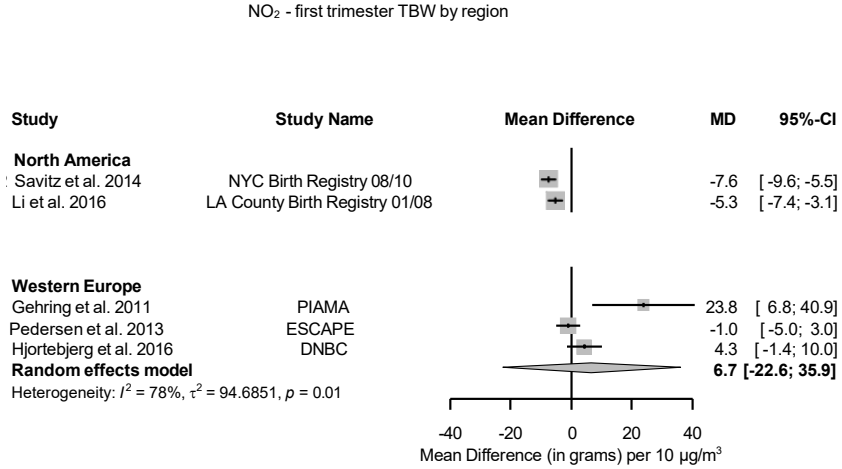


## $NO_2$ First trimester exposure - primary meta-analysis - TBW




Subgroup analysis

By region

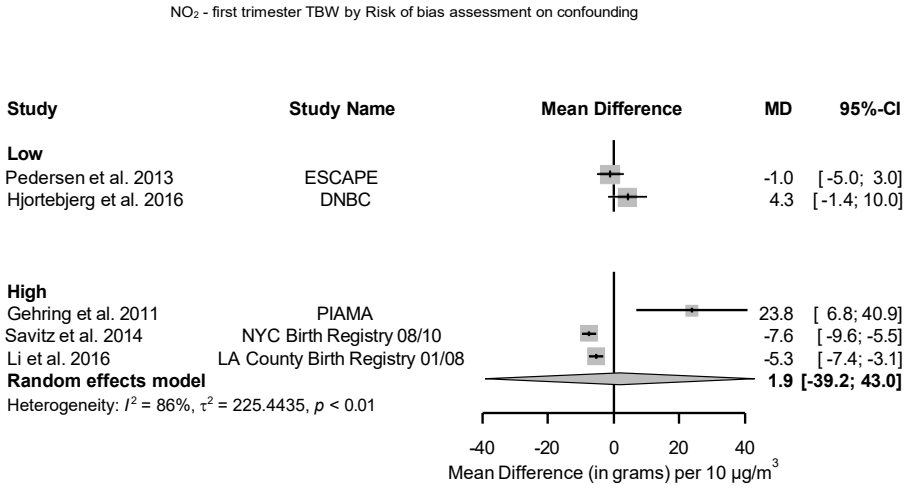



By traffic specificity – all high

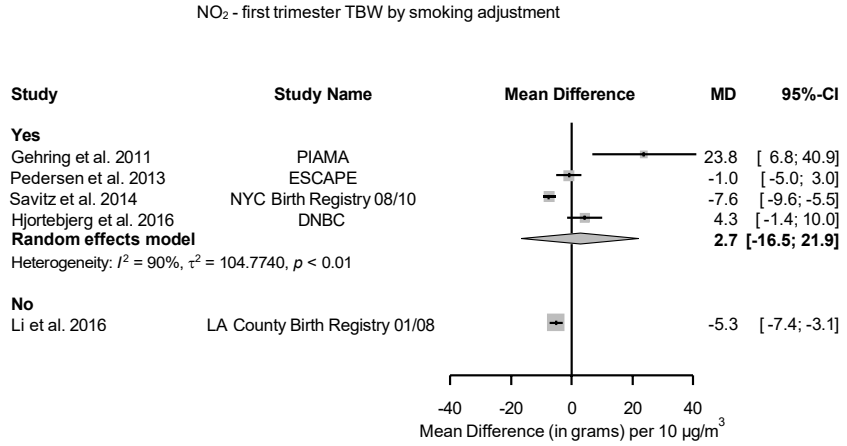
By study design - all cohort studies

By risk of bias

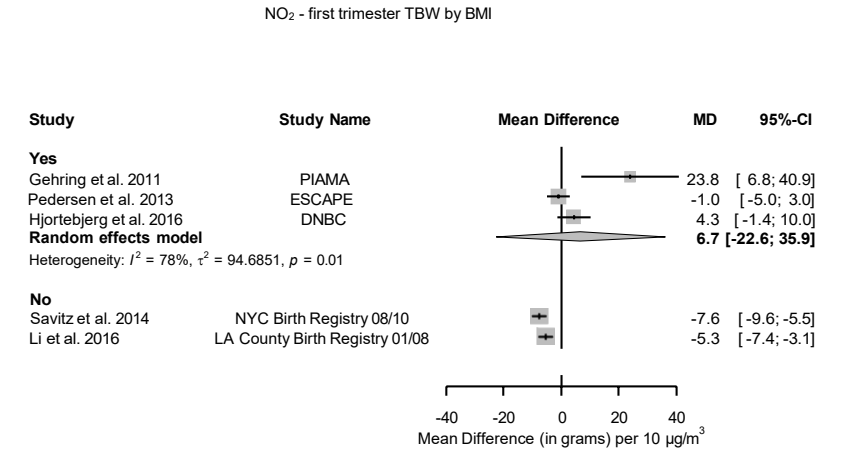
Plots not shown for risk of bias domains if all studies were rated low or moderate



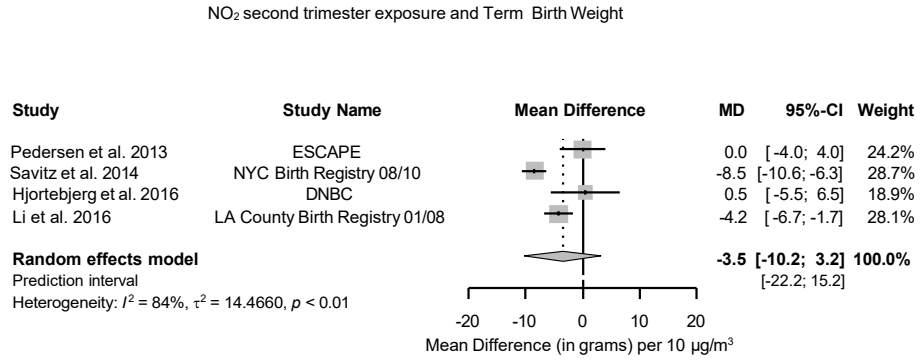
By smoking adjustment




By BMI adjustment



**$NO_2$ Second trimester exposure - primary meta-analysis - TBW**




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

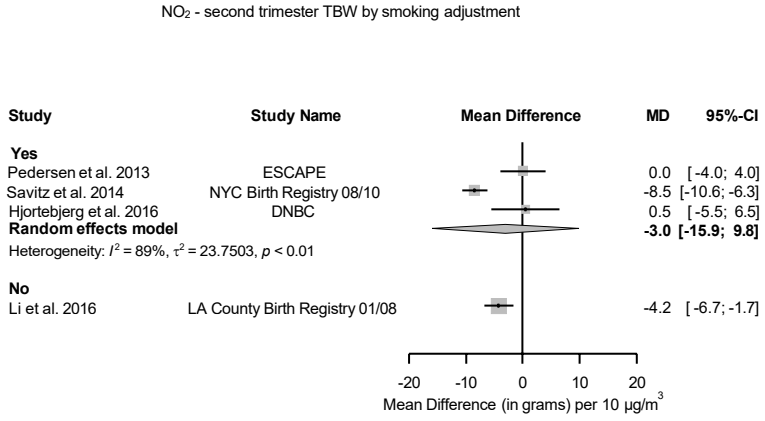
By risk of bias

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.

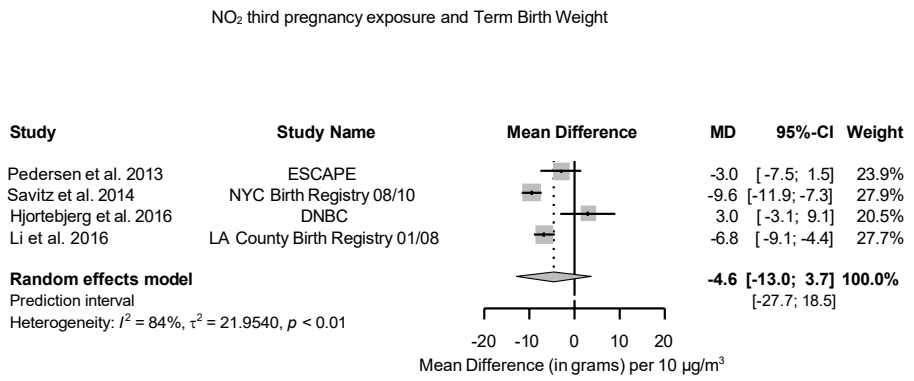
By BMI adjustment

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.

By smoking adjustment



**$NO_2$ Third trimester exposure - primary meta-analysis - TBW**




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

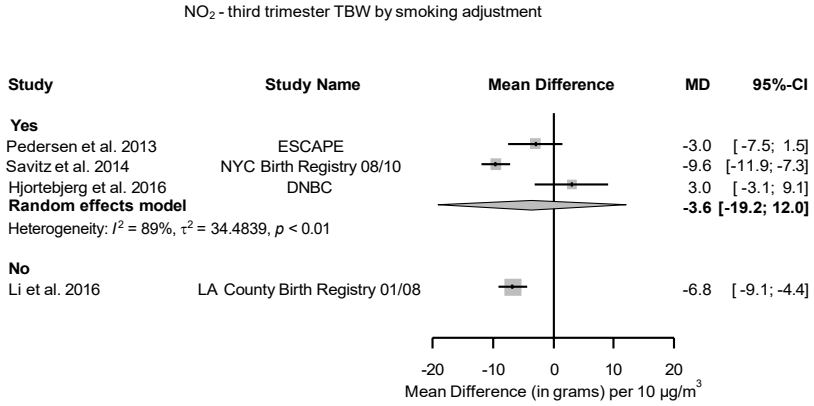
By risk of bias

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.

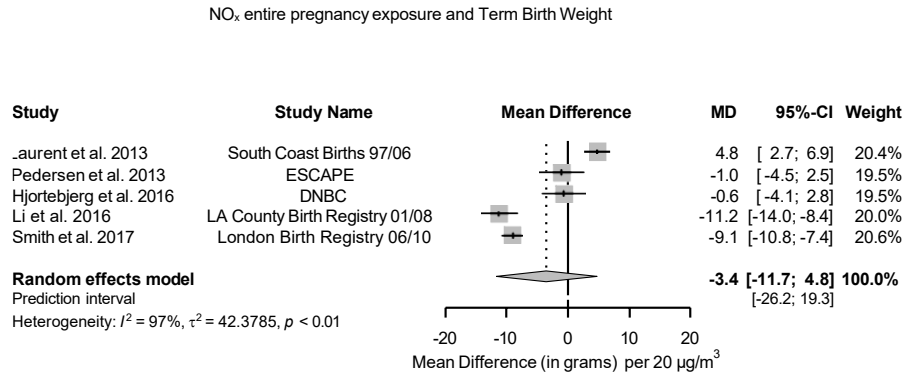
By BMI adjustment

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.

By smoking adjustment

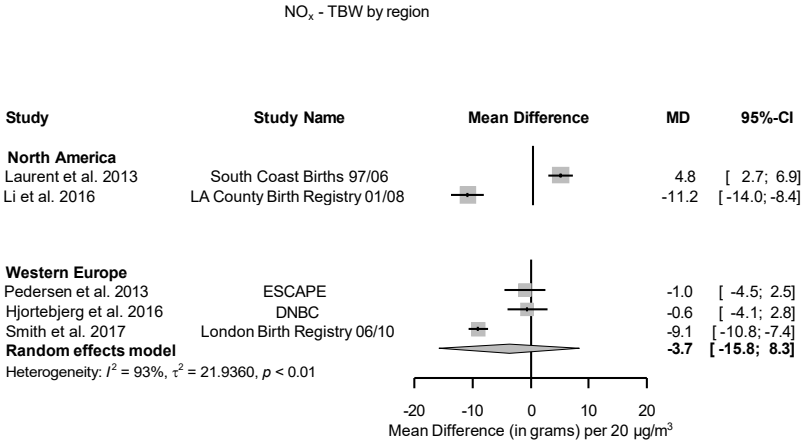


## $NO_x$ Entire pregnancy exposure – primary meta-analysis - TBW




Subgroup analysis – entire trimester exposure

By region

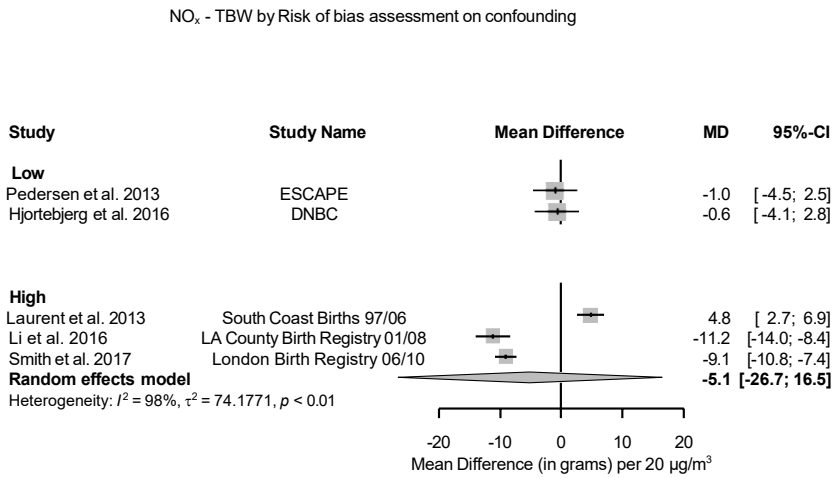



By traffic specificity - all high

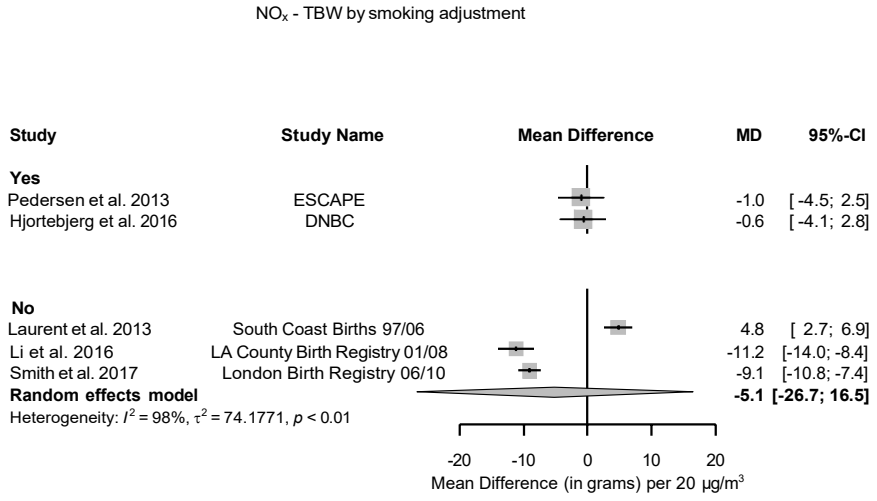
By study design - all cohort studies

By risk of bias

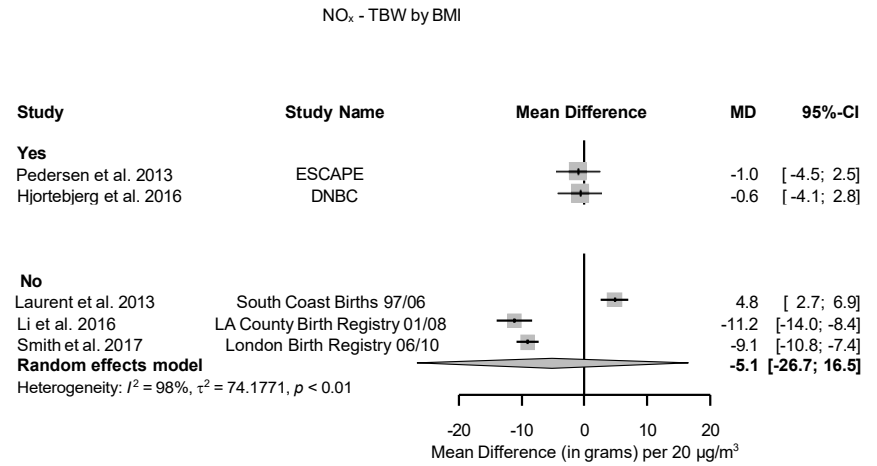
Plots not shown for risk of bias domains if all studies were rated low or moderate



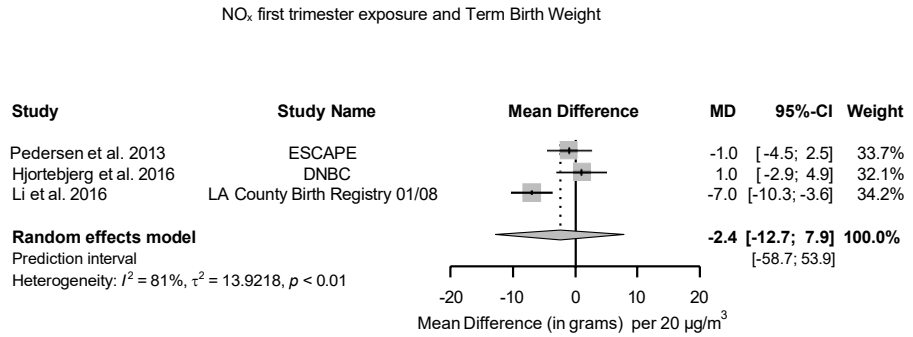
By smoking adjustment




By BMI adjustment

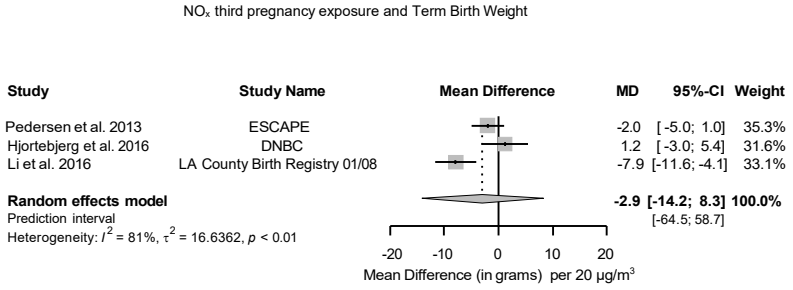


**$NO_x$ First trimester exposure – primary meta-analysis - TBW**




**$NO_x$ Second trimester exposure – primary meta-analysis - TBW**


**$NO_x$ Third trimester exposure – primary meta-analysis - TBW**

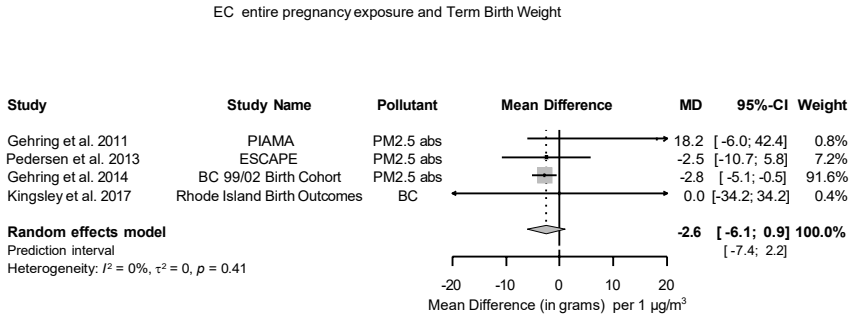



Li et al. 2016 is North American cohort and did not adjust for smoking or BMI, the other two studies Western European studies and did adjust for smoking and BMI.

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**




Subgroup analysis

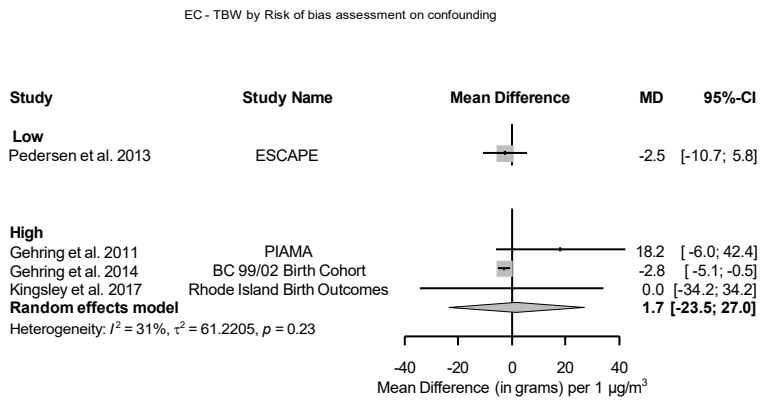
By region

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

By risk of bias

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

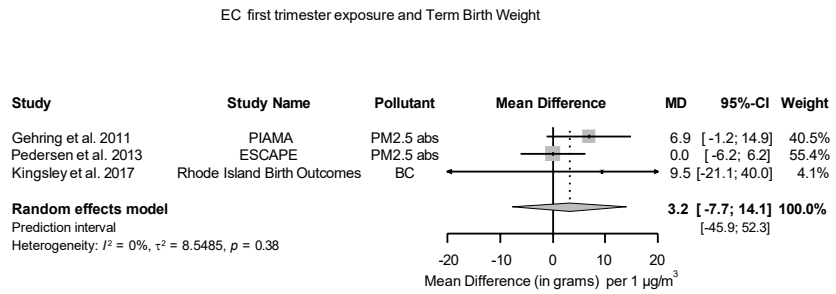



By smoking adjustment – all adjusted for smoking

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**




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.

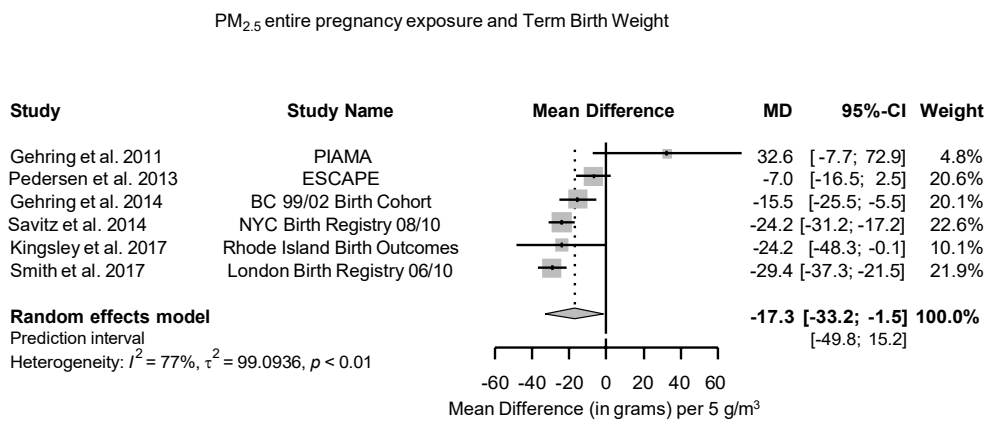
Gehring et al. 2011 and Kingsley et al. 2017 rated high risk of bias for confounding while the other low risk of bias. All rated moderate risk of bias for exposure. Gehring et al. 2011 rated moderate in risk of bias outcome assessment, and the other two studies low risk of bias.

All rated high traffic specificity

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

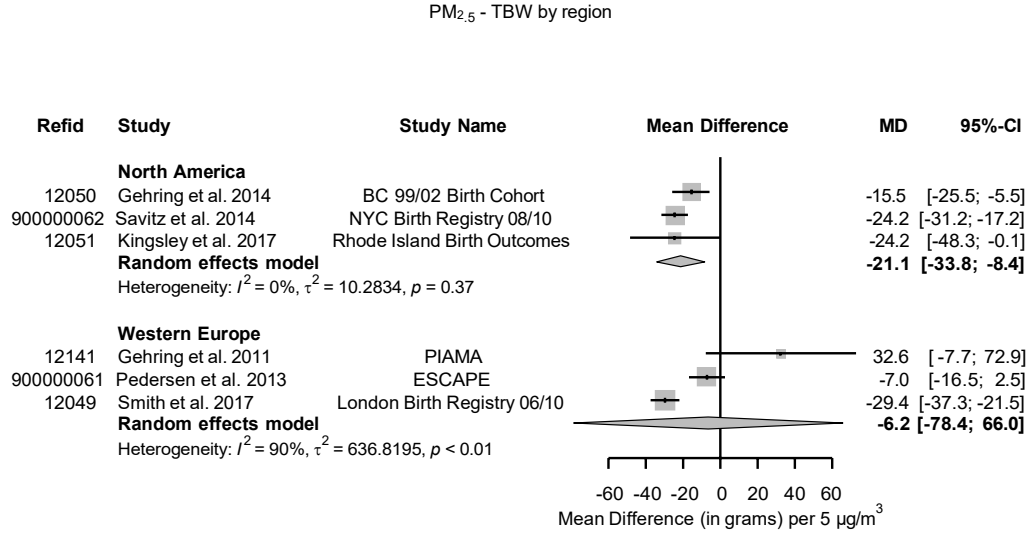
$PM_{10}$ - Not enough TBW studies for meta-analysis

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




Subgroup analysis

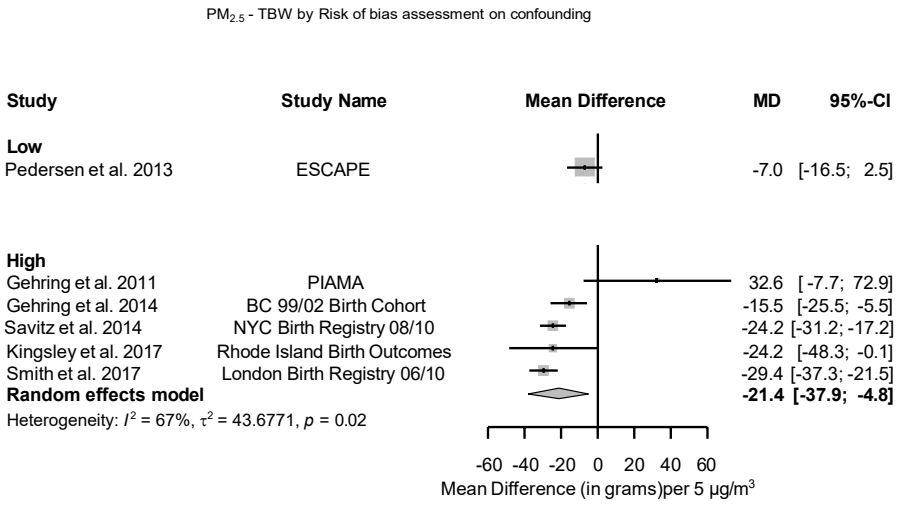
By region



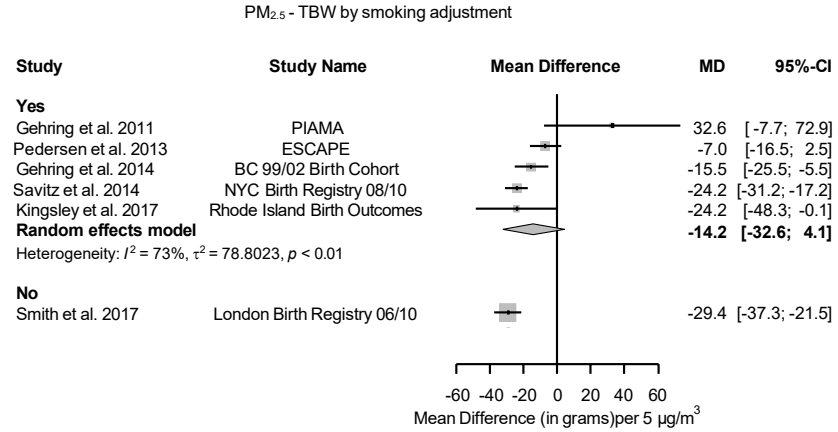

By traffic specificity – all rated moderate

By risk of bias

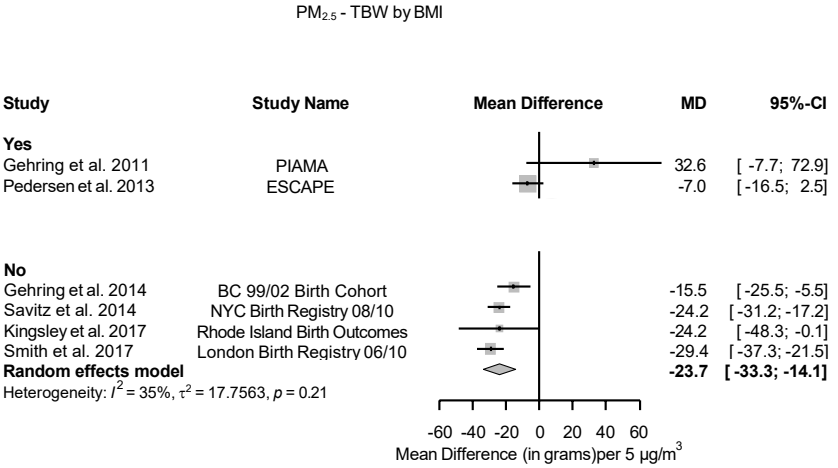
Plots not shown for risk of bias domains if all studies were rated low or moderate



By smoking adjustment

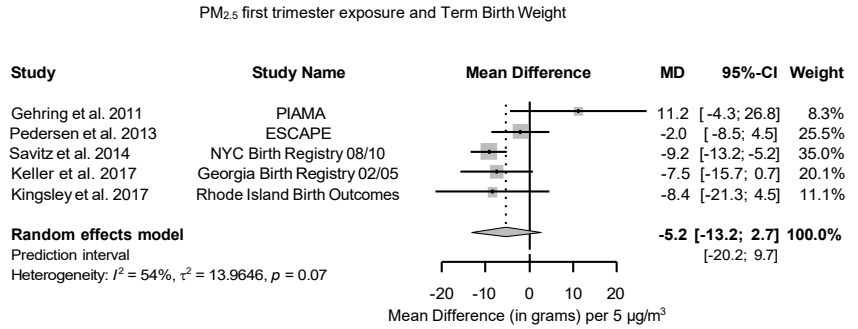



By BMI adjustment



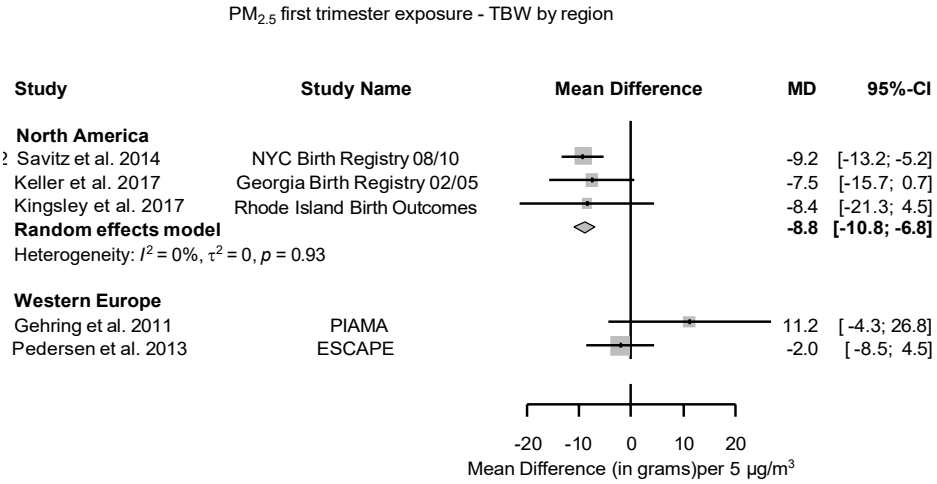

By study design - all cohort studies

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




Subgroup analysis

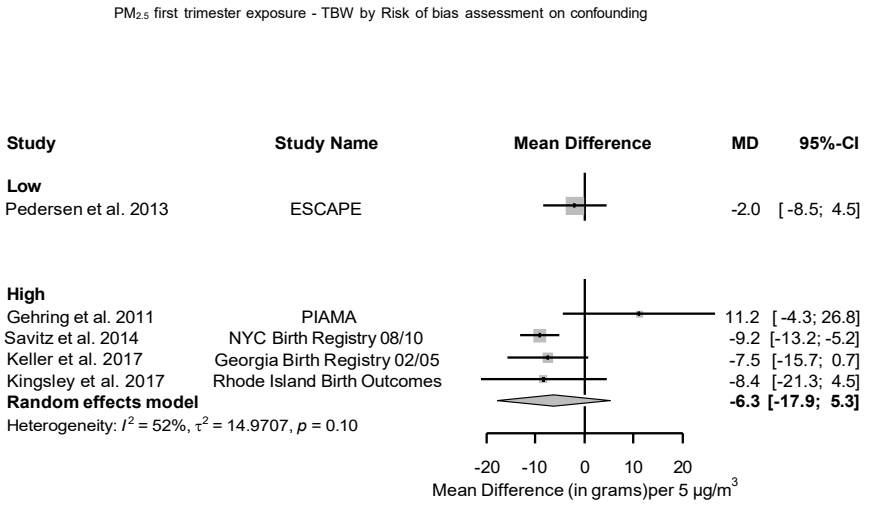
By region




By traffic specificity – all rated moderate

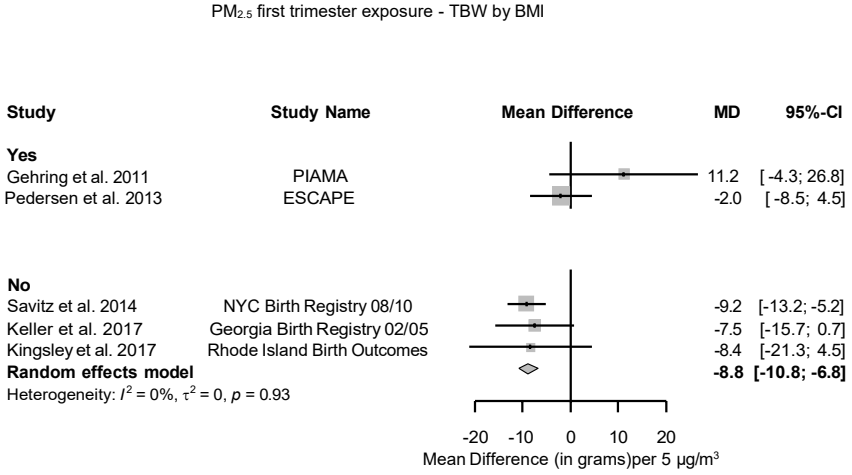
By risk of bias

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



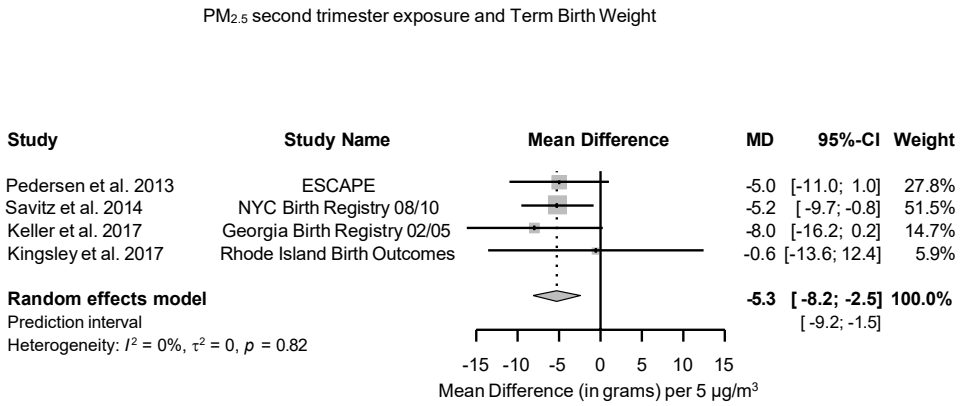

By smoking adjustment – all studies adjusted for smoking

By BMI adjustment

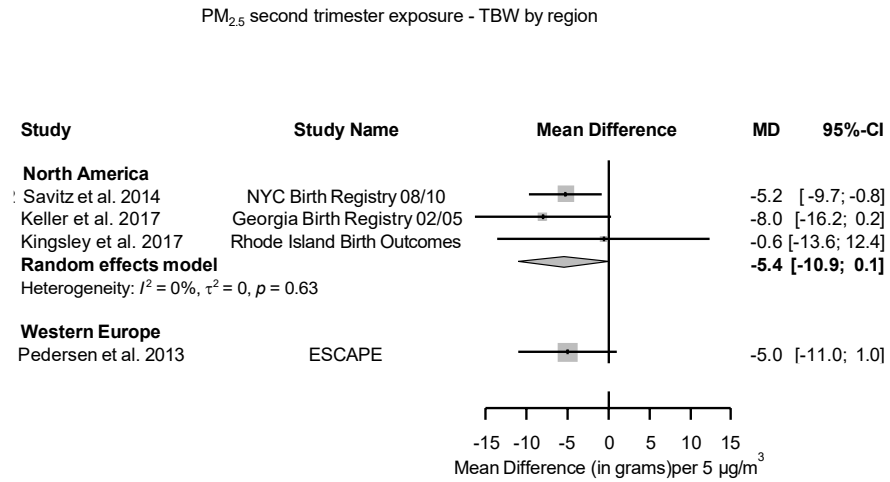


**$PM_{2.5}$ Second trimester exposure – primary meta-analysis - TBW**

Subgroup analysis



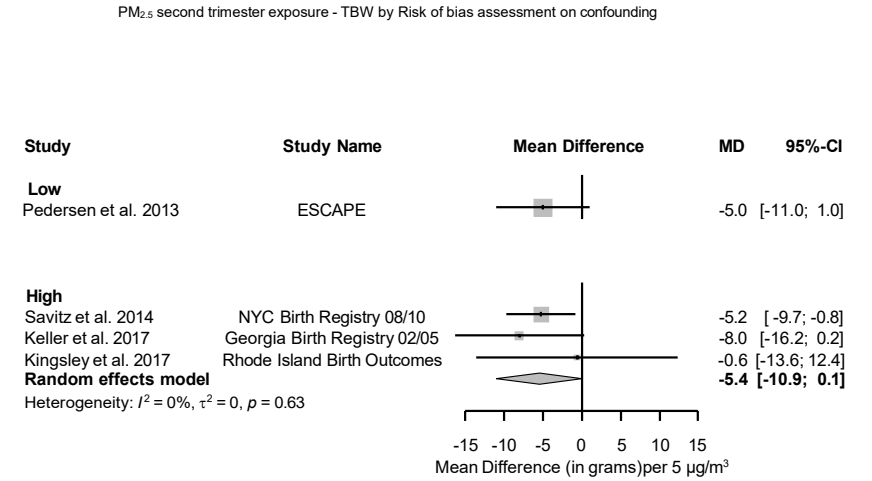

By region




By traffic specificity – all rated moderate

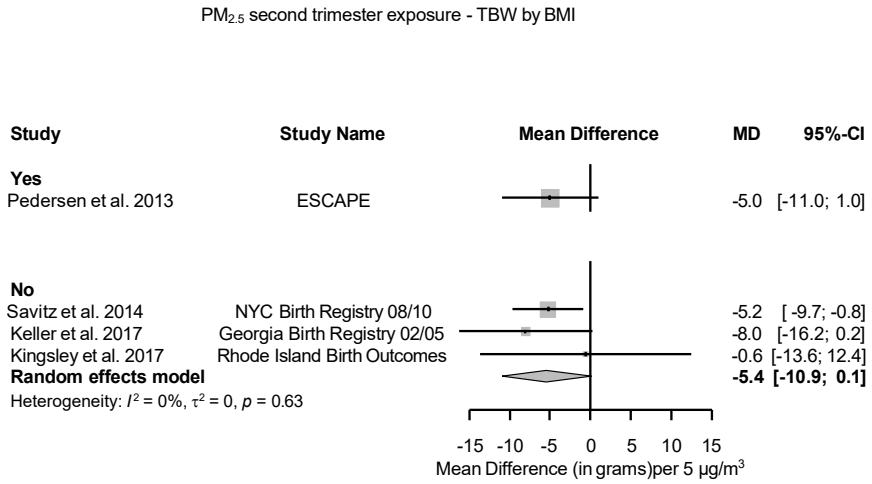
By risk of bias

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

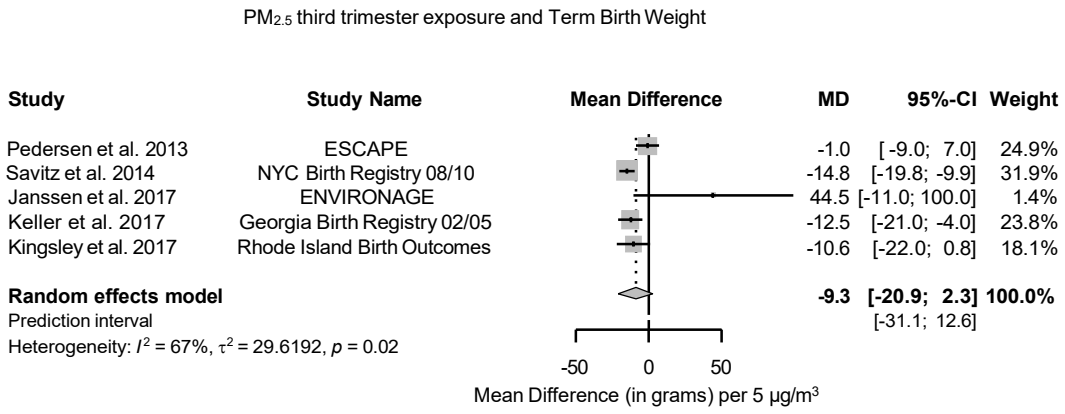



By smoking adjustment – all studies adjusted for smoking

By BMI adjustment

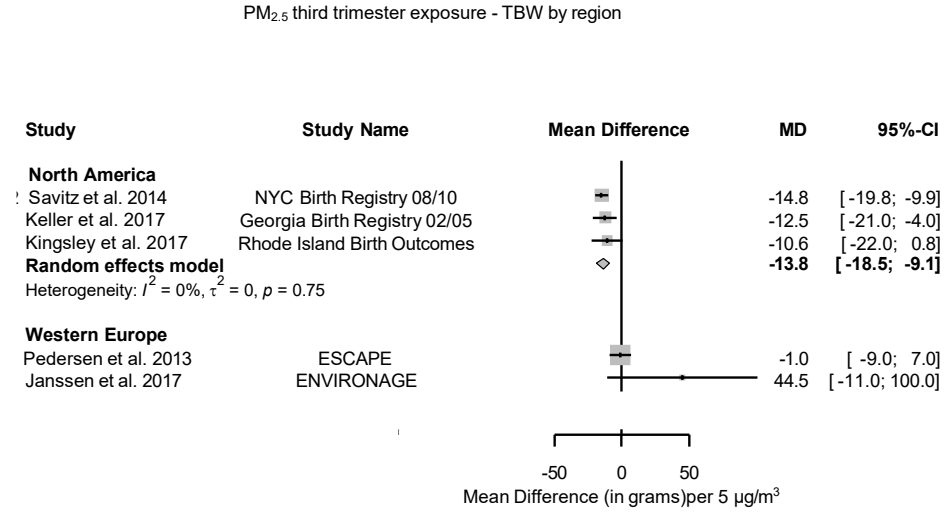


**$PM_{2.5}$ Third trimester exposure – primary meta-analysis - TBW**




Subgroup analysis

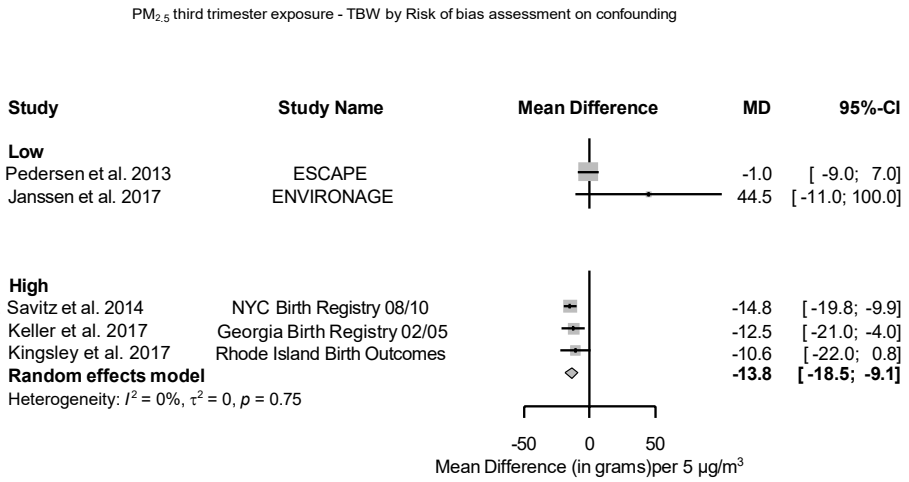
By region




By traffic specificity – all rated moderate

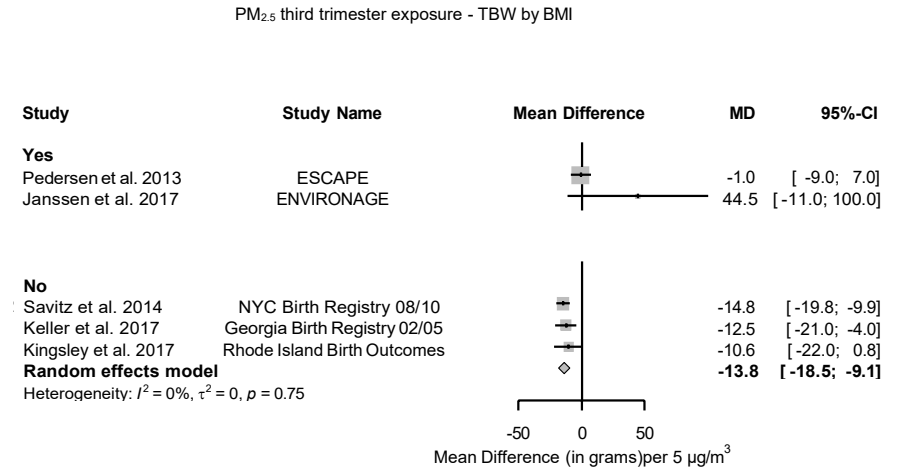
By risk of bias

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



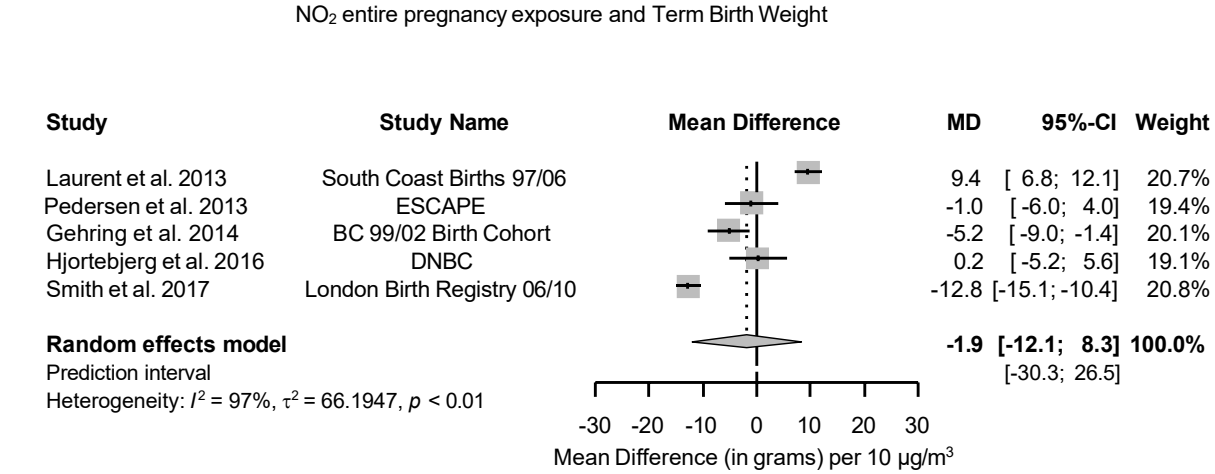

By smoking adjustment – all studies adjusted for smoking

By BMI adjustment

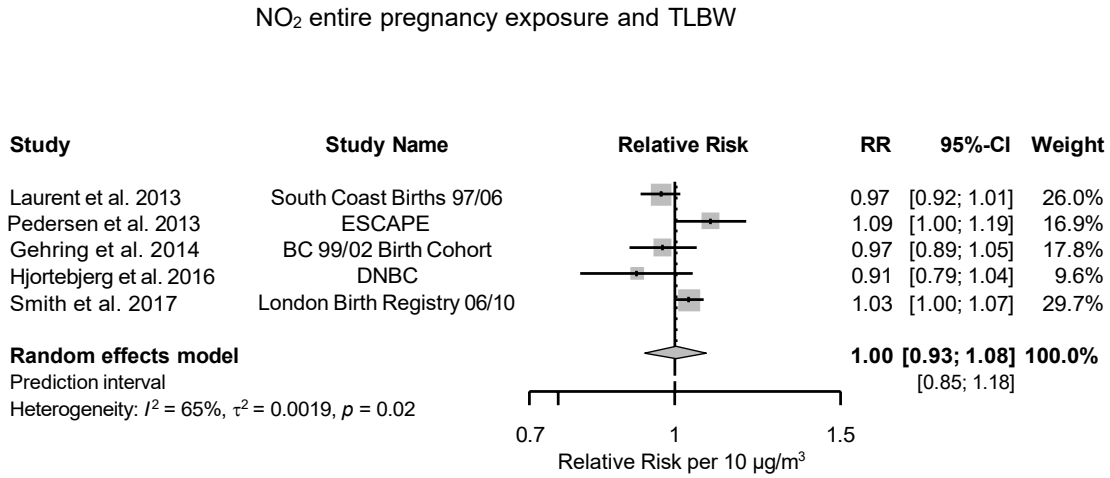


**Meta-analysis results only for studies reporting both TBW and TLBW**

NO2 - TBW

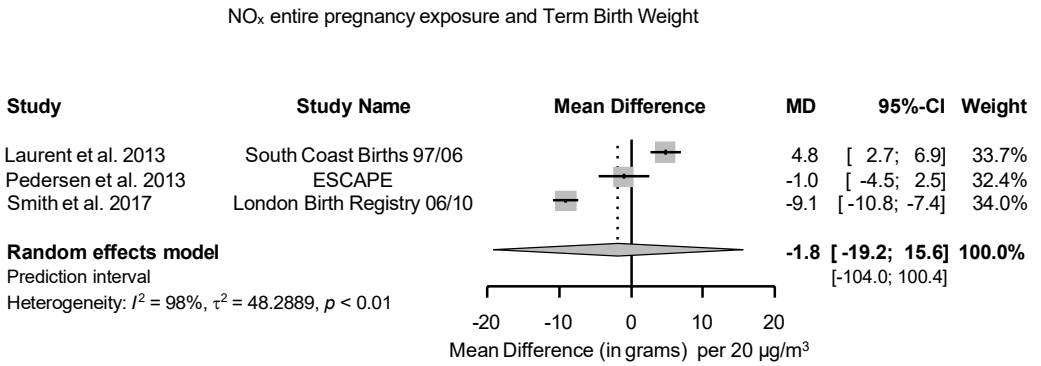



NO2 - TLBW

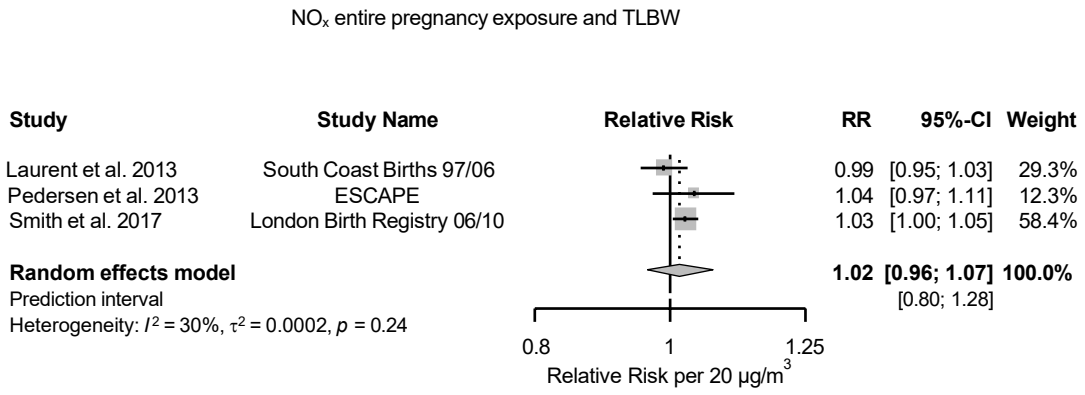


**Meta-analysis results only for studies reporting both TBW and TLBW**

NOx - TBW

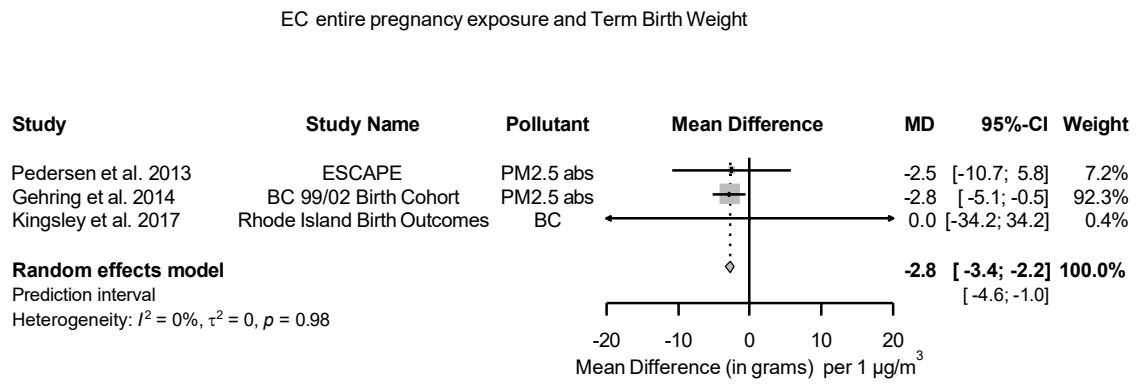



NOx - TLBW

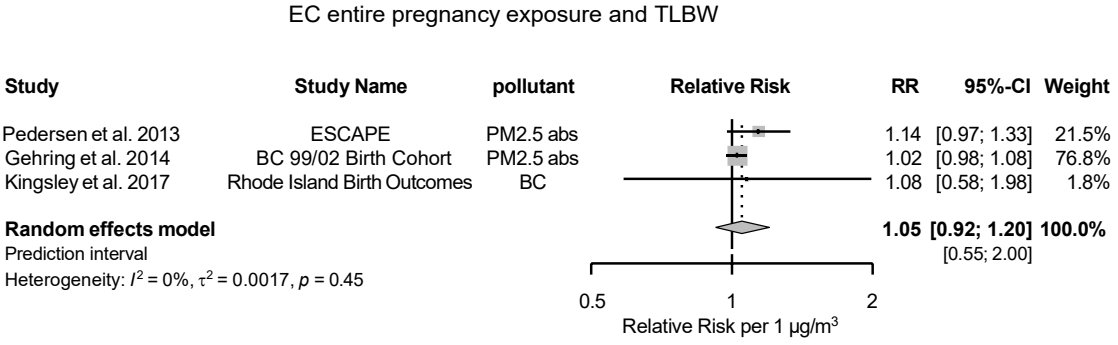


**Meta-analysis results only for studies reporting both TBW and TLBW**

EC - TBW

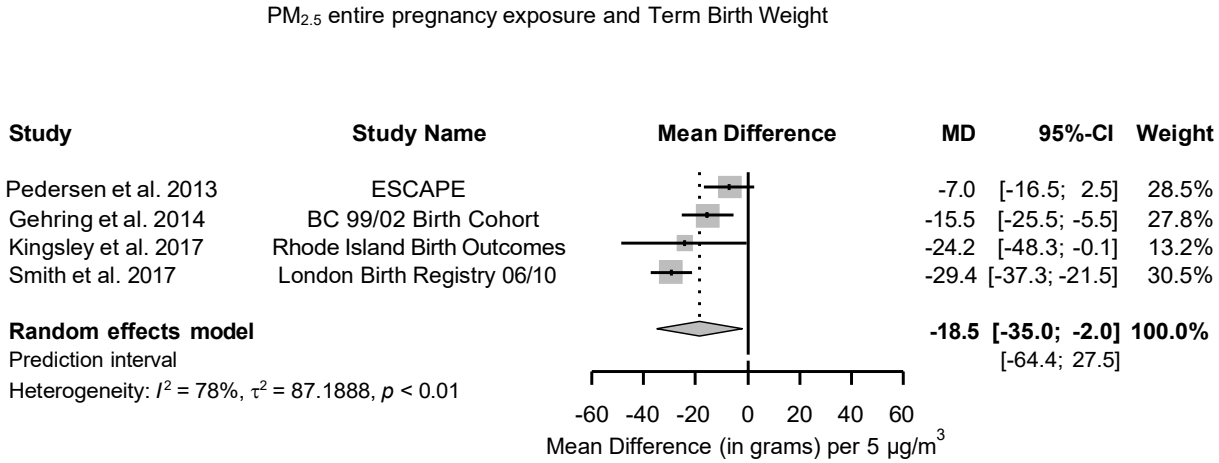



EC - TLBW

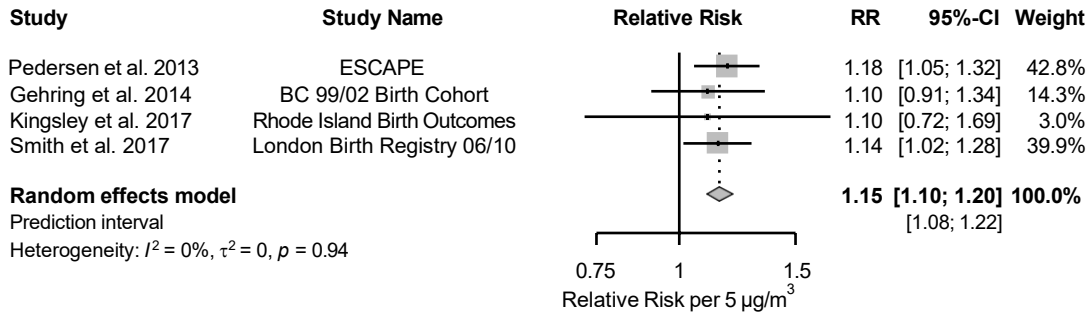


**Meta-analysis results only for studies reporting both TBW and TLBW**

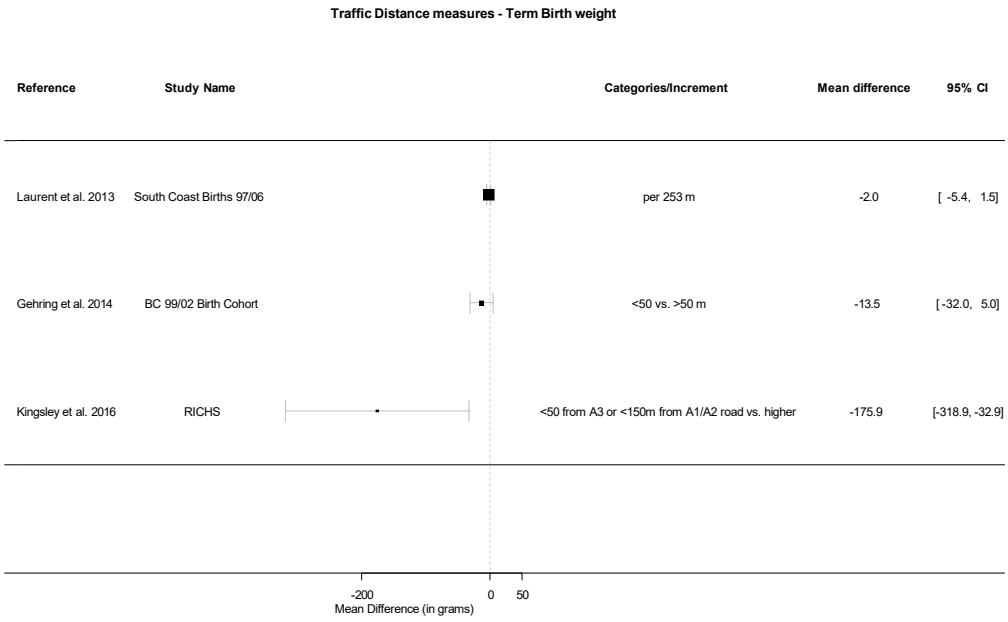
PM2.5 - TBW



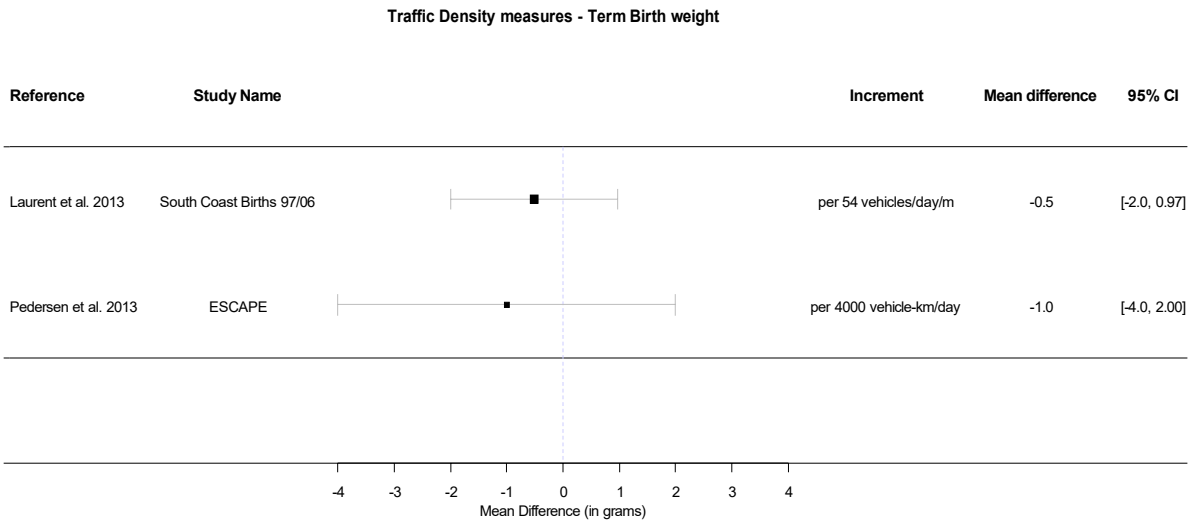

PM2.5 - TLBW



## Distance measures

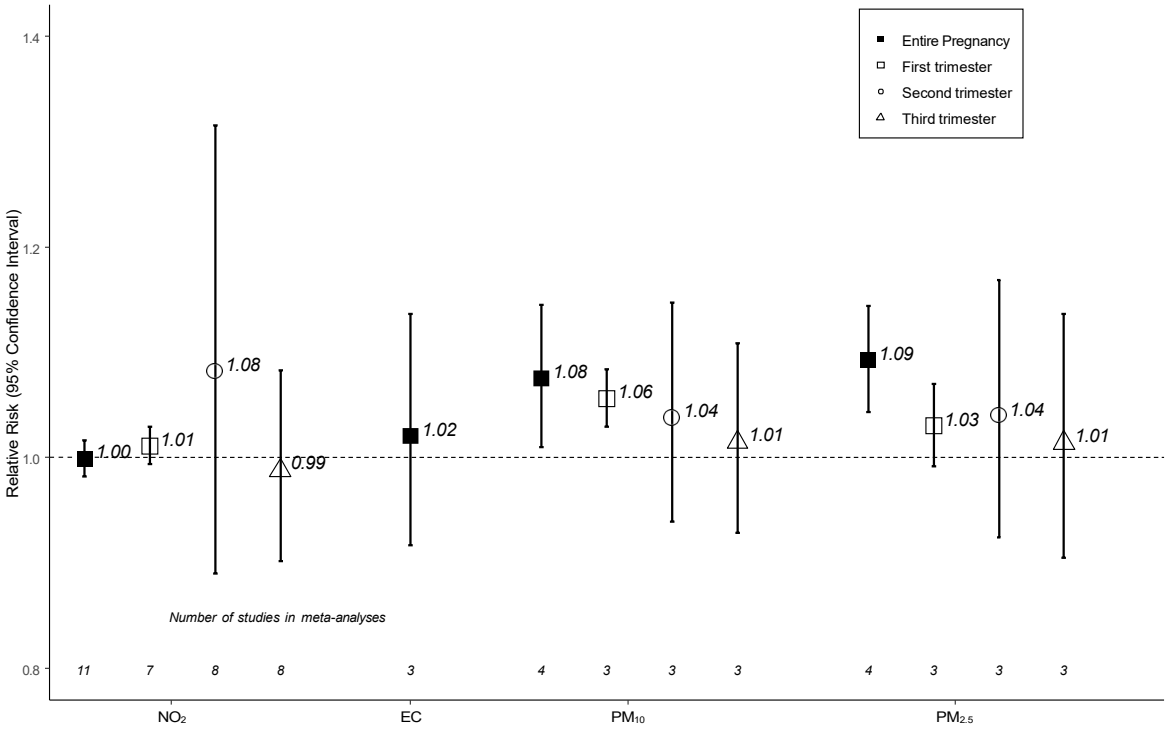



## Density measures



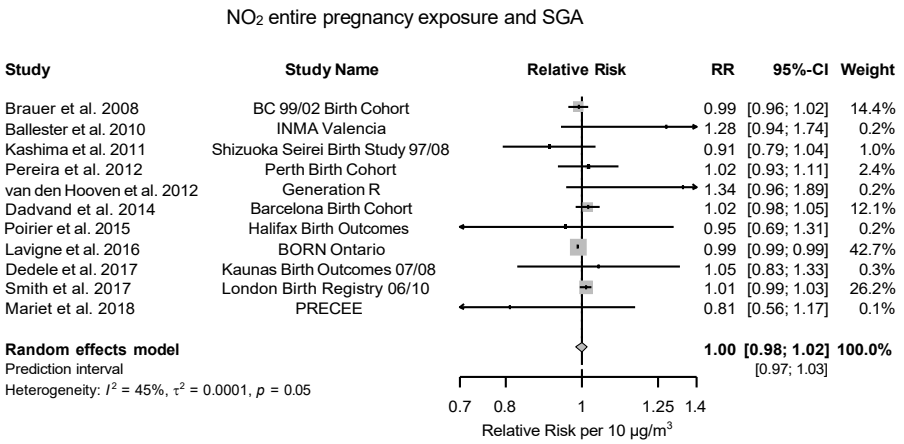
## 8.3 Small for gestational age (SGA)

Summary of meta-analysis

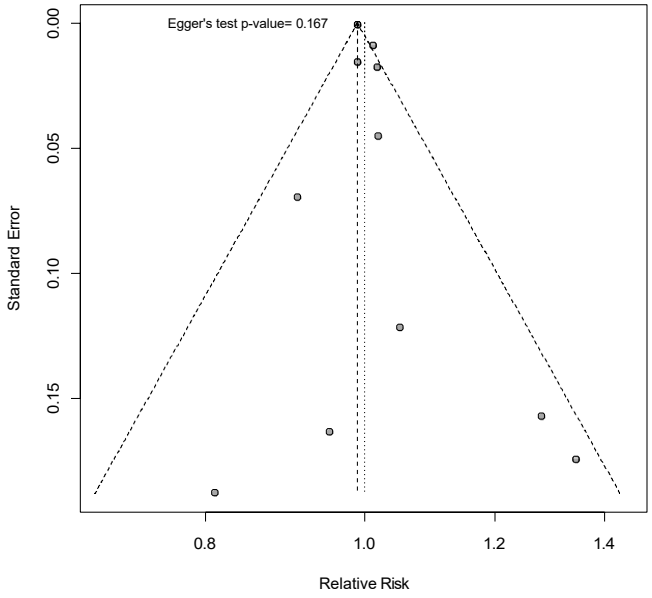



Footnote: The following increments were used: 10 µg/m$^3$ for $NO_2$, 1 µg/m$^3$ for EC, 10 µg/m$^3$ for $PM_{10}$ and 5 µg/m$^3$ for $PM_{2.5}$. Effect estimates cannot be directly compared across the different traffic-related pollutants because the selected increments do not necessarily represent the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

**$NO_2$ Entire pregnancy exposure - primary meta-analysis - SGA**



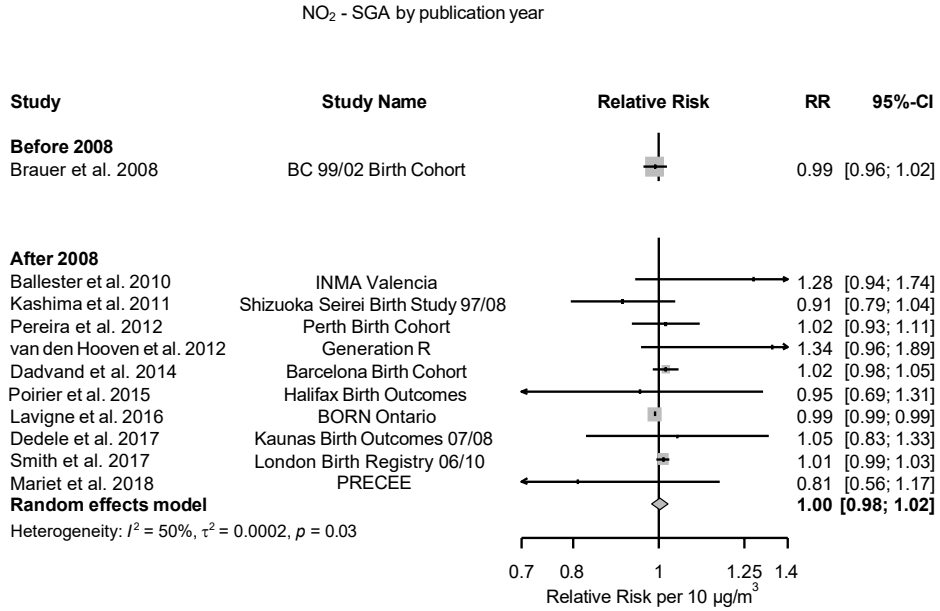

Publication bias – entire pregnancy exposure




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.

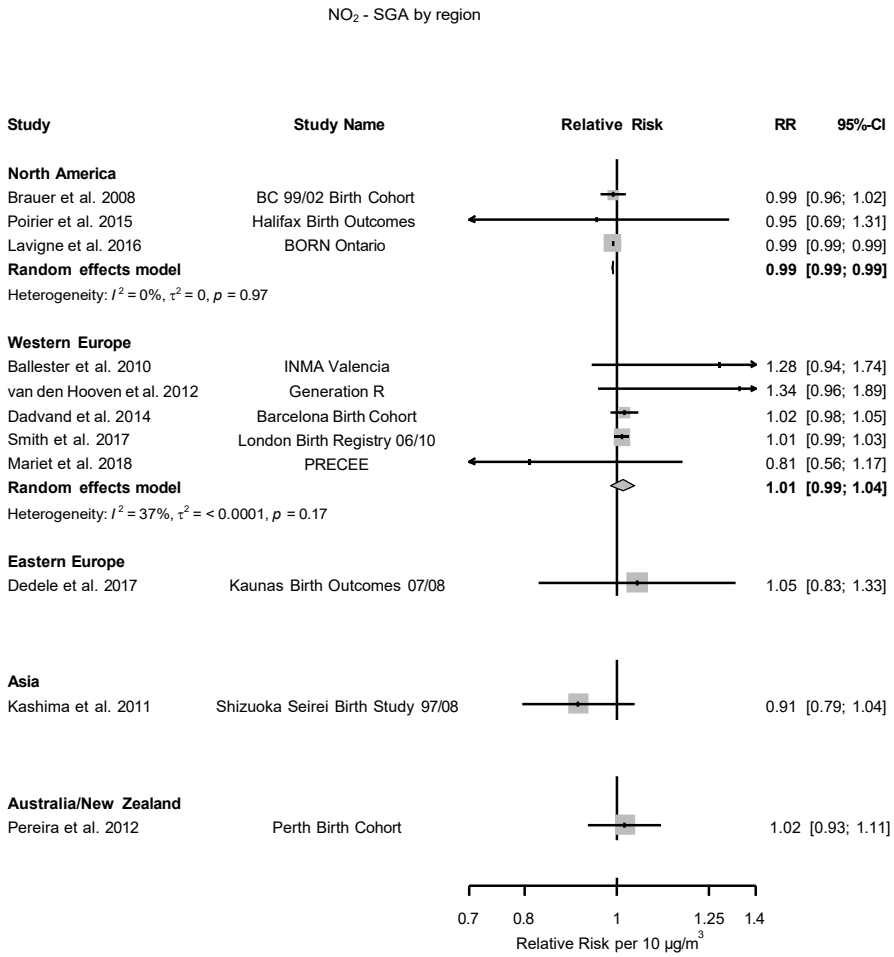
Subgroup analysis – entire pregnancy exposure

By publication year

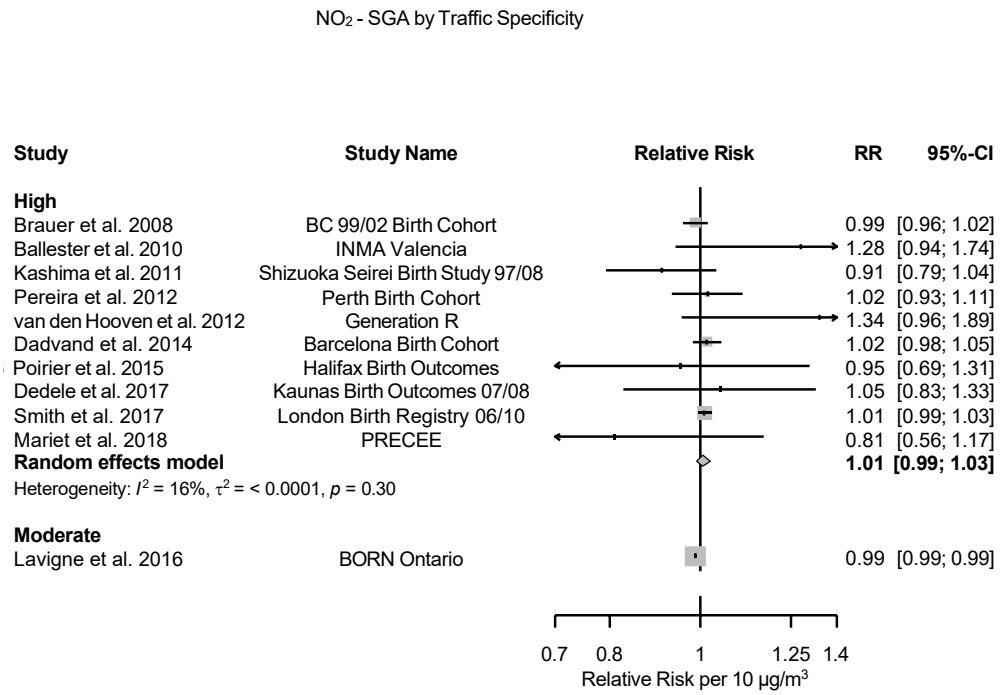



By study design – all cohort studies

By region

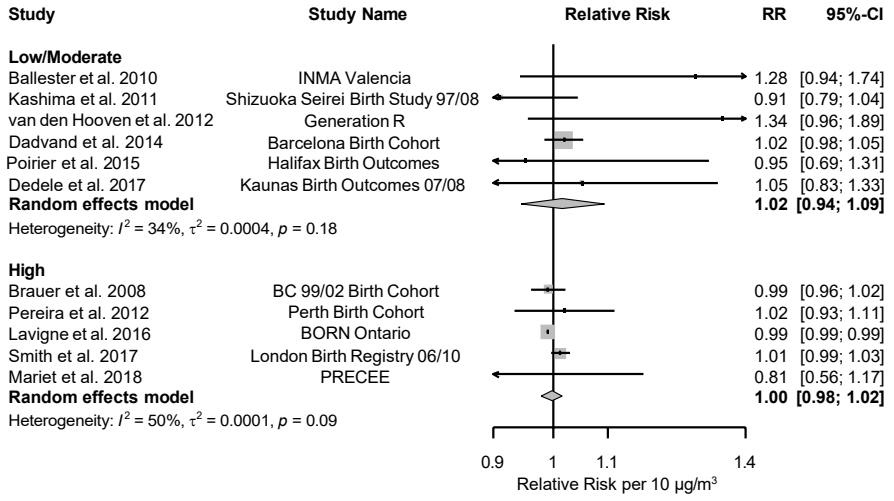

$NO_2$ - SGA by region
Study
Study Name
Relative Risk
RR
95%-CI
North America
Brauer et al. 2008
BC 99/02 Birth Cohort
0.99 [0.96; 1.02]
Poirier et al. 2015
Halifax Birth Outcomes
0.95 [0.69; 1.31]
Lavigne et al. 2016
BORN Ontario
0.99 [0.99; 0.99]
Random effects model
0.99 [0.99; 0.99]
Heterogeneity: $I^2$ = 0%, $\tau^2$ = 0, $p$ = 0.97
Western Europe
Ballester et al. 2010
INMA Valencia
1.28 [0.94; 1.74]
van den Hooven et al. 2012
Generation R
1.34 [0.96; 1.89]
Dadvand et al. 2014
Barcelona Birth Cohort
1.02 [0.98; 1.05]
Smith et al. 2017
London Birth Registry 06/10
1.01 [0.99; 1.03]
Mariet et al. 2018
PRECEE
0.81 [0.56; 1.17]
Random effects model
1.01 [0.99; 1.04]
Heterogeneity: $I^2$ = 37%, $\tau^2$ = < 0.0001, $p$ = 0.17
Eastern Europe
Dedele et al. 2017
Kaunas Birth Outcomes 07/08
1.05 [0.83; 1.33]
Asia
Kashima et al. 2011
Shizuoka Seirei Birth Study 97/08
0.91 [0.79; 1.04]
Australia/New Zealand
Pereira et al. 2012
Perth Birth Cohort
1.02 [0.93; 1.11]
0.7
0.8
1
1.25
1.4
Relative Risk per 10 µg/m$^3$

By traffic specificity

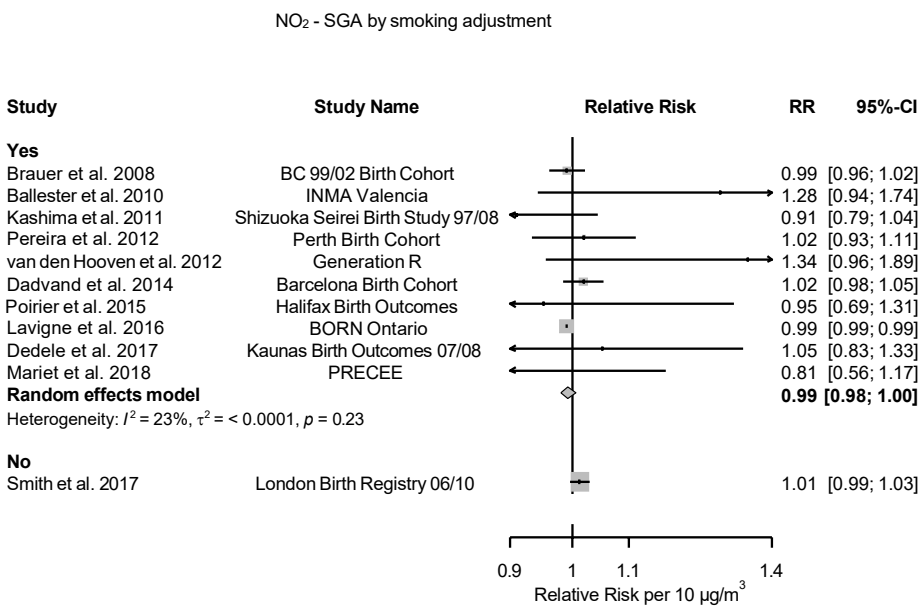



By risk of bias

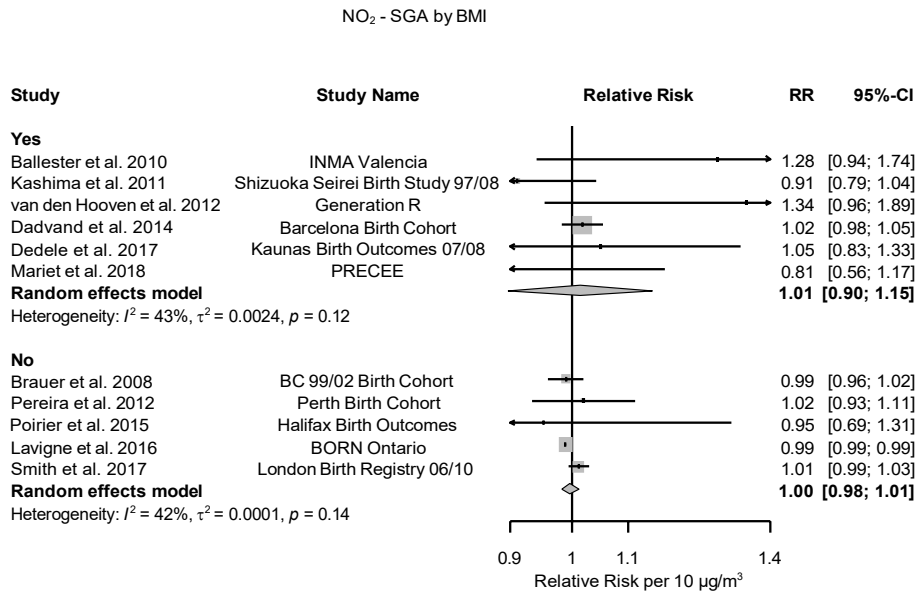
Plots not shown for risk of bias domains if all studies were rated low or moderate



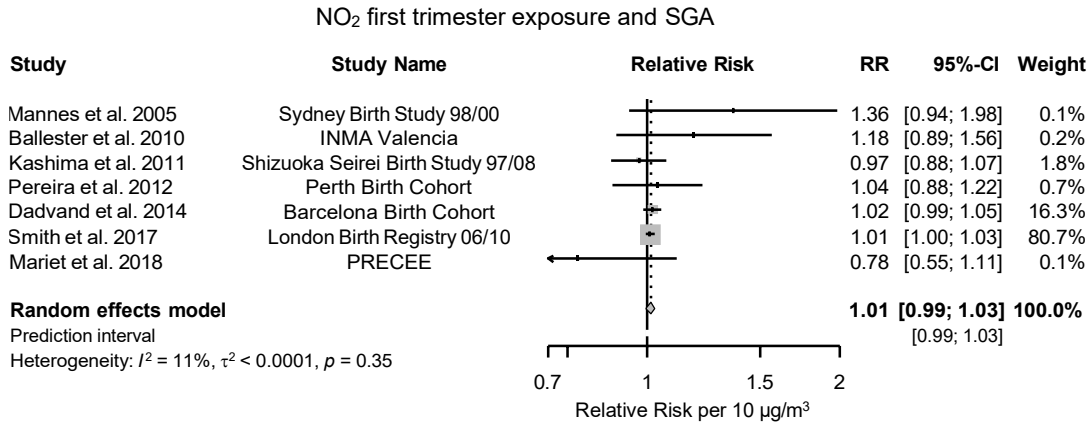
By smoking adjustment




By BMI adjustment



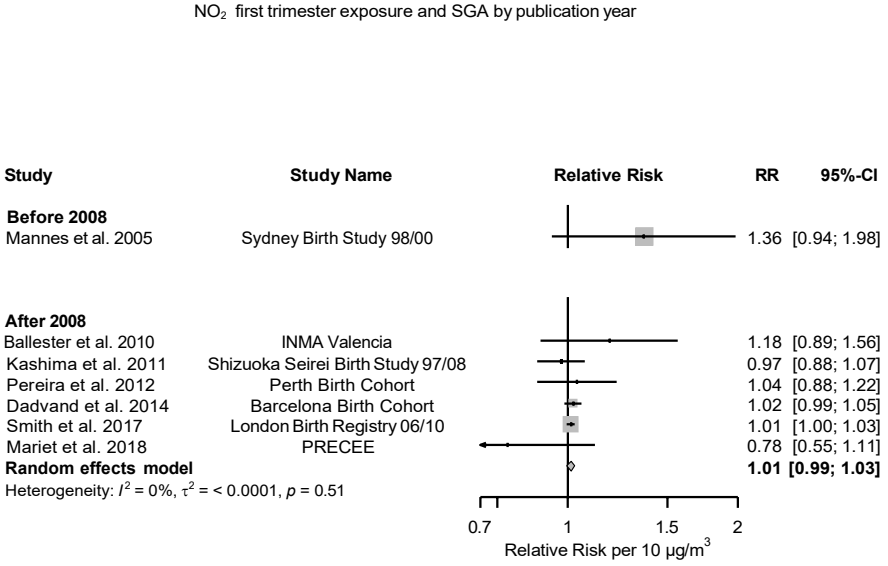
**$NO_2$ First trimester exposure - primary meta-analysis - SGA**



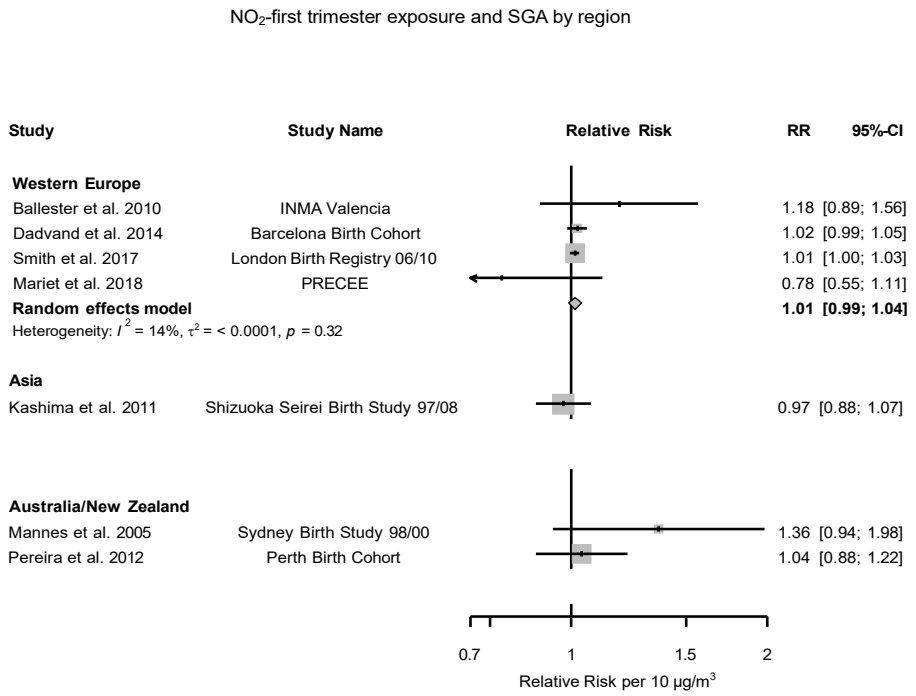

Subgroup analysis – first trimester exposure

By study design – all cohort studies

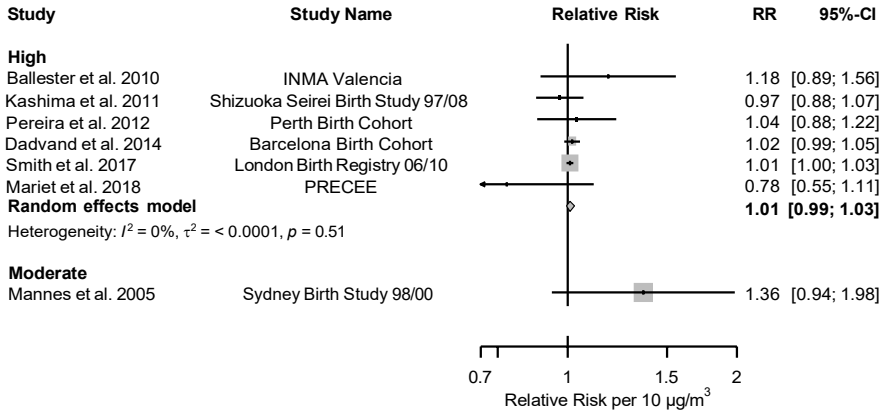
By publication year



By region

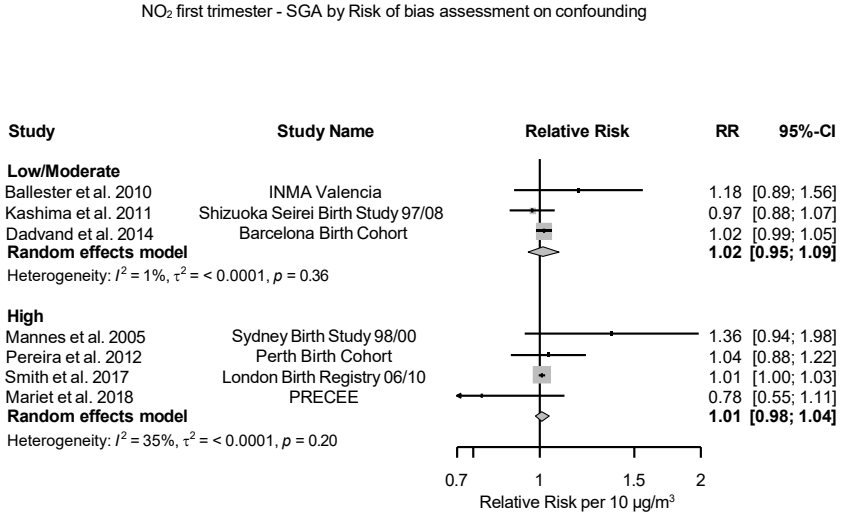



By traffic specificity

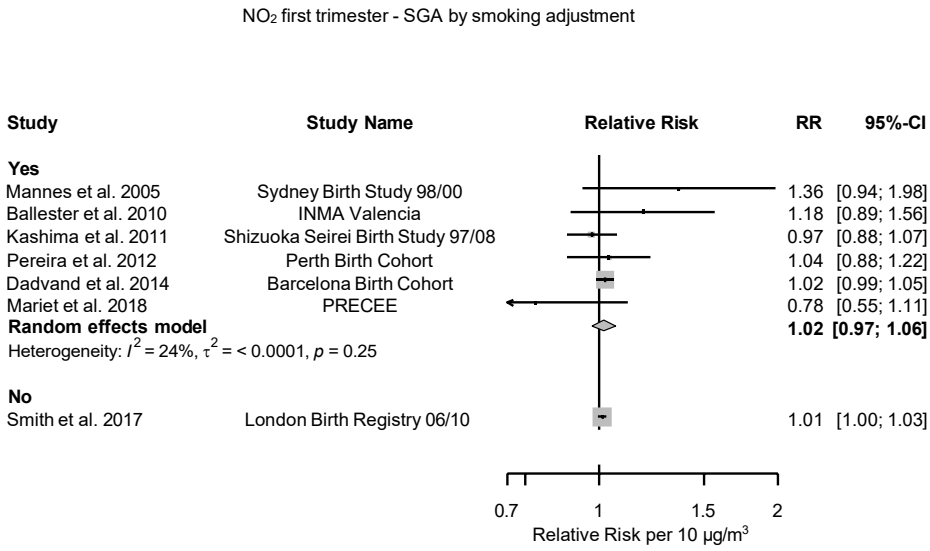


By risk of bias

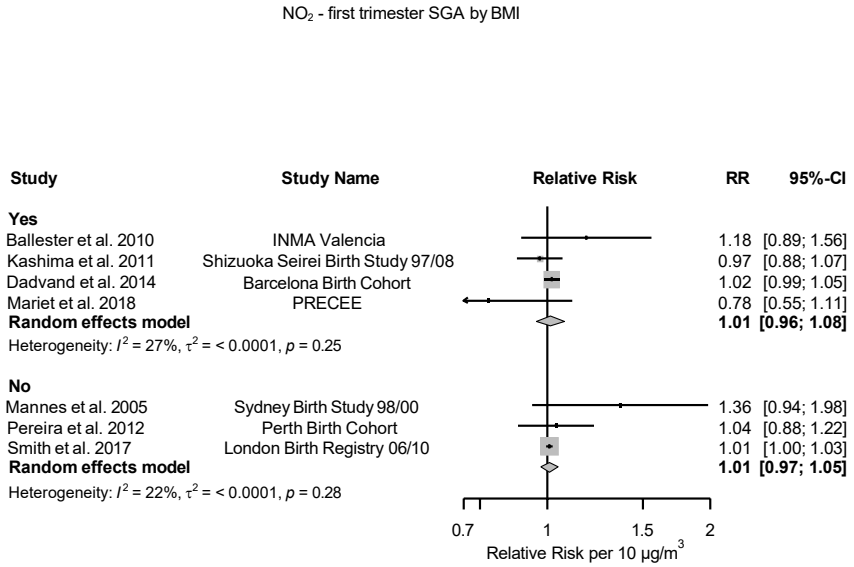
Plots not shown for risk of bias domains if all studies were rated low or moderate



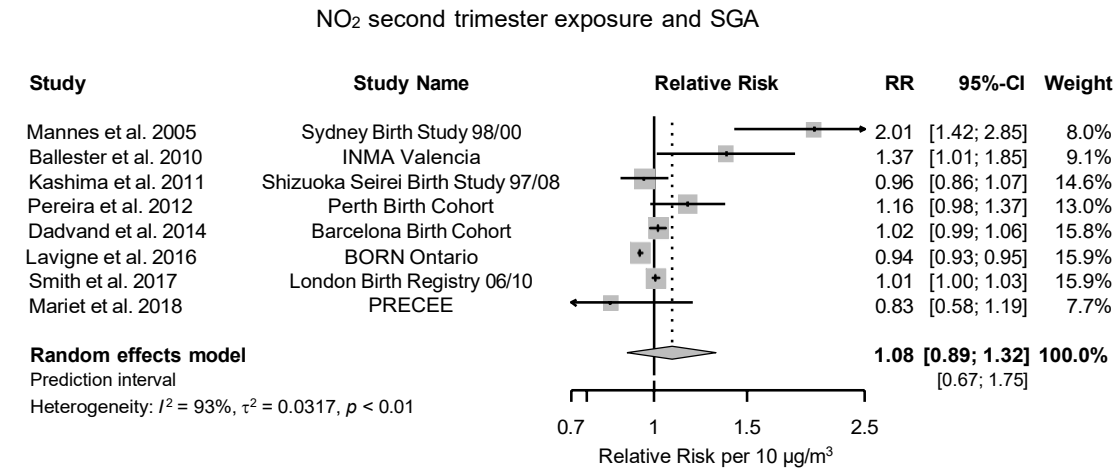
By smoking adjustment




By BMI adjustment

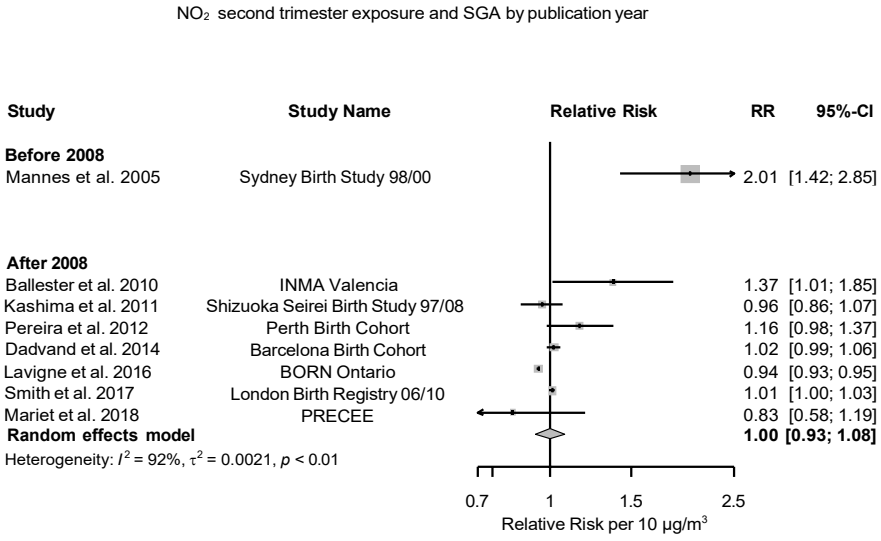


**$NO_2$ Second trimester exposure - primary meta-analysis - SGA**

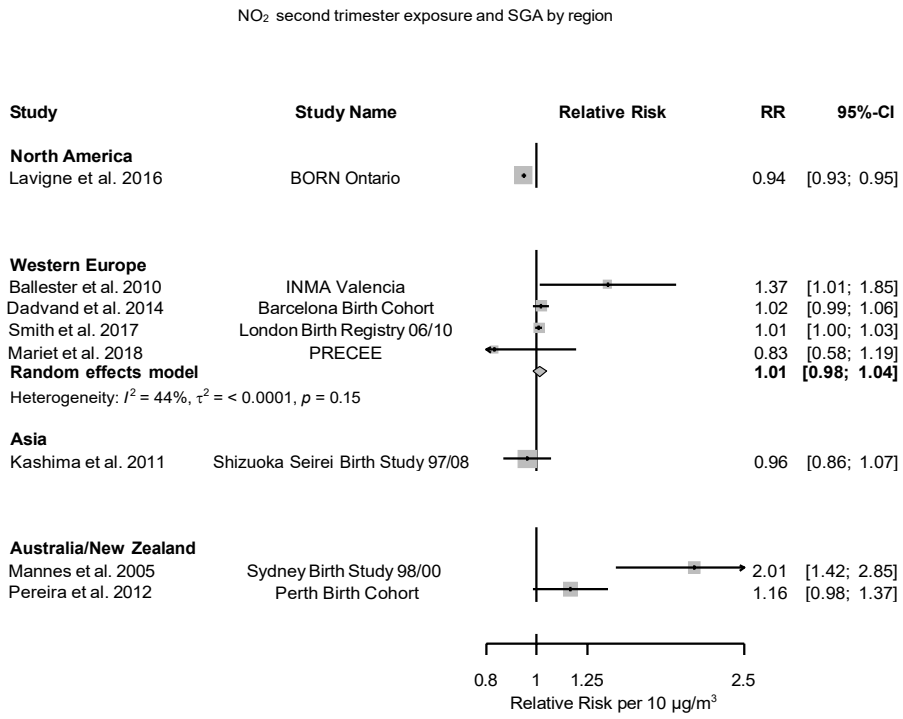



Subgroup – second trimester exposure

By publication year

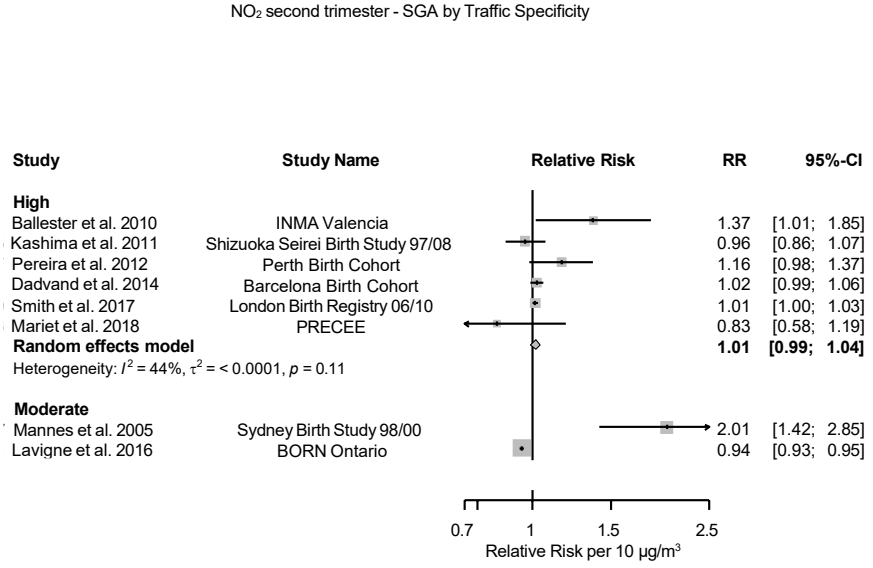


By region



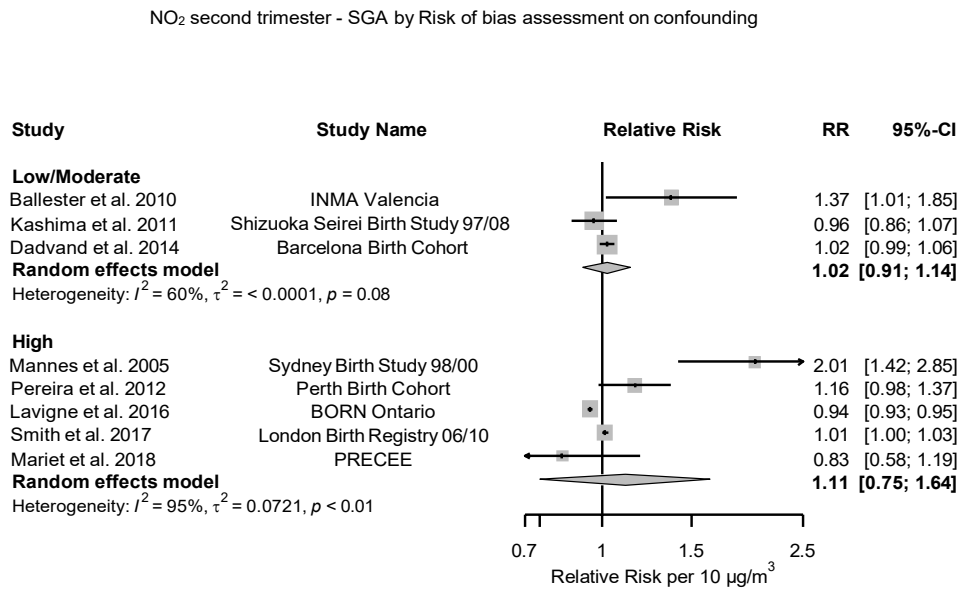

By study design – all cohort studies

By traffic specificity

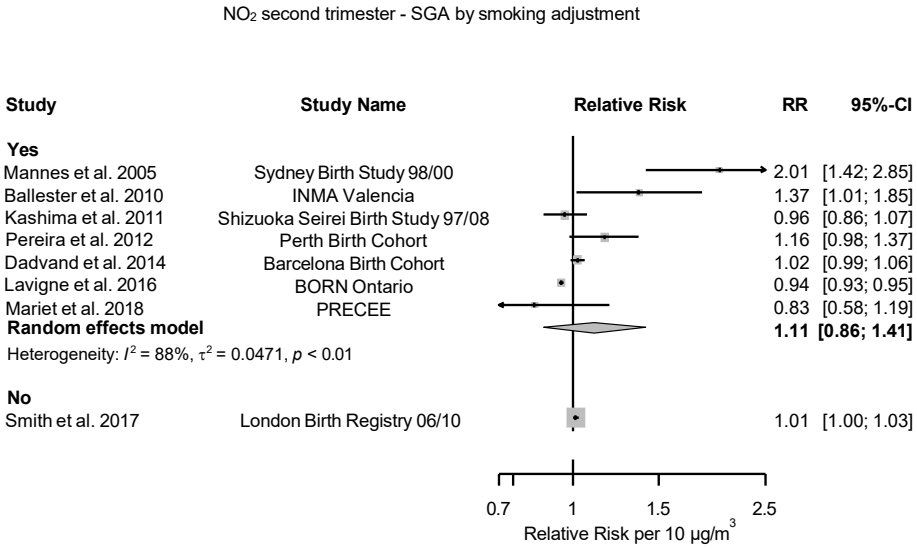


By risk of bias

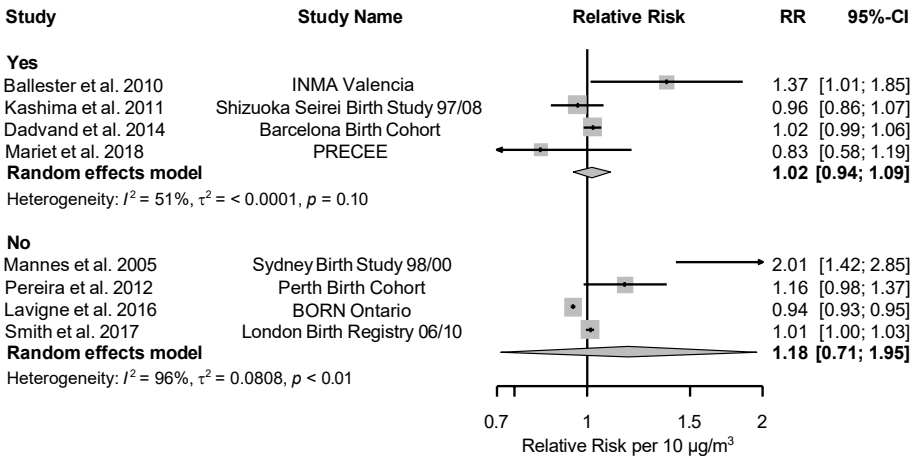
Plots not shown for risk of bias domains if all studies were rated low or moderate



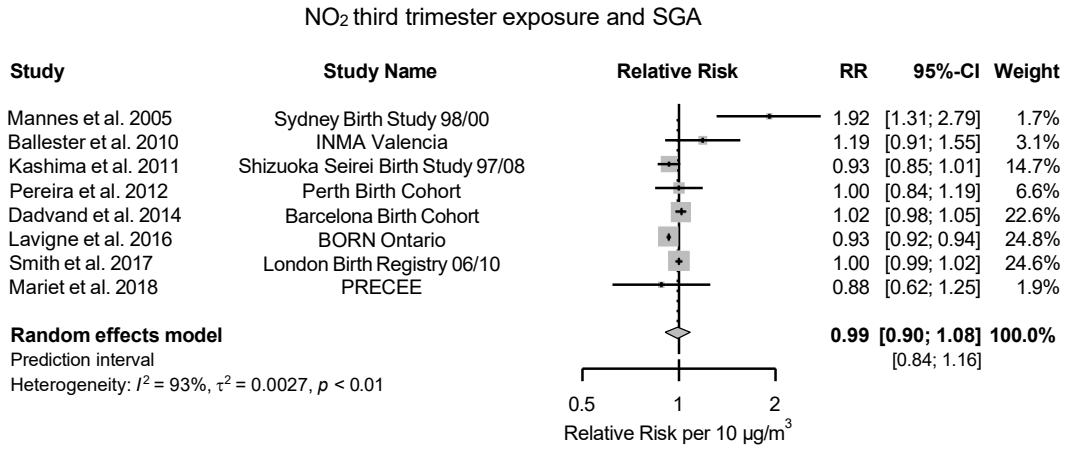
By smoking adjustment




By BMI adjustment

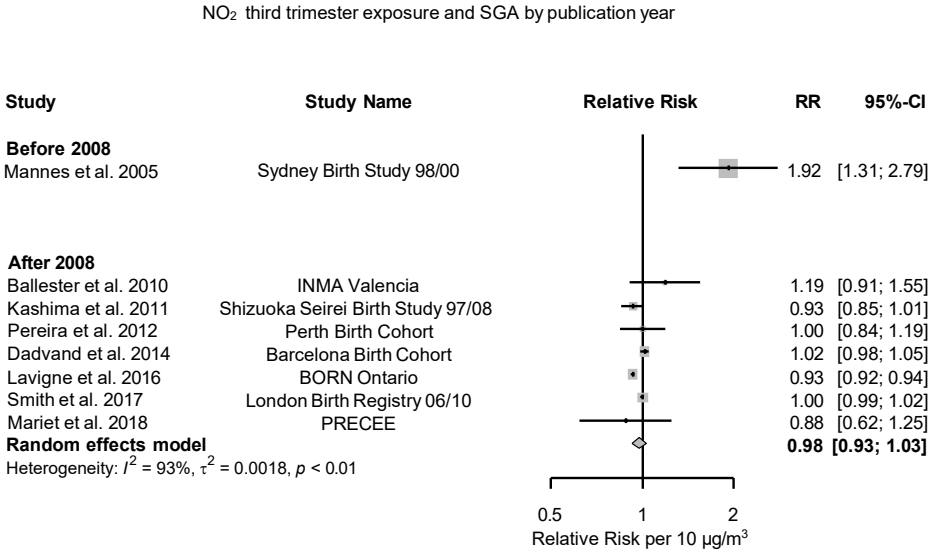


**$NO_2$ Third trimester exposure - primary meta-analysis - SGA**

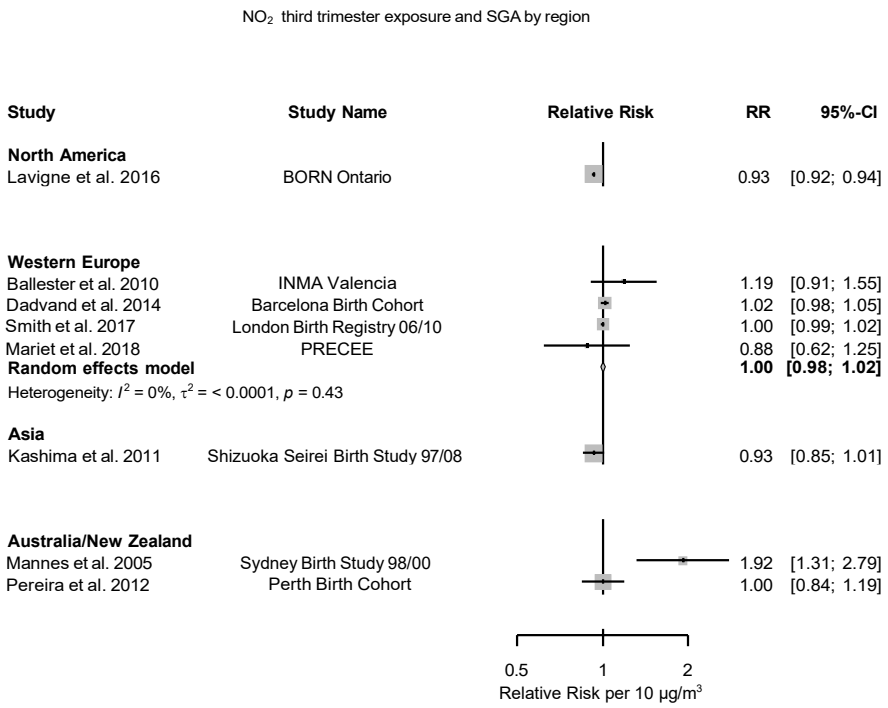



Subgroup analysis – third trimester exposure

By publication year

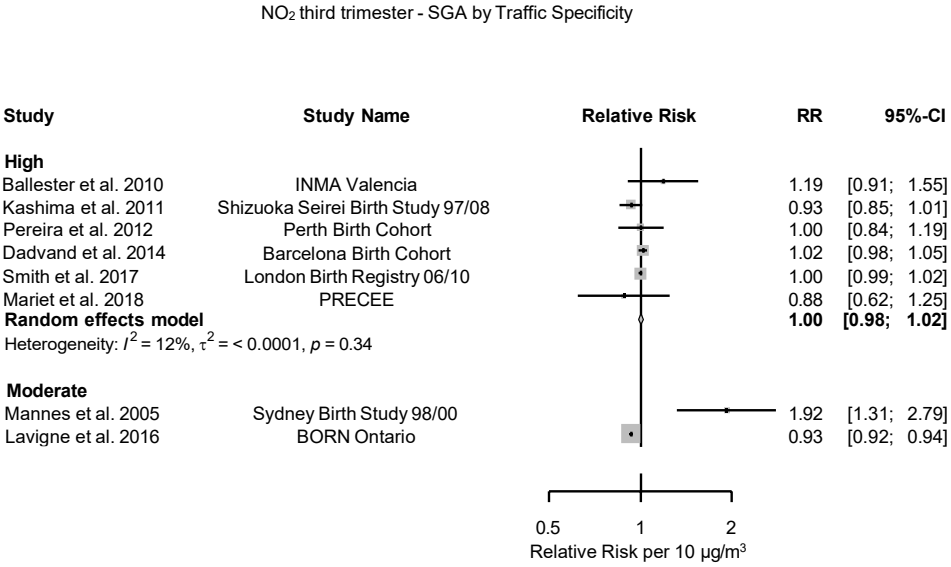


By region



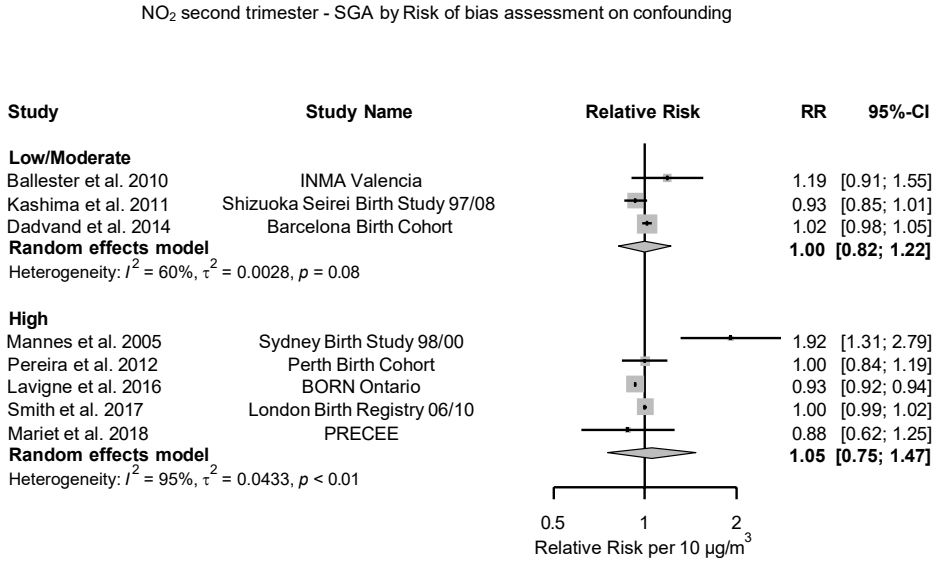

By study design – all cohort studies

By traffic specificity

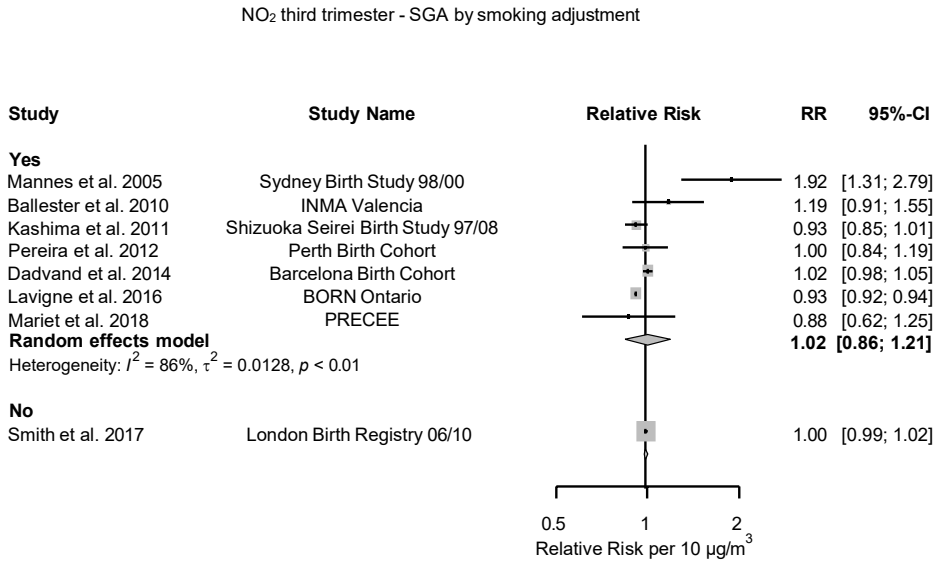


By risk of bias

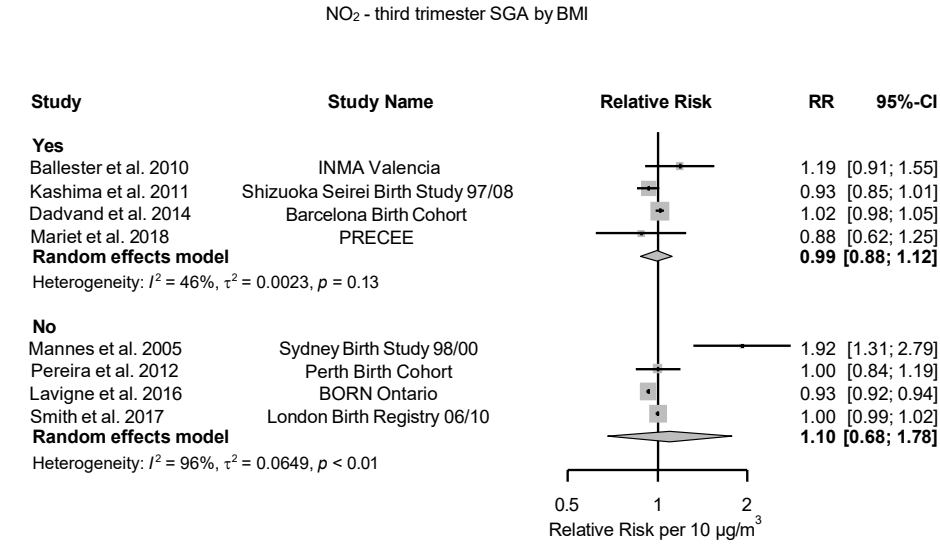
Plots not shown for risk of bias domains if all studies were rated low or moderate



By smoking adjustment



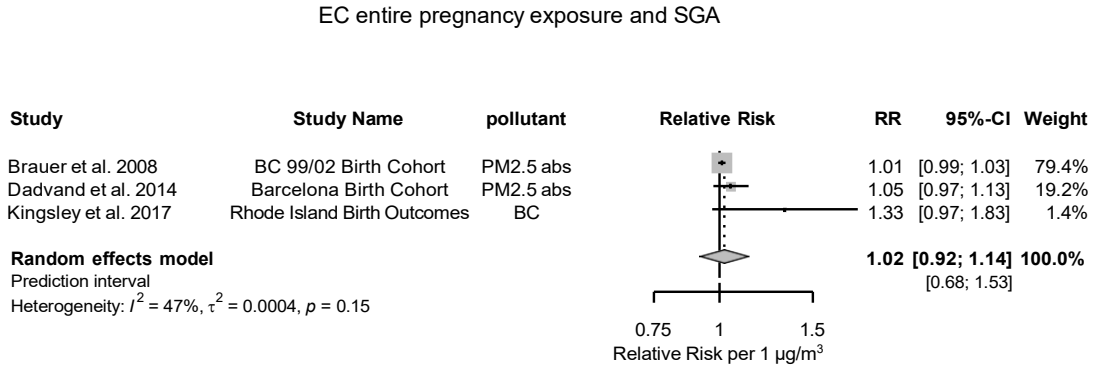

By BMI adjustment




**$NO_x$**

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**



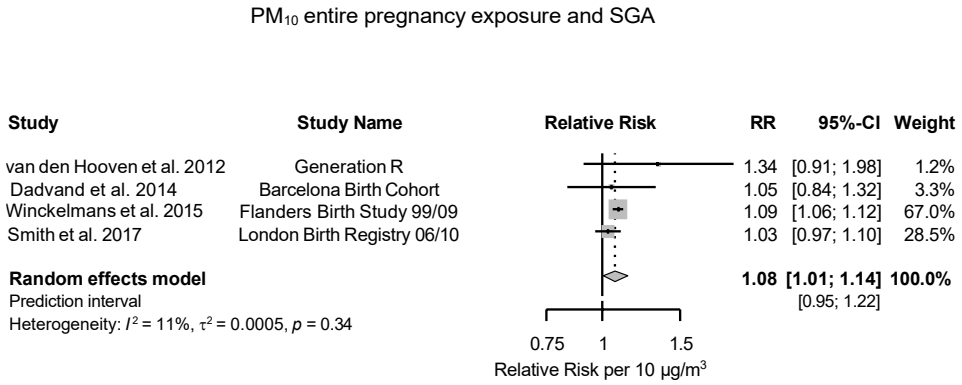

Subgroup analysis

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.

**$PM_{10}$ Entire pregnancy exposure - primary meta-analysis - SGA**




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.

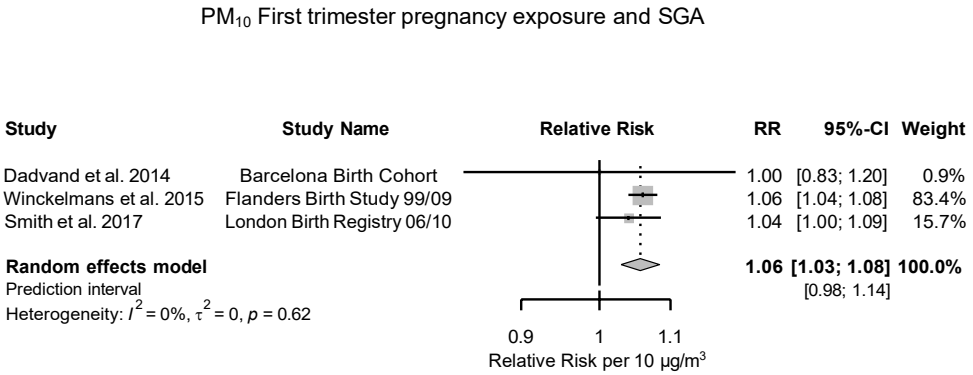
By smoking adjustment

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.

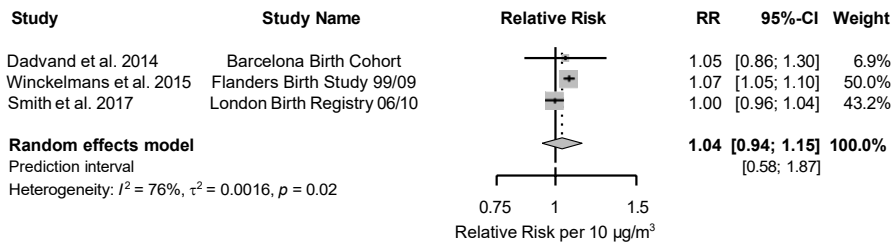
By BMI adjustment

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.

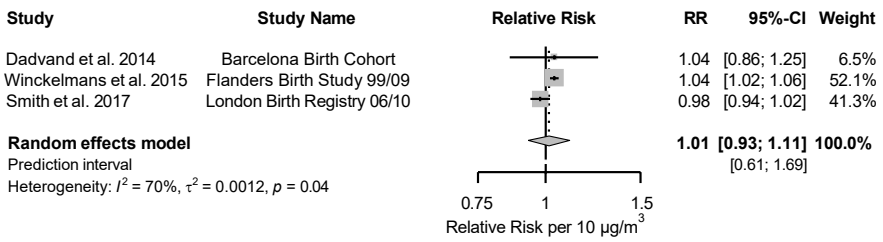
**$PM_{10}$ First trimester exposure - primary meta-analysis - SGA**




**$PM_{10}$ Second trimester exposure - primary meta-analysis - SGA**




**$PM_{10}$ Third trimester exposure - primary meta-analysis - SGA**

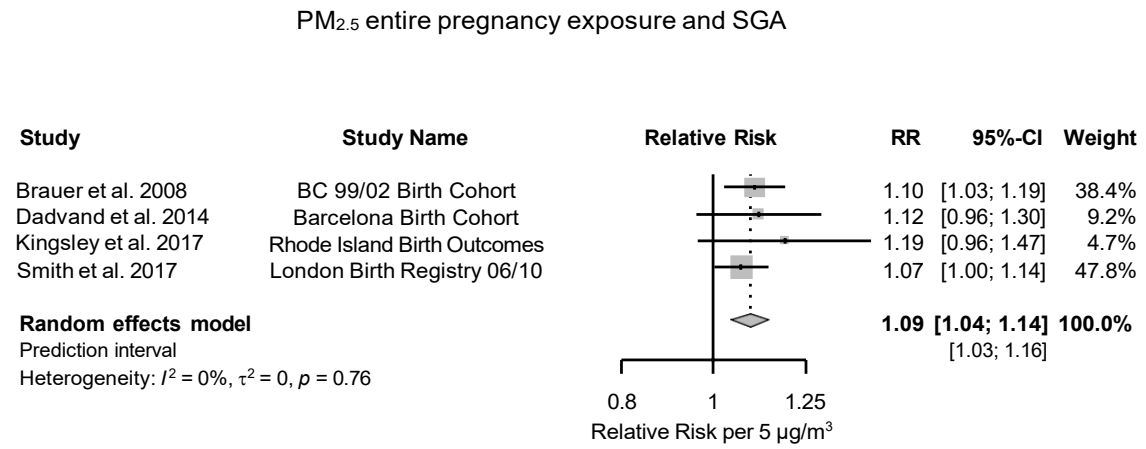



All were Western European cohorts that rated moderate for traffic specificity.

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**




Subgroup analysis – entire pregnancy exposure

By region

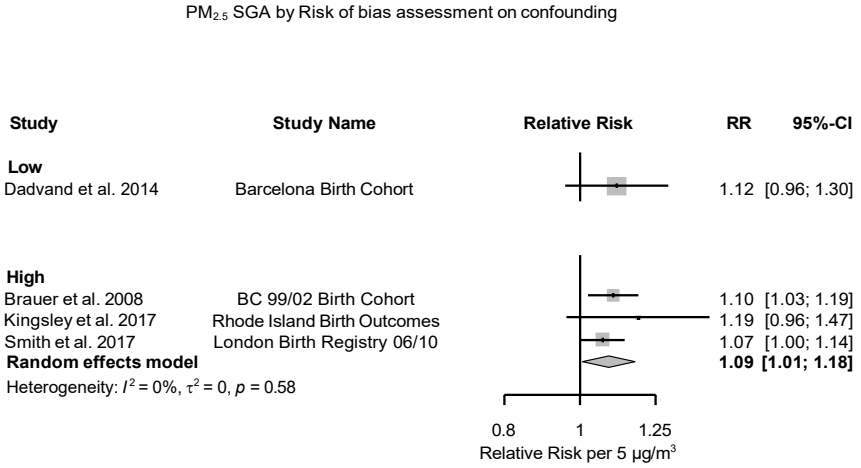
Brauer et al. 2008 and Kingsley et al. 2017 from North America, Dadvand et al. 2013 and Smith et al. 2017 from Western Europe.

By study design – all cohort studies

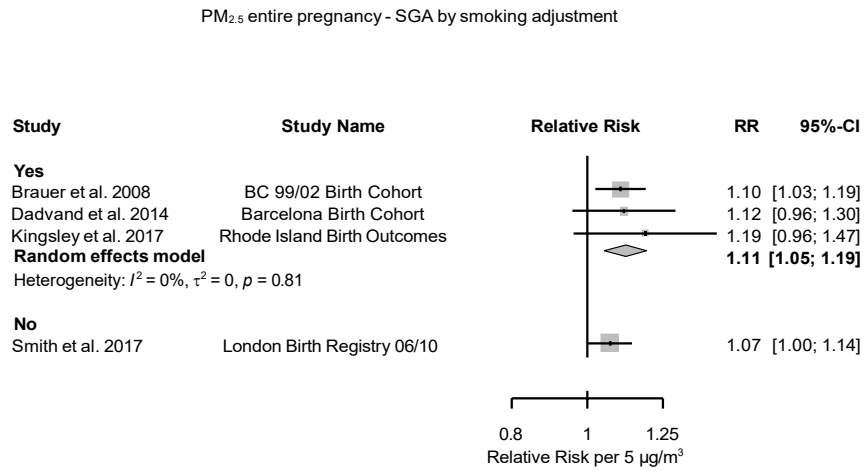
By traffic specificity - all rated moderate

By risk of bias

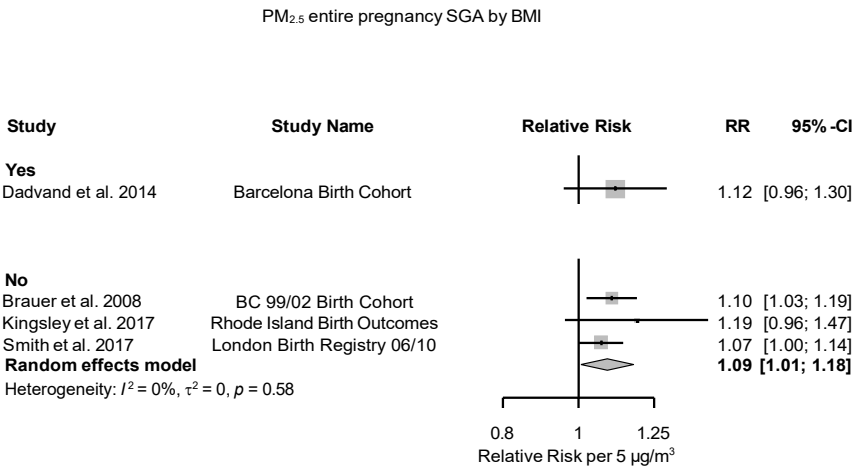
Plots not shown for risk of bias domains if all studies were rated low or moderate



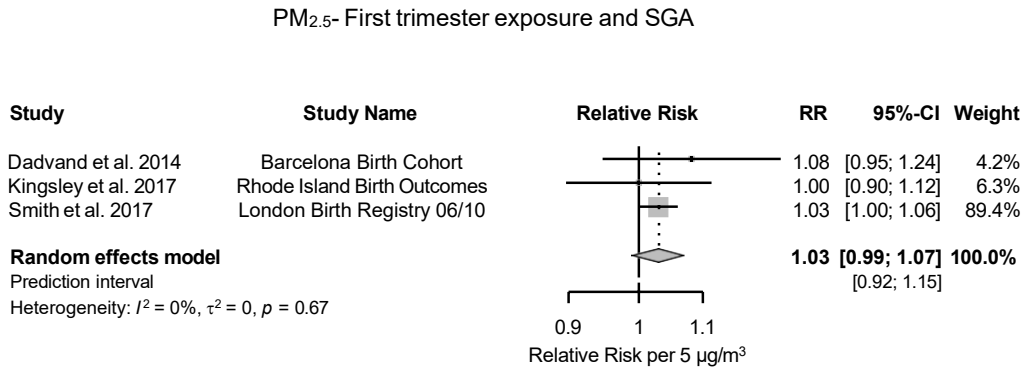
By smoking adjustment



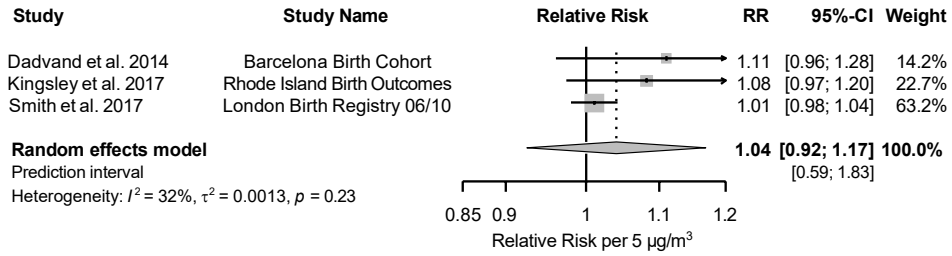

By BMI adjustment



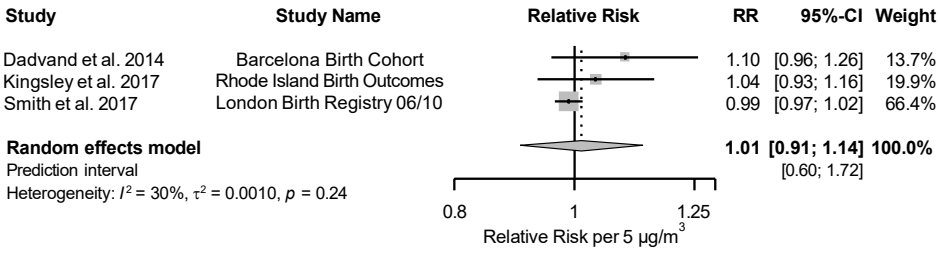
**$PM_{2.5}$ First trimester exposure - primary meta-analysis - SGA**




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




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

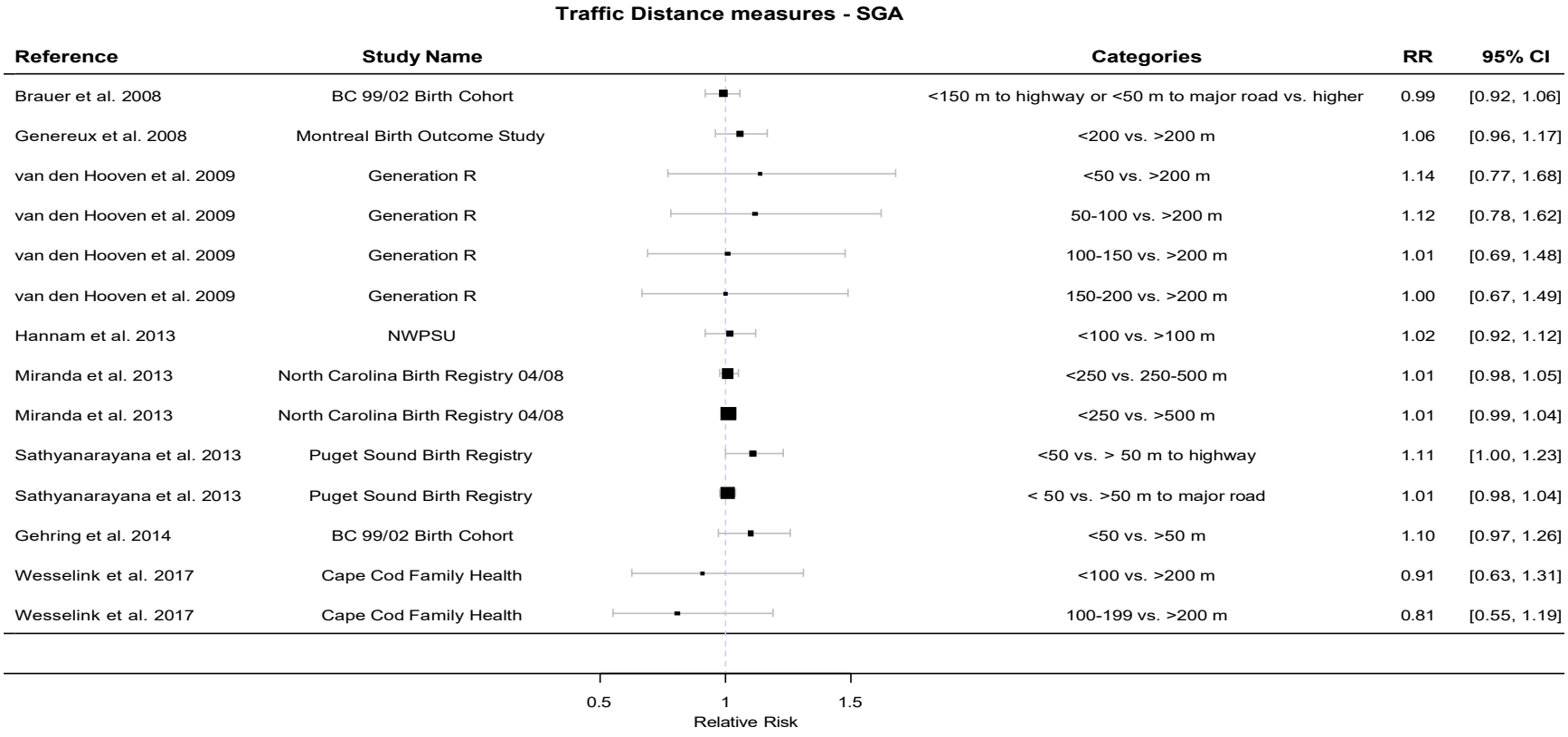



2 Western European and 1 North American cohort. All rated moderate in traffic specificity.

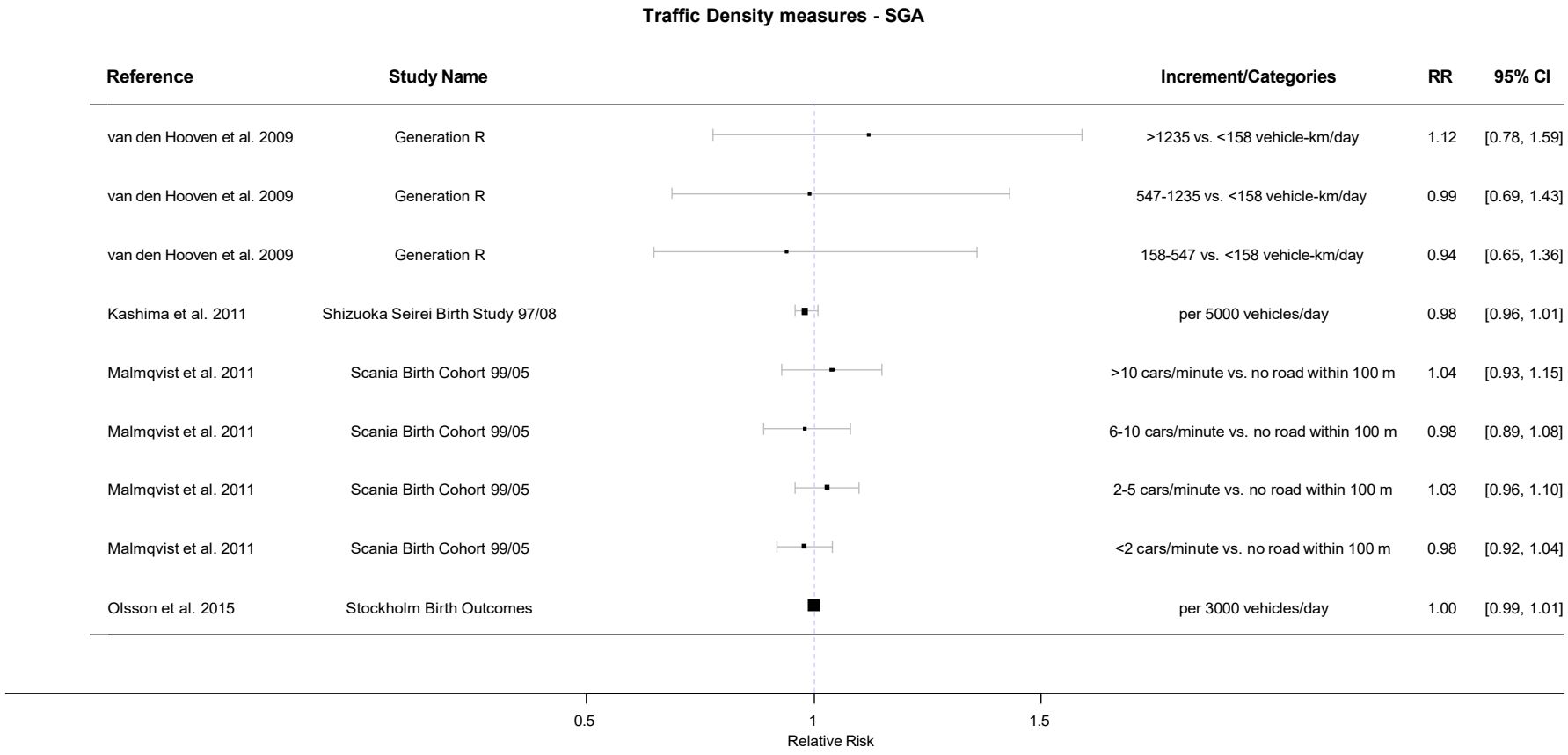
Dadvand et al. 2014 adjusted for smoking and BMI. Smith et al. 2017 did not adjust for smoking.

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**

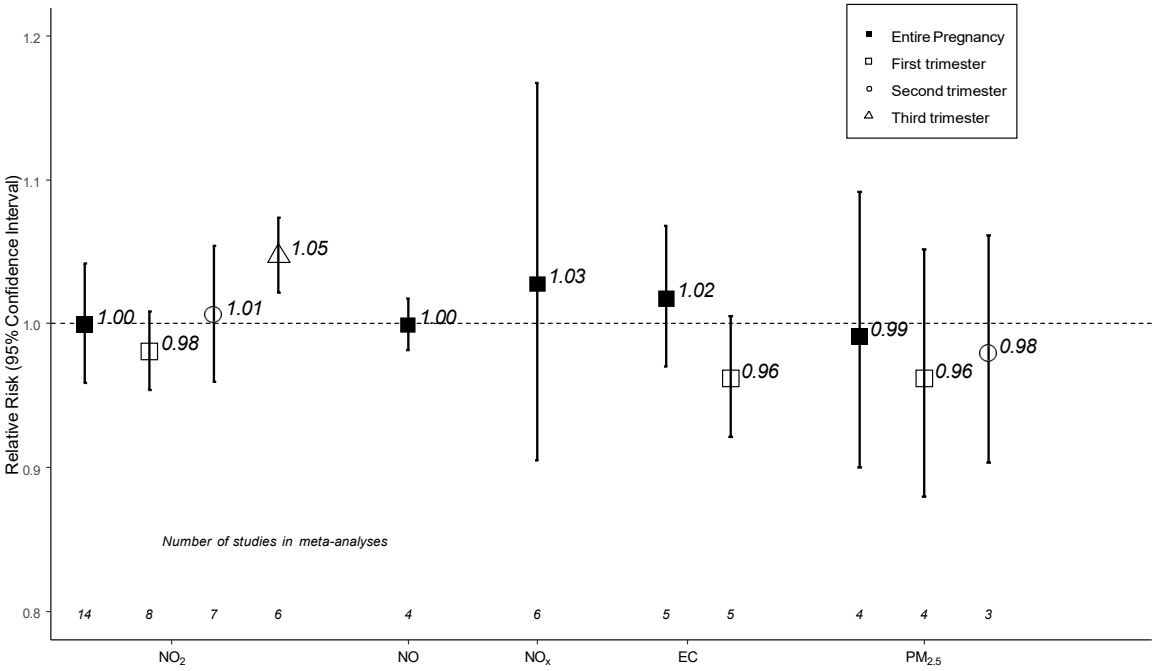


**Density measures**



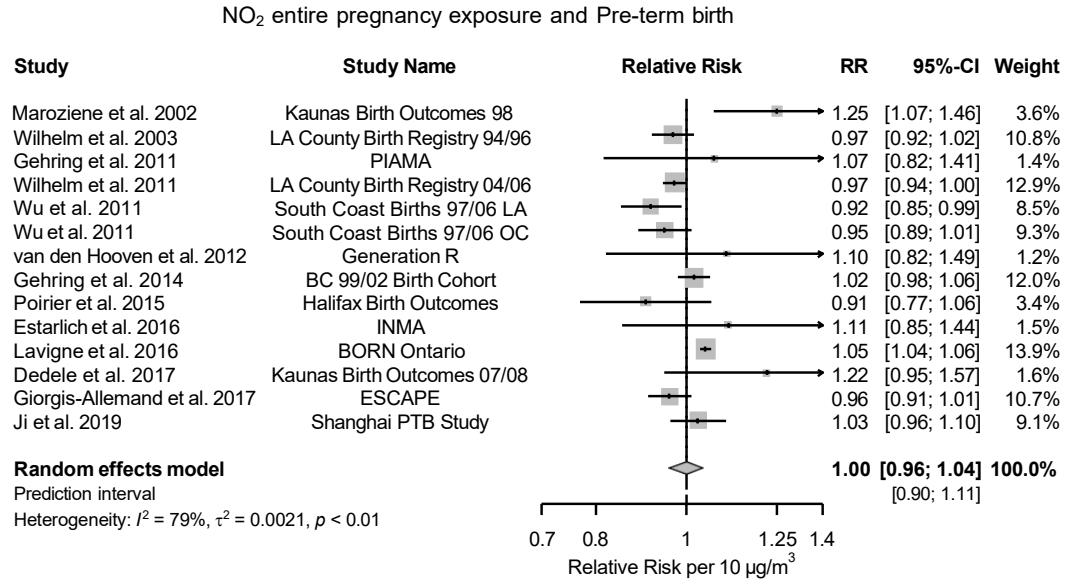
## 8.4 Preterm birth (PTB)

Summary of meta-analysis

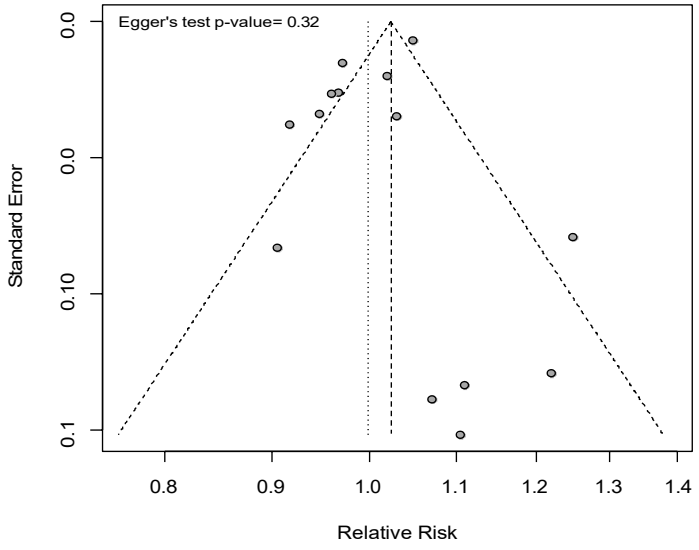



Footnote: The following increments were used: 10 µg/m$^3$ for $NO_2$, 10 µg/m$^3$ for NO, 20 µg/m$^3$ for $NO_x$, 1 µg/m$^3$ for EC and 5 µg/m$^3$ for $PM_{2.5}$. Effect estimates cannot be directly compared across the different traffic-related pollutants because the selected increments do not necessarily represent the same contrast in exposure.

**$NO_2$ Entire pregnancy exposure - primary meta-analysis - PTB**



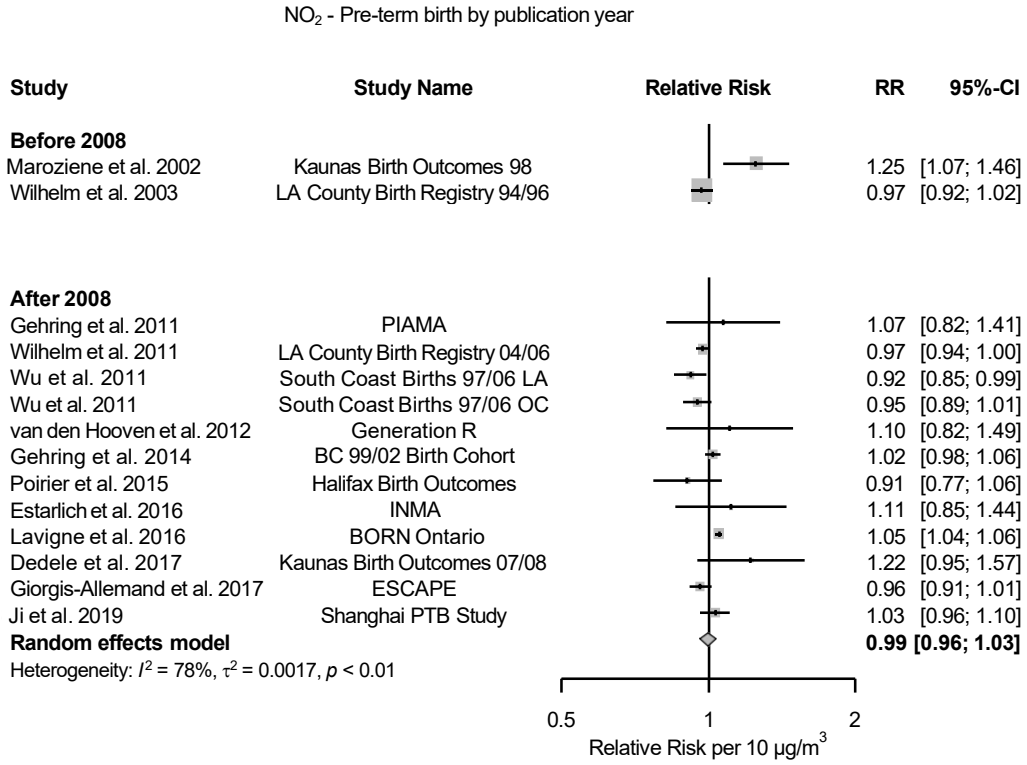

Publication bias – entire pregnancy exposure



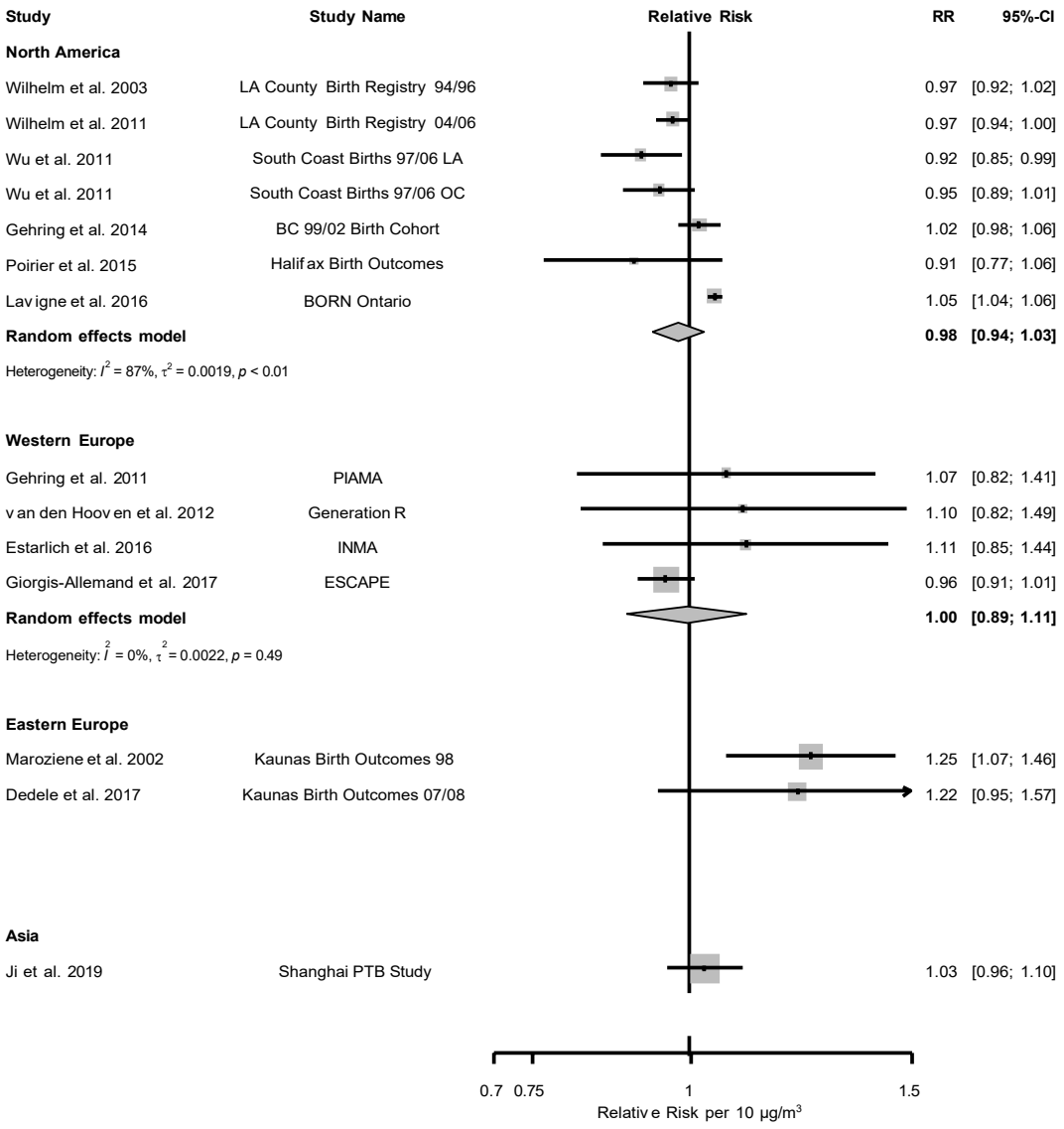

Footnote: The vertical lines in the funnel plots represent the pooled fixed and random effect estimates. The vertical dashed line in the middle of the funnel shows the fixed effect estimate. As the Panel applied a random-effects model, the funnel plot also presents the random-effects estimate with the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

Subgroup analysis – entire pregnancy exposure

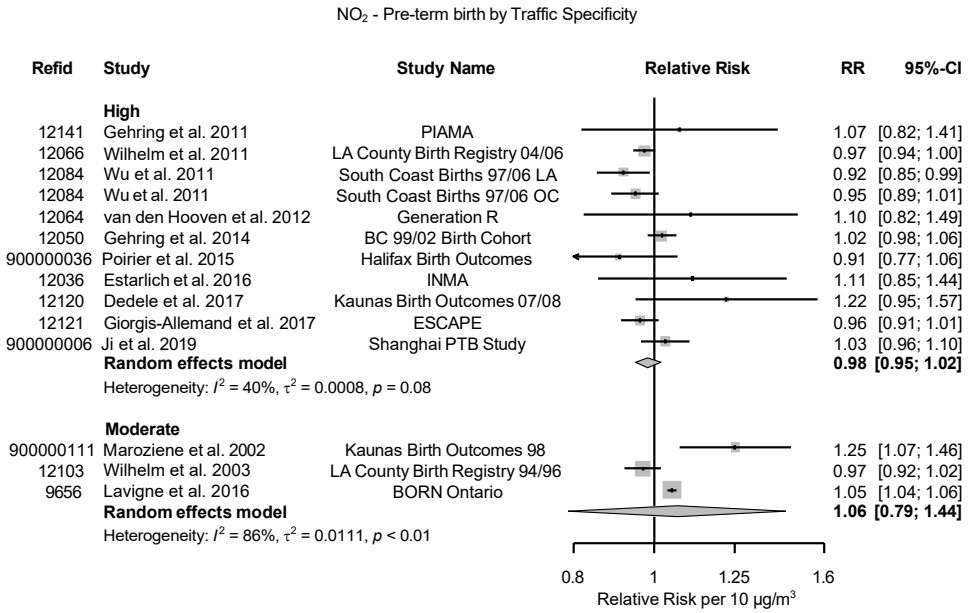
By publication year



By region

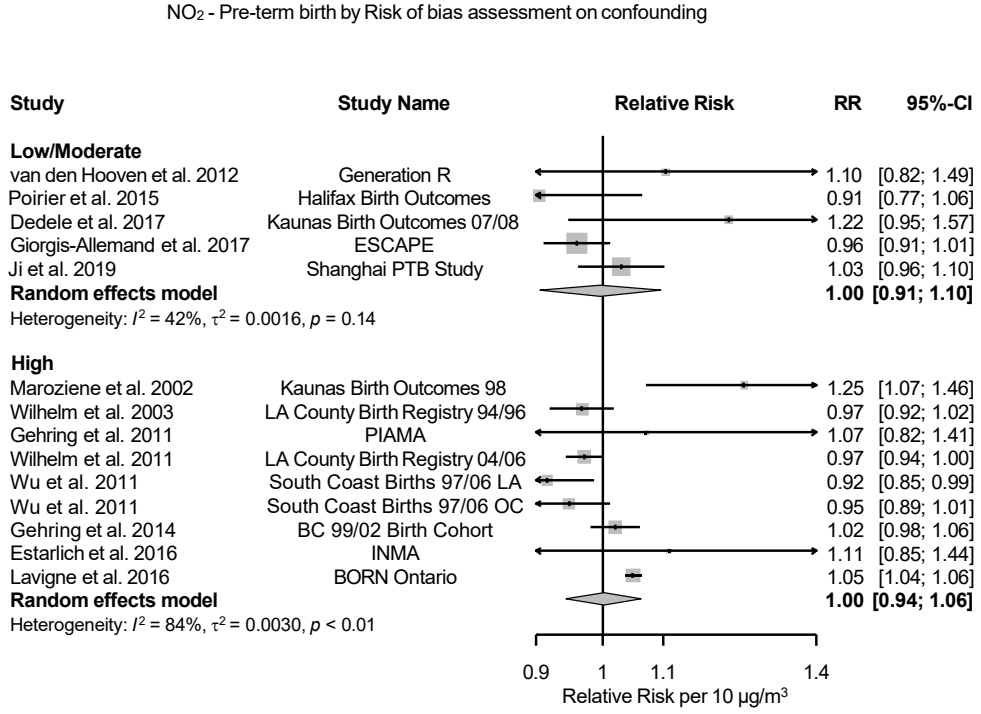

Study
Study Name
Relative Risk
RR
95%-CI
North America
Wilhelm et al. 2003
LA County Birth Registry 94/96
0.97 [0.92; 1.02]
Wilhelm et al. 2011
LA County Birth Registry 04/06
0.97 [0.94; 1.00]
Wu et al. 2011
South Coast Births 97/06 LA
0.92 [0.85; 0.99]
Wu et al. 2011
South Coast Births 97/06 OC
0.95 [0.89; 1.01]
Gehring et al. 2014
BC 99/02 Birth Cohort
1.02 [0.98; 1.06]
Poirier et al. 2015
Halifax Birth Outcomes
0.91 [0.77; 1.06]
Lavigne et al. 2016
BORN Ontario
1.05 [1.04; 1.06]
Random effects model
0.98 [0.94; 1.03]
Heterogeneity: $I^2$ = 87%, $\tau^2$ = 0.0019, $p$ < 0.01
Western Europe
Gehring et al. 2011
PIAMA
1.07 [0.82; 1.41]
van den Hooven et al. 2012
Generation R
1.10 [0.82; 1.49]
Estarlich et al. 2016
INMA
1.11 [0.85; 1.44]
Giorgis-Allemand et al. 2017
ESCAPE
0.96 [0.91; 1.01]
Random effects model
1.00 [0.89; 1.11]
Heterogeneity: $I^2$ = 0%, $\tau^2$ = 0.0022, $p$ = 0.49
Eastern Europe
Maroziene et al. 2002
Kaunas Birth Outcomes 98
1.25 [1.07; 1.46]
Dedele et al. 2017
Kaunas Birth Outcomes 07/08
1.22 [0.95; 1.57]
Asia
Ji et al. 2019
Shanghai PTB Study
1.03 [0.96; 1.10]
0.7
0.75
1
1.5
Relative Risk per 10 µg/m3

By traffic specificity

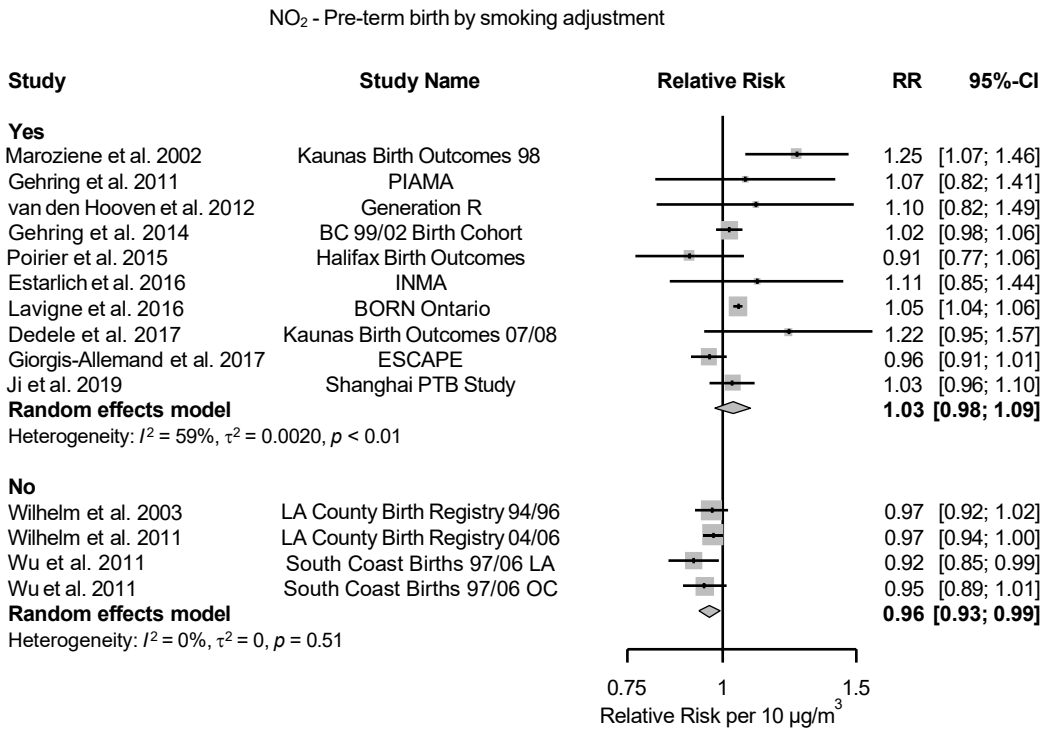



By risk of bias

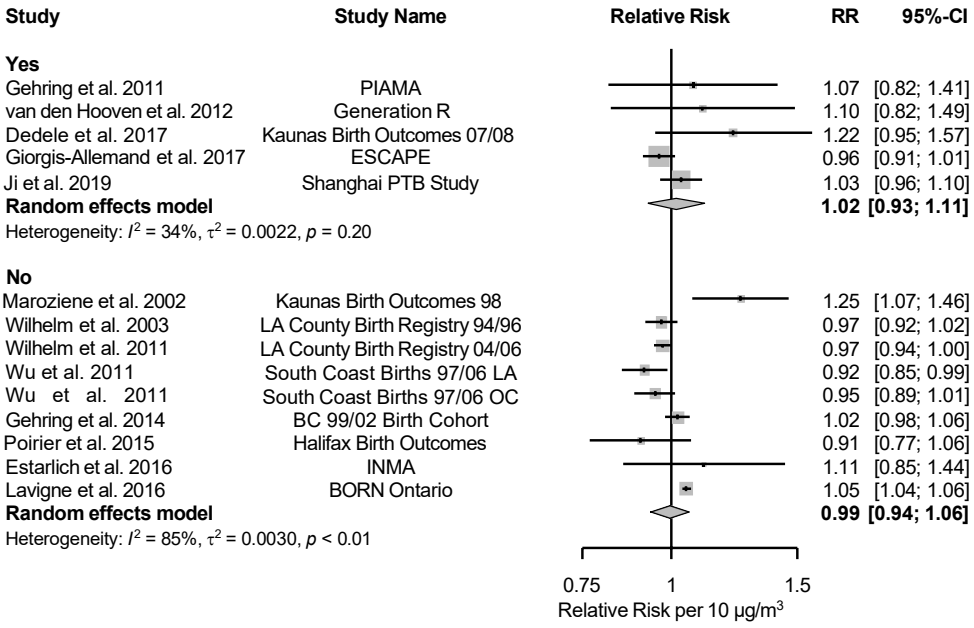
Plots not shown for risk of bias domains if all studies were rated low or moderate



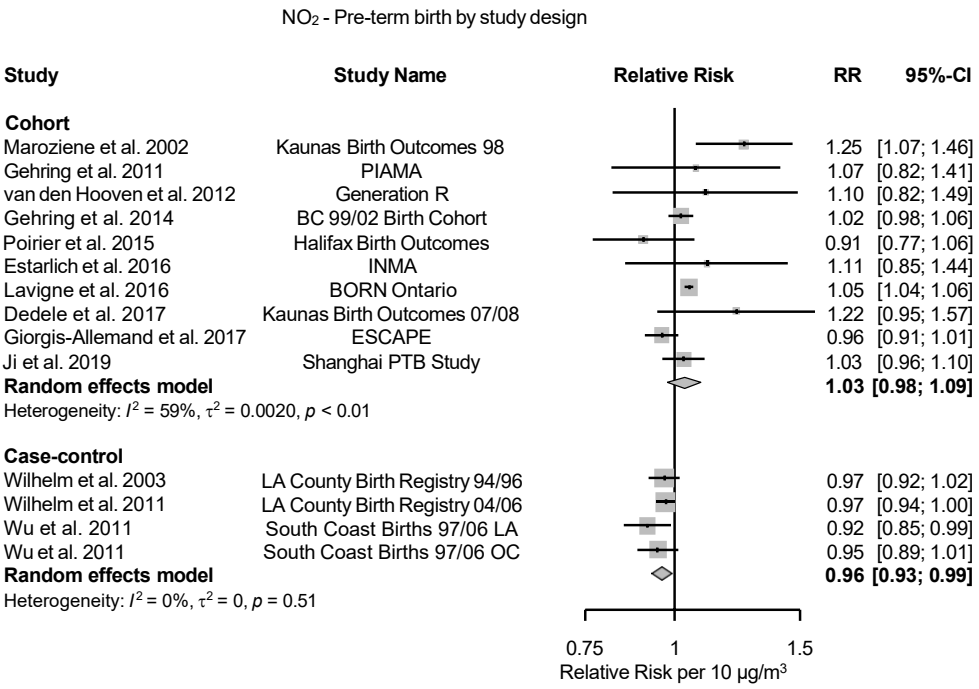
By smoking adjustment



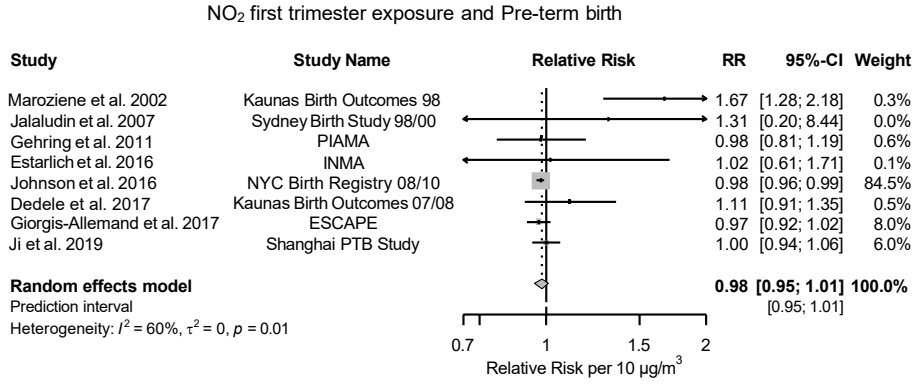

By BMI adjustment



By study design

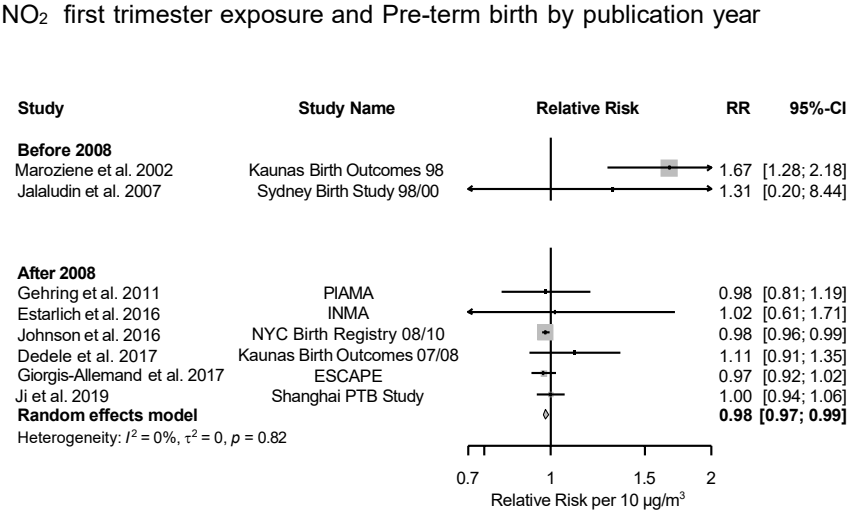


**$NO_2$ First trimester exposure - primary meta-analysis - PTB**

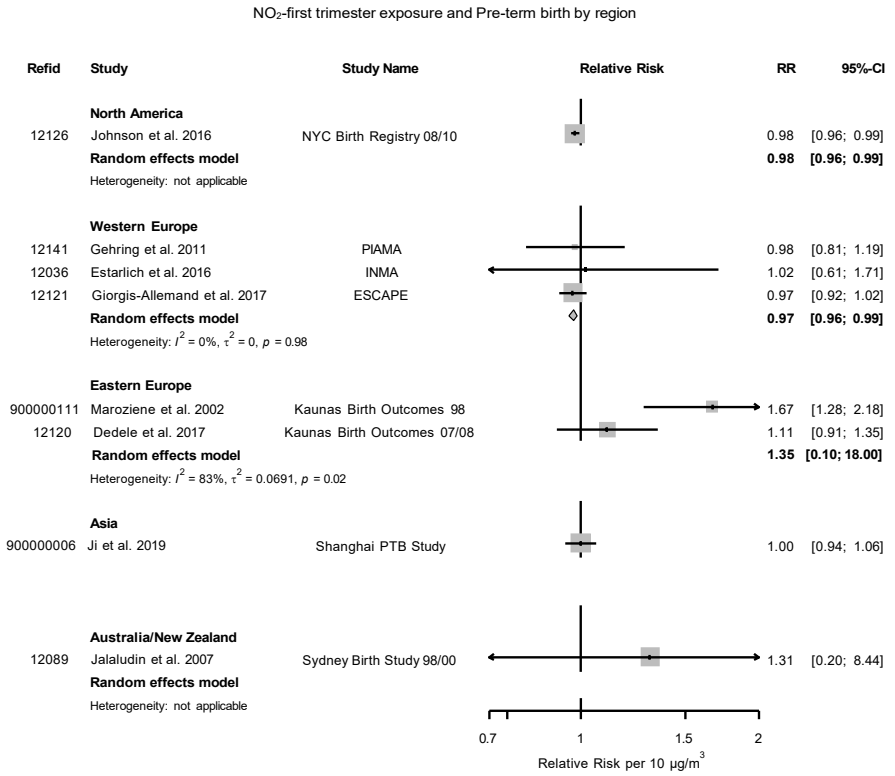



Subgroup analysis – first trimester exposure

By publication year

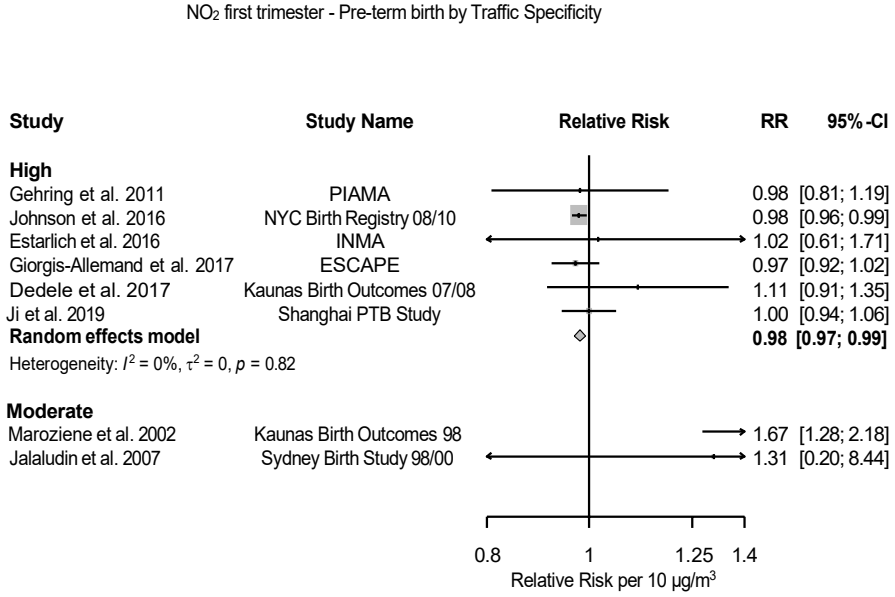


By region



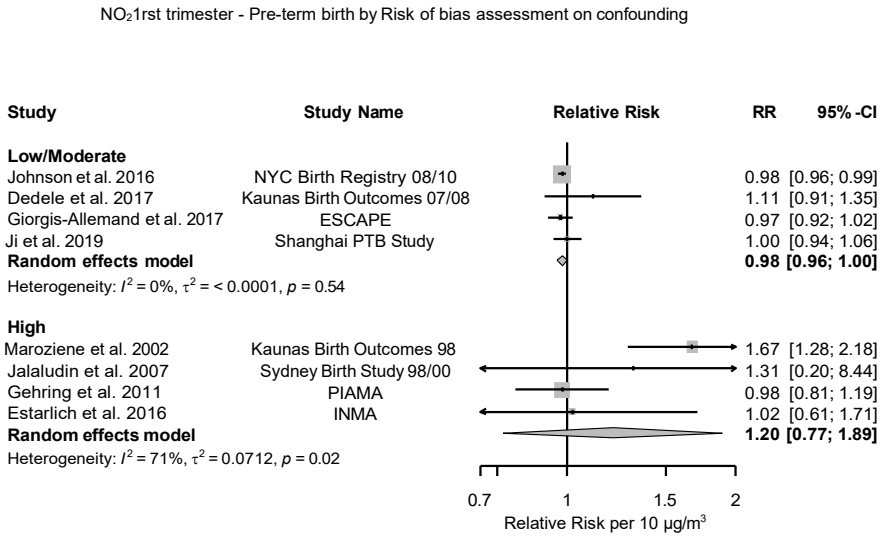

By study design – all cohort studies

By traffic specificity



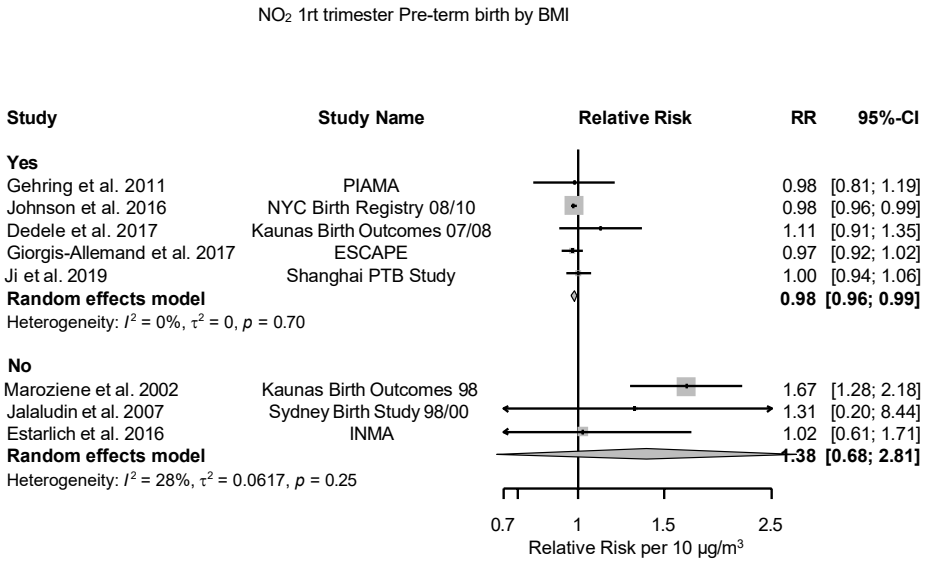
By risk of bias

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

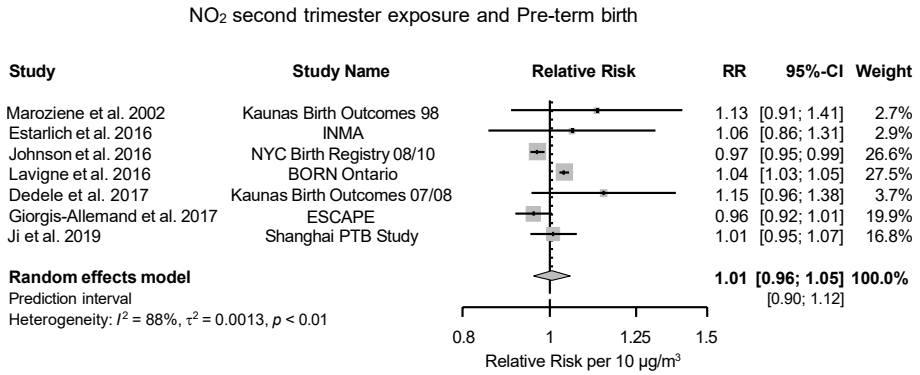



By smoking adjustment - all studies adjusted for smoking

By BMI adjustment

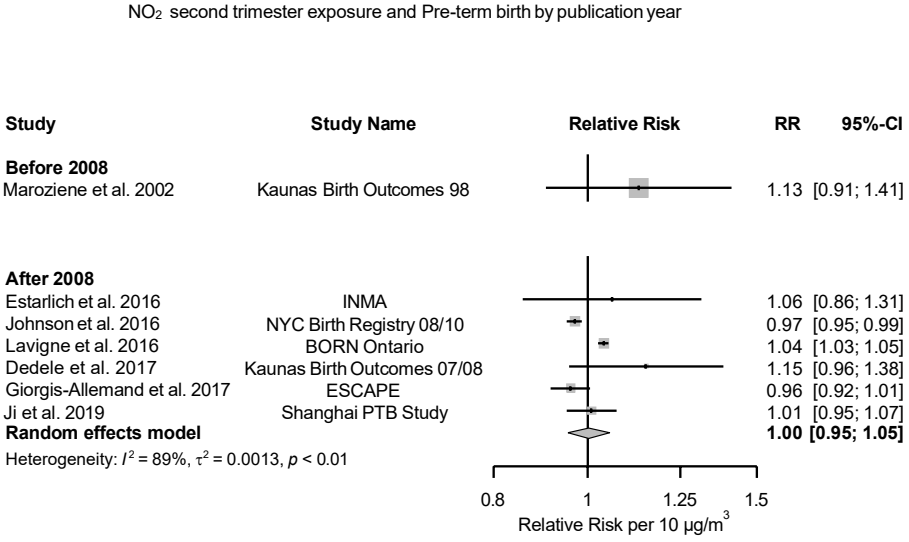


**$NO_2$ Second trimester exposure - primary meta-analysis - PTB**




Subgroup – second trimester exposure

By publication year

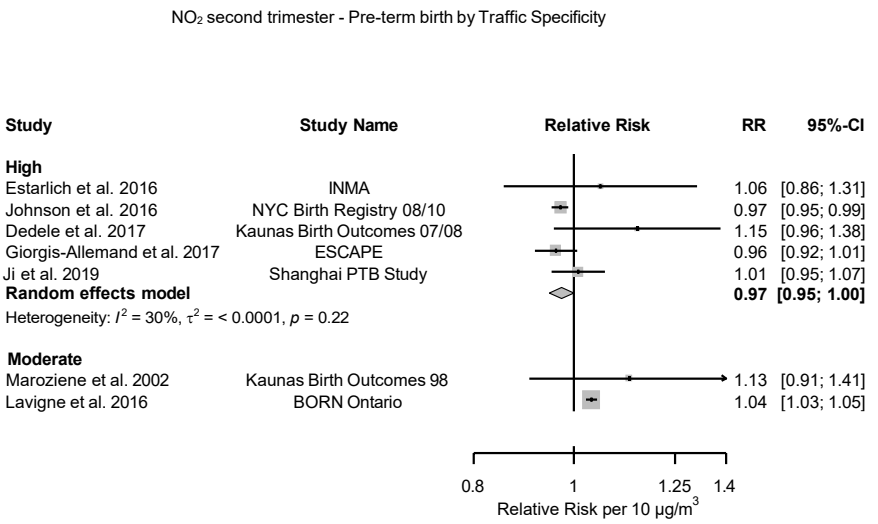



By region

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.

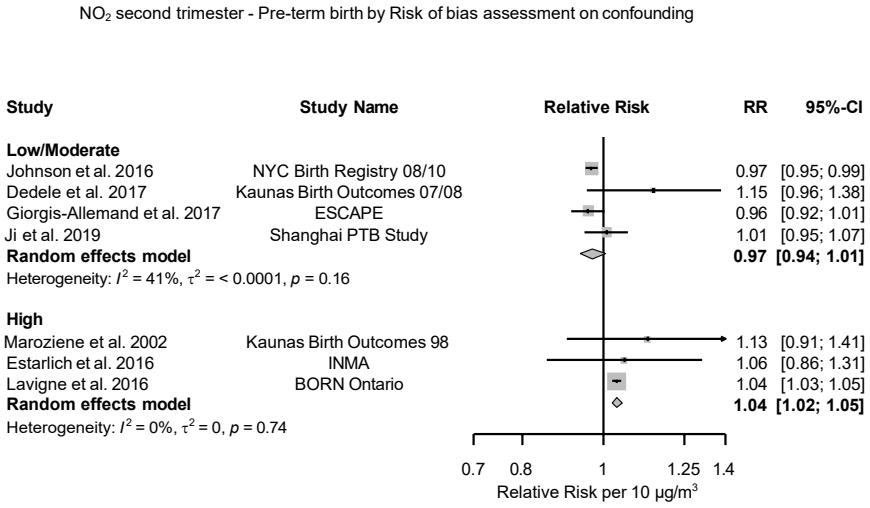
By study design – all cohort studies

By traffic specificity



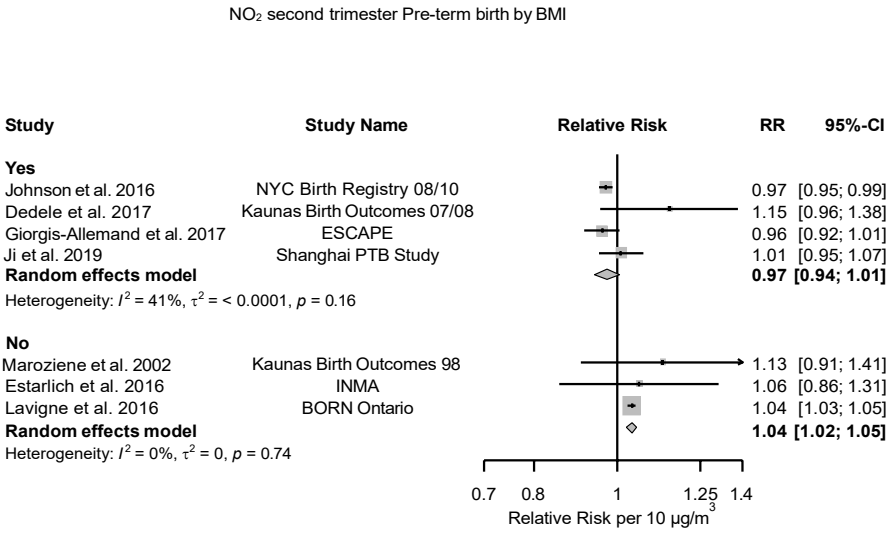

By risk of bias

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

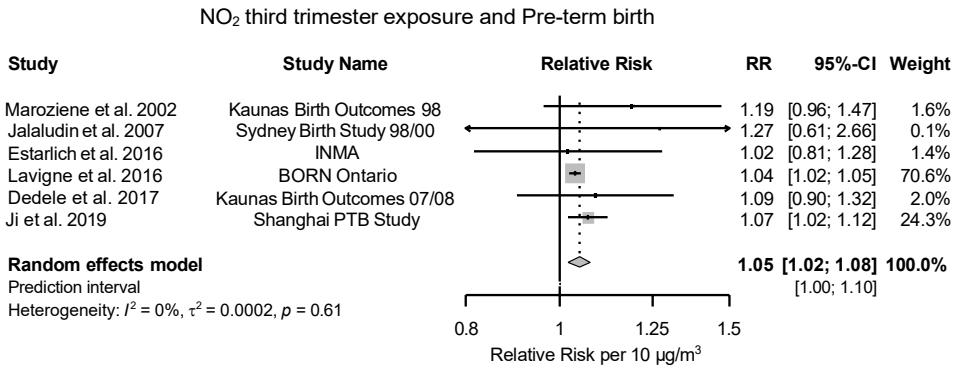


By smoking adjustment - all adjusted for smoking

By BMI adjustment

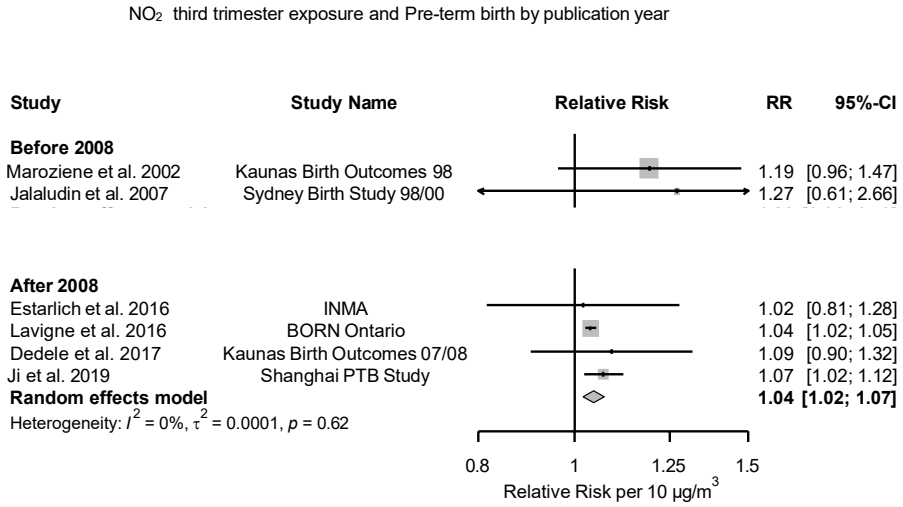


**$NO_2$ Third trimester exposure - primary meta-analysis - PTB**




Subgroup analysis – third trimester exposure

By publication year

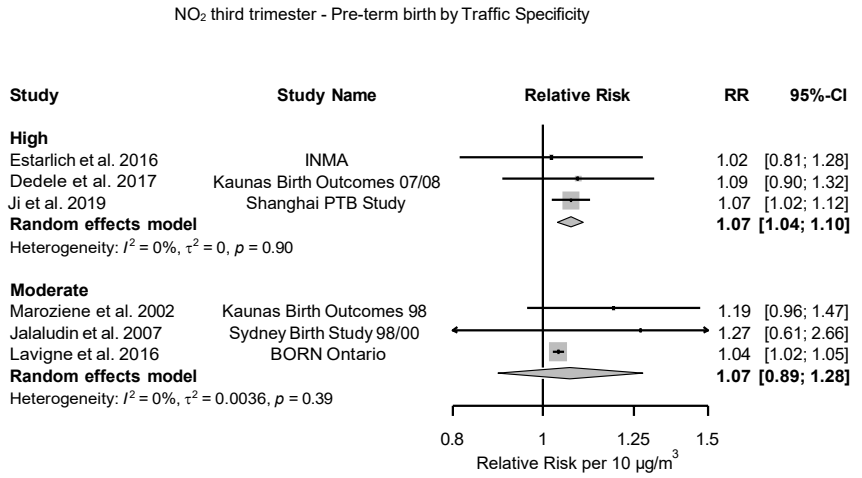



By study design – all cohort studies

By region

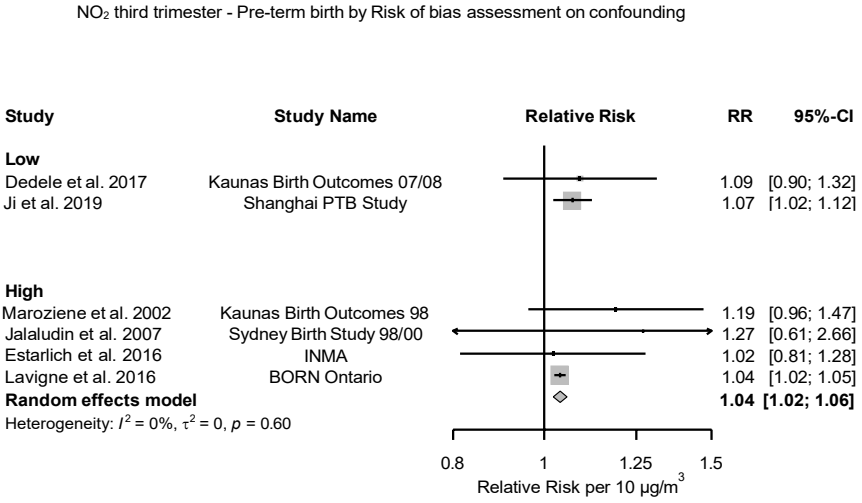
Lavigne et al. 2016 from North America; Estarlich et al. 2016 from Western Europe; Maroziene et al. 2002 and Dedele et al. 2017 from Eastern Europe, Ji et al. 2019 from Asia and Jalaludin et al. 2007 from Australia.

By traffic specificity



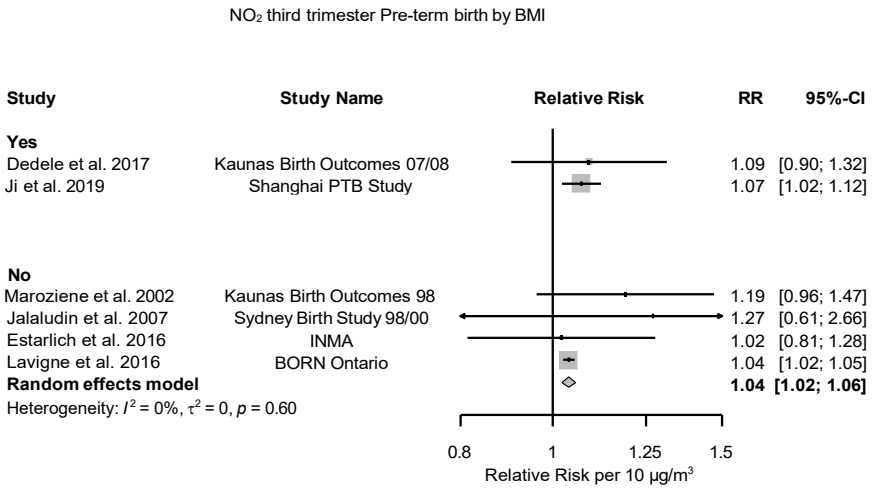

By risk of bias

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

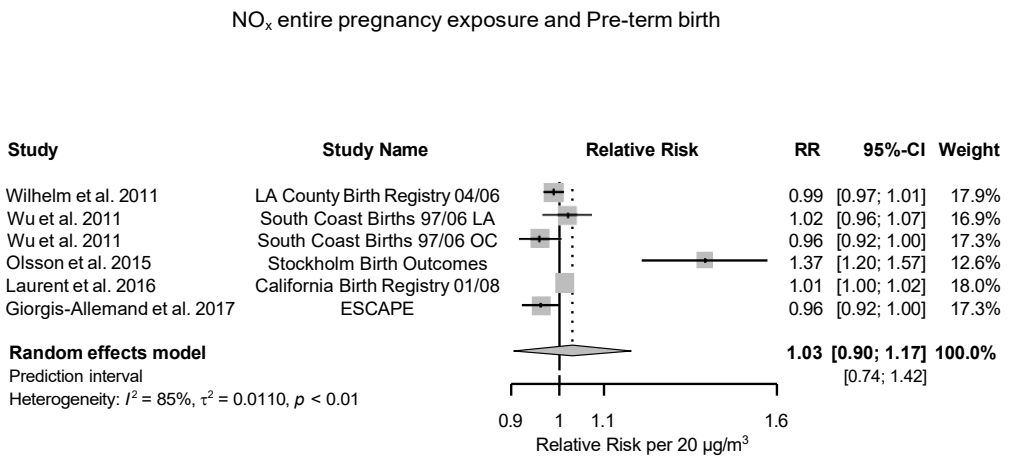


By smoking adjustment - all adjusted for smoking

By BMI adjustment

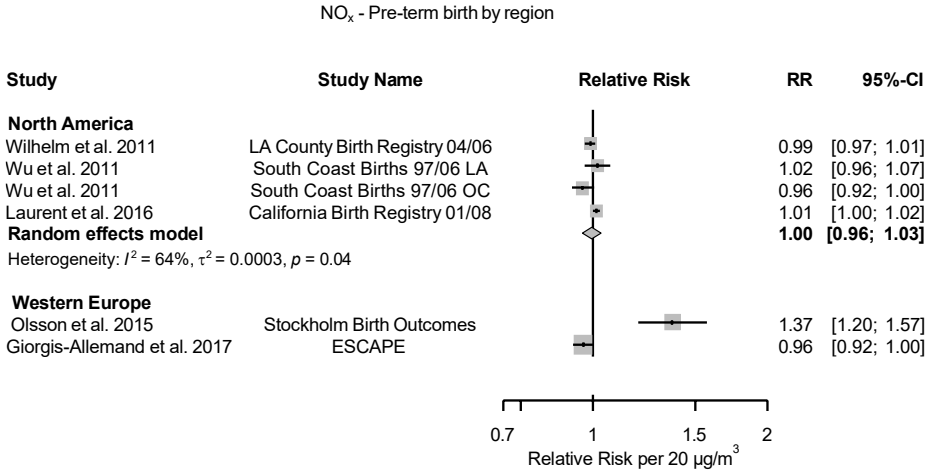


**$NO_x$ Entire pregnancy exposure - primary meta-analysis - PTB**

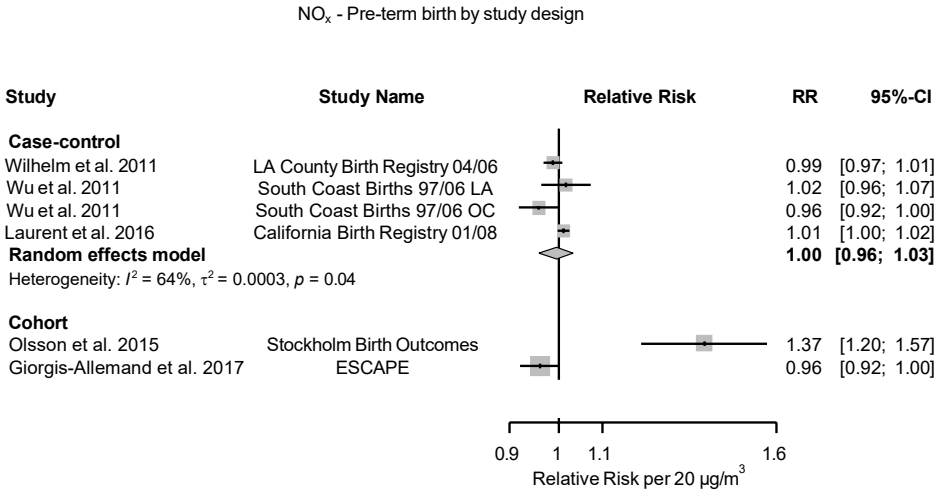



Subgroup analysis – entire pregnancy exposure

By region



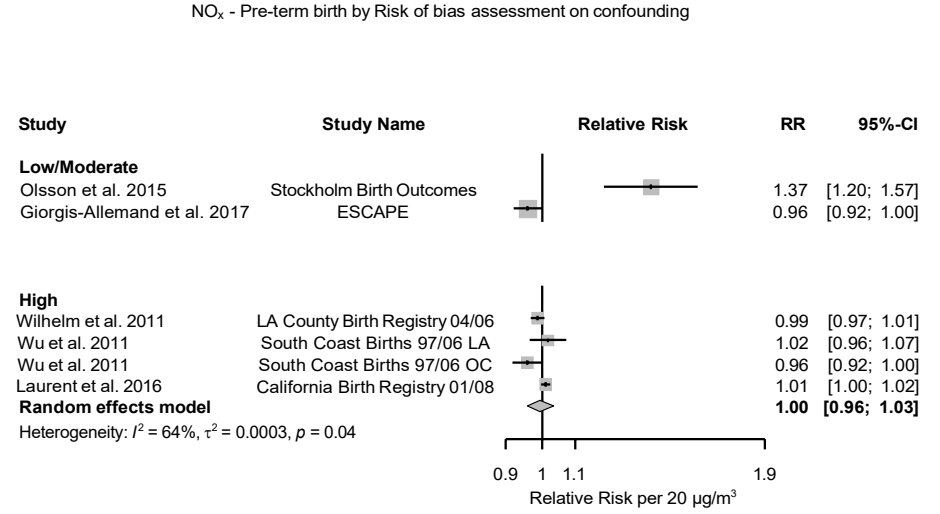
By study design



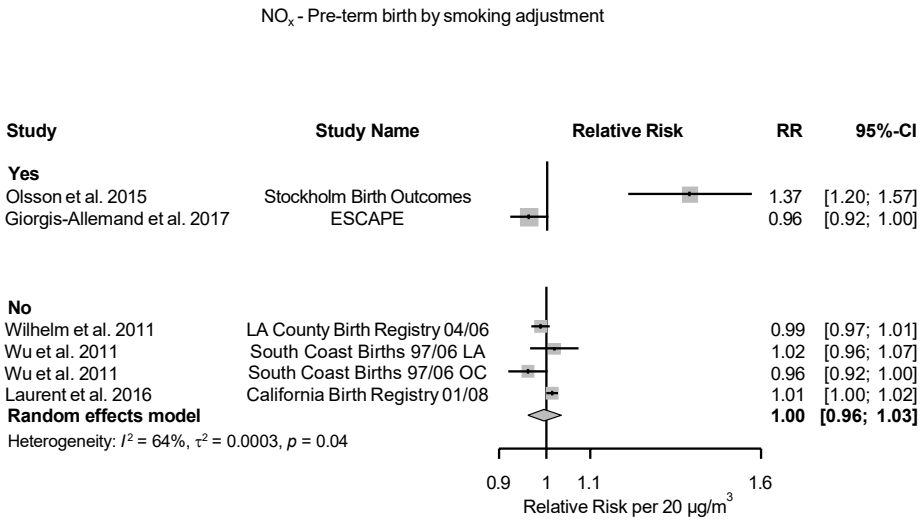

By traffic specificity - all high traffic specificity

By risk of bias

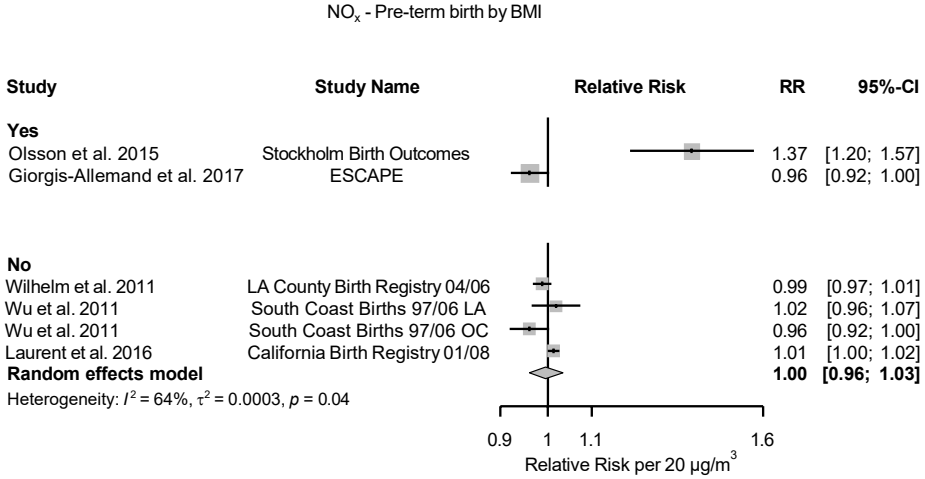
Plots not shown for risk of bias domains if all studies were rated low or moderate



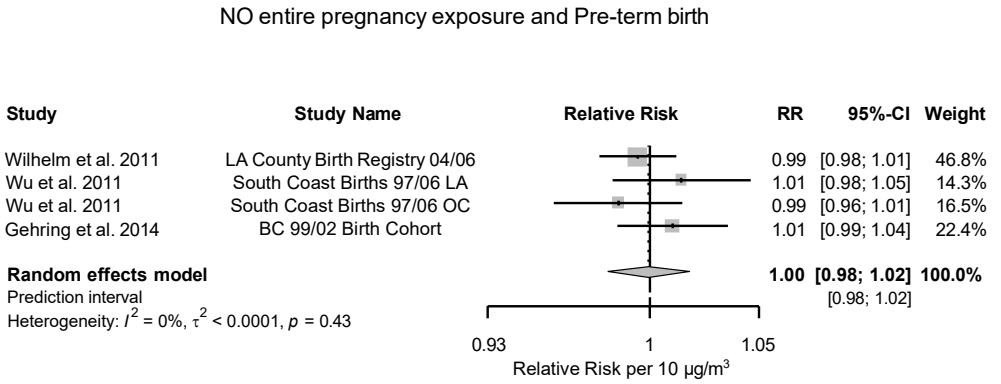
By smoking adjustment




By BMI adjustment



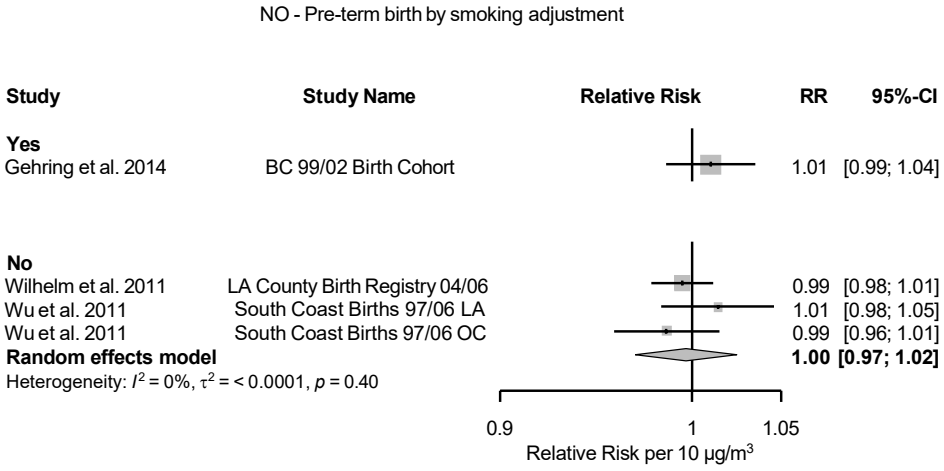
**NO Entire pregnancy exposure - primary meta-analysis - PTB**




By traffic specificity - all high traffic specificity

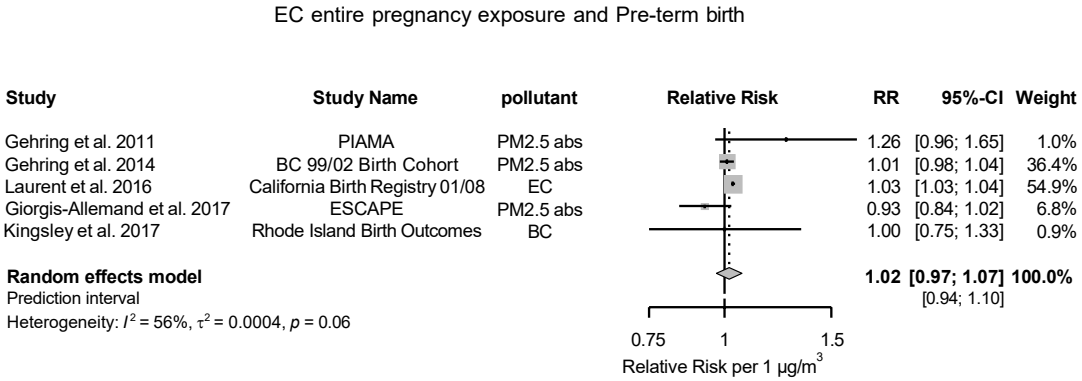
By risk of bias - all high risk of bias for confounding and low or moderate for other categories.

By smoking adjustment



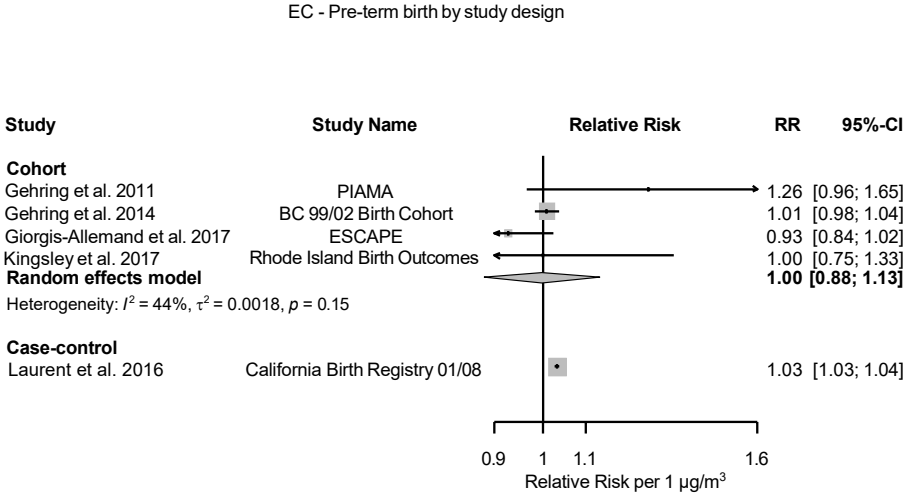

By BMI adjustment - no studies adjusted for BMI

**EC Entire pregnancy exposure - primary meta-analysis - PTB**

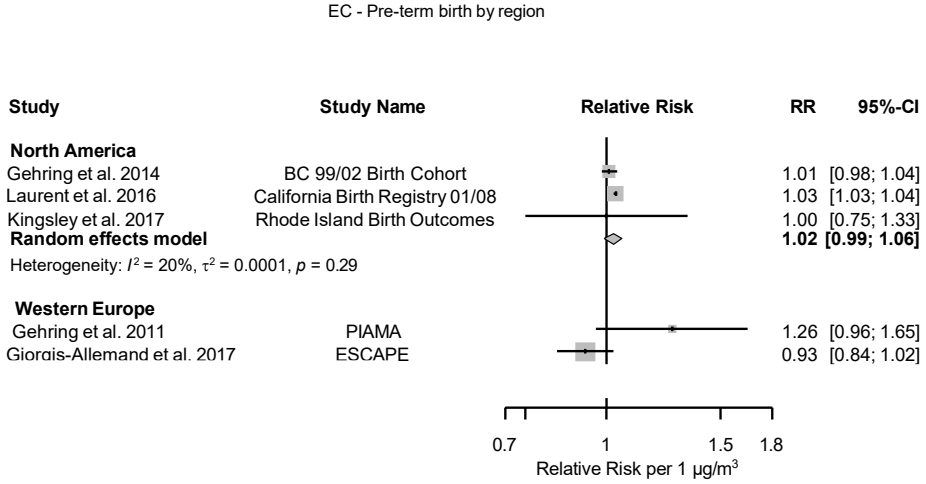



Subgroup analysis – entire pregnancy exposure

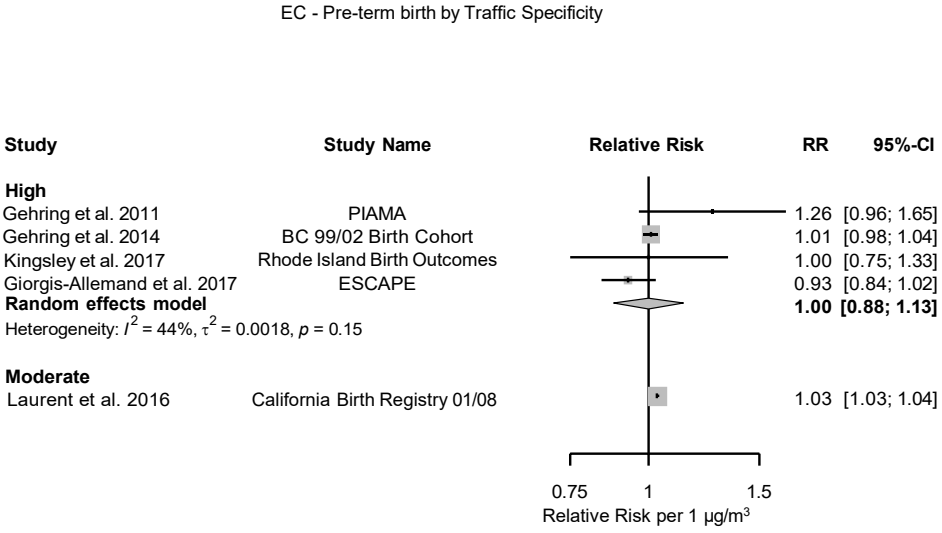
By study design



By region

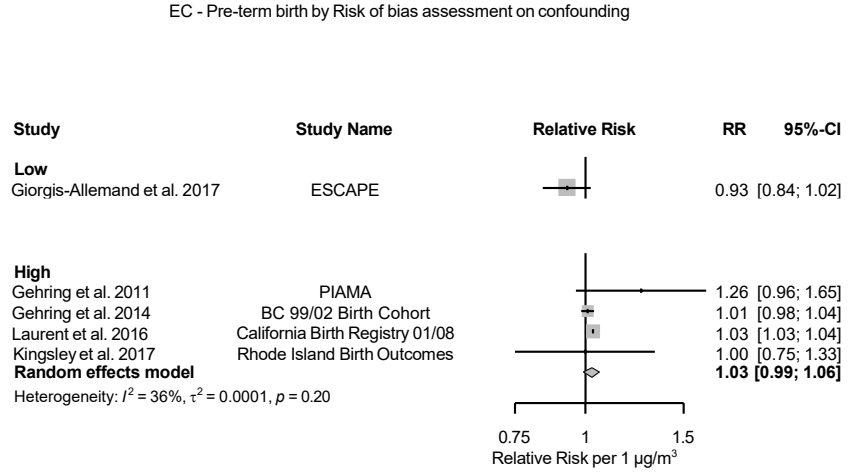



By traffic specificity

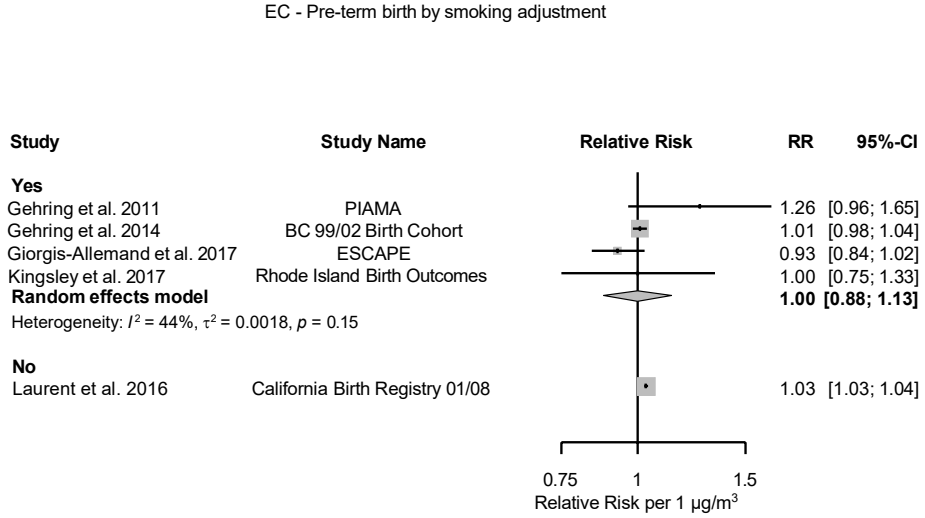


By risk of bias

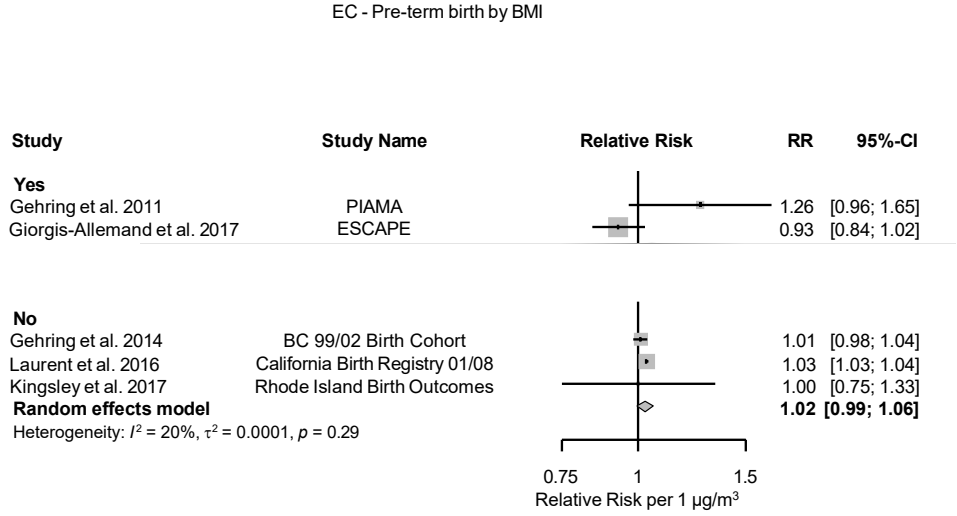
Plots not shown for risk of bias domains if all studies were rated low or moderate



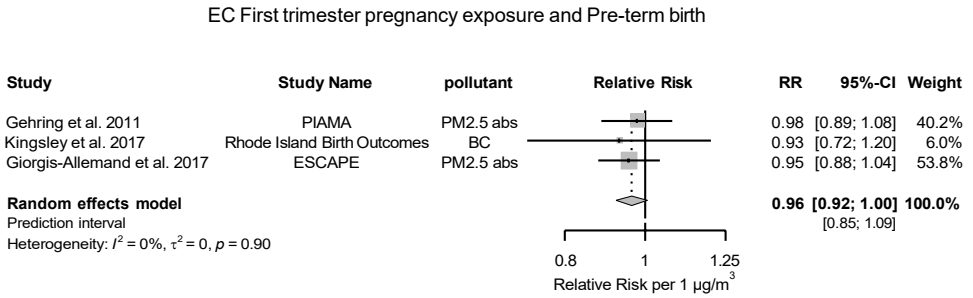
By smoking adjustment




By BMI adjustment



**EC First trimester exposure – primary meta-analysis - PTB**

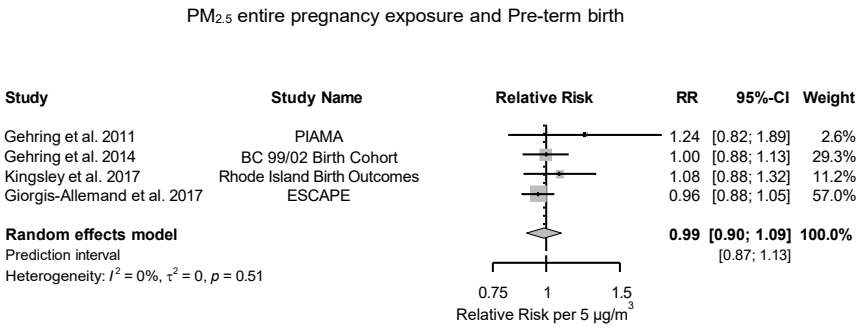



Subgroup analyses

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**




Subgroup analysis – entire pregnancy exposure

By region

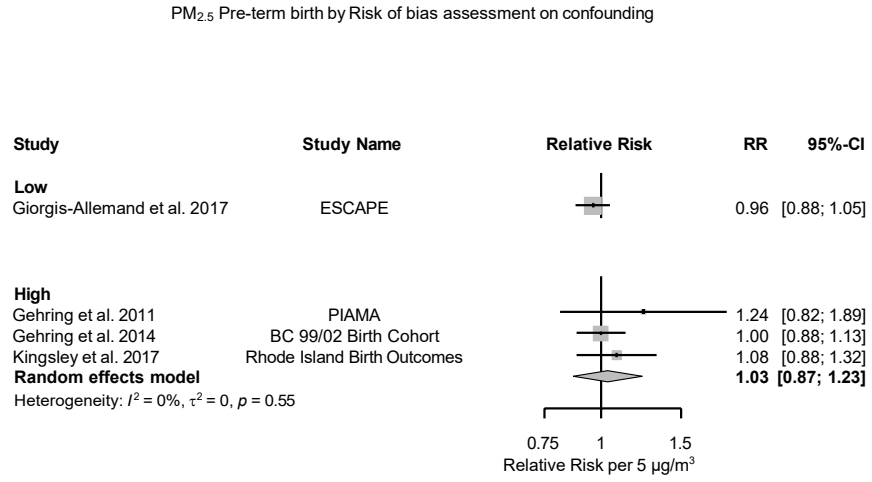
Gehring et al. 2014 and Kingsley et al. 2017 from North America, Gehring et al. 2011 and Giorgis-Allemand et al. 2017 from Western Europe.

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

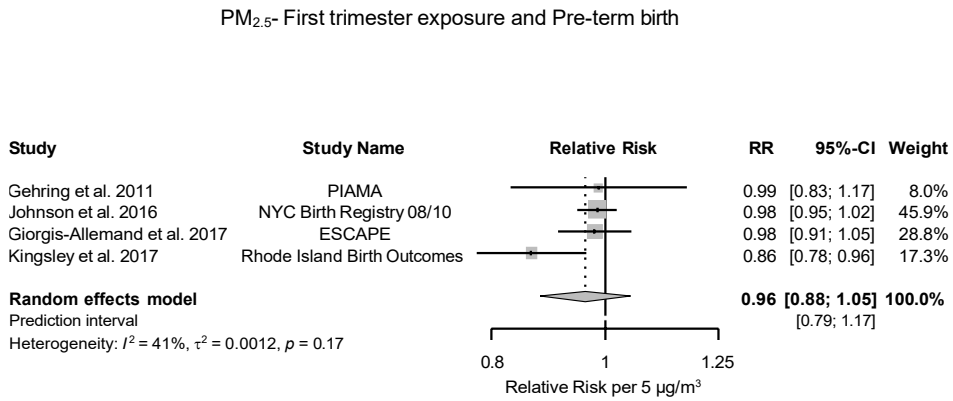



By smoking adjustment – all studies adjusted for smoking

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**




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.

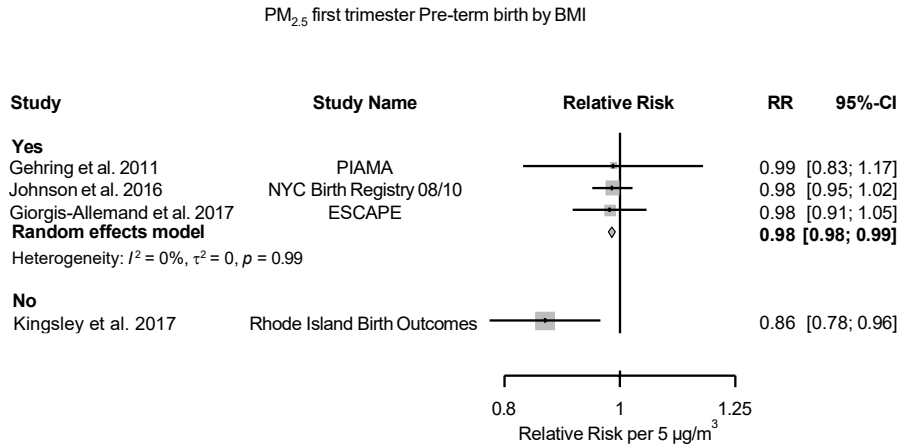
By study design - all cohort studies

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




By smoking adjustment – all studies adjusted for smoking

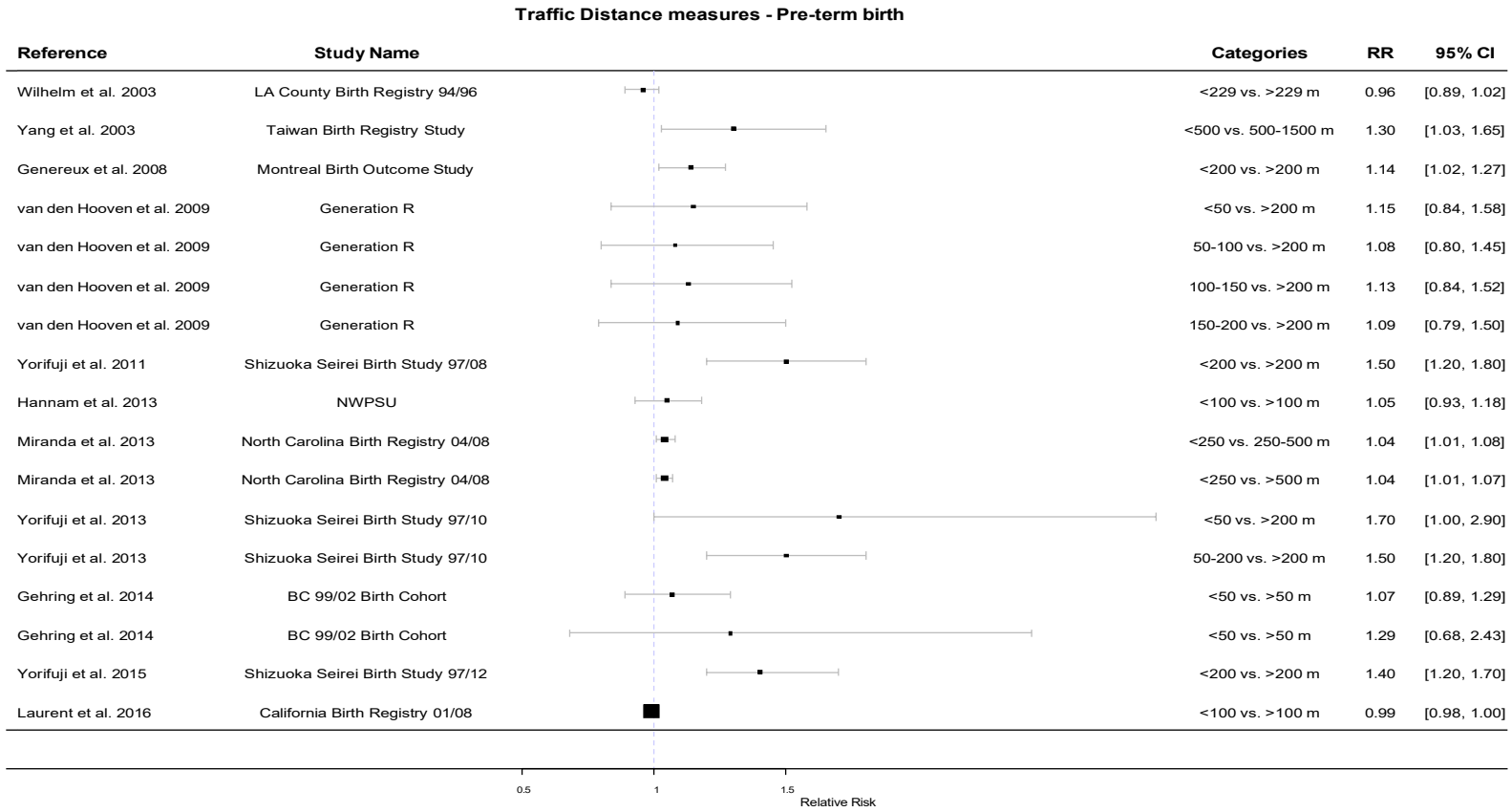
**$PM_{2.5}$ Second trimester exposure – primary meta-analysis - PTB**


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



## Density measures

**Traffic Density measures - Pre-term birth**

| Reference | Study Name | Increment/Categories | RR | 95% CI |
|---|---|---|---|---|
| van den Hooven et al. 2009 | Generation R | >1235 vs. <158 vehicle-km/day | 1.18 | [0.87, 1.59] |
| van den Hooven et al. 2009 | Generation R | 547-1235 vs. <158 vehicle-km/day | 1.33 | [0.98, 1.79] |
| van den Hooven et al. 2009 | Generation R | 158-547 vs. <158 vehicle-km/day | 1.37 | [1.02, 1.84] |
| Malmqvist et al. 2011 | Scania Birth Cohort 99/05 | >10 cars/minute vs. no road within 100 m | 0.88 | [0.76, 1.02] |
| Malmqvist et al. 2011 | Scania Birth Cohort 99/05 | 6-10 cars/minute vs. no road within 100 m | 0.94 | [0.82, 1.07] |
| Malmqvist et al. 2011 | Scania Birth Cohort 99/05 | 2-5 cars/minute vs. no road within 100 m | 0.97 | [0.88, 1.06] |
| Malmqvist et al. 2011 | Scania Birth Cohort 99/05 | <2 cars/minute vs. no road within 100 m | 1.01 | [0.94, 1.10] |
| Wu et al. 2011 | South Coast Births 97/06 LA | per 76.6 vehicles/day/m | 1.02 | [1.00, 1.04] |
| Wu et al. 2011 | South Coast Births 97/06 OC | per 76.6 vehicles/day/m | 1.00 | [0.98, 1.03] |
| Padula et al. 2014 | San Joaquin Valley Birth Study | >13561 vs. <13561 vehicles/day | 1.25 | [1.00, 1.56] |
| Padula et al. 2014 | San Joaquin Valley Birth Study | >13561 vs. <13561 vehicles/day | 1.13 | [0.96, 1.33] |
| Padula et al. 2014 | San Joaquin Valley Birth Study | >13561 vs. <13561 vehicles/day | 1.05 | [0.95, 1.15] |
| Padula et al. 2014 | San Joaquin Valley Birth Study | >13561 vs. <13561 vehicles/day | 1.10 | [1.01, 1.19] |
| Padula et al. 2014 | San Joaquin Valley Birth Study | >13561 vs. <13561 vehicles/day | 1.04 | [1.00, 1.07] |
| Olsson et al. 2015 | Stockholm Birth Outcomes | per 3000 vehicles/day | 1.00 | [0.99, 1.02] |
| Laurent et al. 2016 | California Birth Registry 01/08 | per 10000 vehicles/day/m | 0.97 | [0.94, 1.00] |
| Giorgis-Allemand et al. 2017 | ESCAPE | per 4000 vehicle-km/day | 0.96 | [0.89, 1.03] |