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## Supplemental Material

# Fine Particulate Air Pollution and Adverse Birth Outcomes: Effect Modification by Regional Nonvolatile Oxidative Potential

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**Table S1.** Pearson correlation coefficients across time periods for air pollution measures.

| Air pollutant | $PM_{2.5}$ ($\mu g/m^3$) | | | | | Oxidative potential | |
|---|---|---|---|---|---|---|---|
| | 1st trimester | 2nd trimester | 3rd trimester | Pregnancy average | | $OP^{GSH}$ | $OP^{AA}$ |
| $PM_{2.5}$ ($\mu g/m^3$) | | | | | | | |
| $1^{st}$ trimester | 1.00 | | | | | | |
| $2^{nd}$ trimester | 0.60 | 1.00 | | | | | |
| $3^{rd}$ trimester | 0.57 | 0.57 | 1.00 | | | | |
| Pregnancy average | 0.85 | 0.85 | 0.83 | 1.00 | | | |
| Oxidative potential | | | | | | | |
| $OP^{GSH}$ | -0.04 | -0.04 | -0.04 | -0.05 | | 1.00 | |
| $OP^{AA}$ | 0.15 | 0.15 | 0.15 | 0.17 | | 0.03 | 1.00 |

**Table S2.** Associations between exposure to $PM_{2.5}$ and $PM_{2.5}$ oxidative burden with additional adjustment for $NO_2$, $O_3$ and their combined oxidant capacity over the first trimester of exposure during pregnancy and birth outcomes in Ontario, Canada (2006 – 2012).

| **Model** | **$PM_{2.5}$** | | **$PM_{2.5}$*$OP^{GSH}$** | | **$PM_{2.5}$*$OP^{AA}$** |
|---|---|---|---|---|---|
| **Term low birth weight OR (95% CI)** | | | | | |
| Base model | 1.08 (1.01, 1.15) | | 1.31 (1.07, 1.61) | | 1.12 (0.95, 1.32) |
| NO2 | 1.06 (0.98, 1.15) | | 1.27 (1.01, 1.61) | | 1.09 (0.93, 1.28) |
| O3 | 1.05 (0.98, 1.14) | | 1.28 (1.03, 1.59) | | 1.09 (0.92, 1.28) |
| NO2 and O3 | 1.06 (0.97, 1.15) | | 1.25 (0.96, 1.62) | | 1.09 (0.91, 1.30) |
| $O_x$ | 1.05 (0.97, 1.15) | | 1.27 (0.99, 1.63) | | 1.07 (0.91, 1.27) |
| $O_x^{wt}$ | 1.05 (0.97, 1.14) | | 1.26 (0.99, 1.61) | | 1.07 (0.90, 1.26) |
| **Preterm birth OR (95% CI)** | | | | | |
| Base model | 0.95 (0.77, 1.18) | | 0.70 (0.36, 1.36) | | 0.90 (0.53, 1.54) |
| NO2 | 0.97 (0.91, 1.04) | | 0.98 (0.87, 1.10) | | 0.88 (0.69, 1.12) |
| O3 | 0.92 (0.74, 1.15) | | 0.61 (0.30, 1.24) | | 0.80 (0.45, 1.42) |
| NO2 and O3 | 0.92 (0.81, 1.05) | | 0.66 (0.42, 1.05) | | 0.77 (0.53, 1.11) |
| $O_x$ | 0.86 (0.69, 1.07) | | 0.47 (0.23, 0.99) | | 0.67 (0.37, 1.21) |
| $O_x^{wt}$ | 0.85 (0.68, 1.05) | | 0.45 (0.22, 0.93) | | 0.64 (0.36, 1.14) |
| **Term birth weight β (95% CI)** | | | | | |
| Base model | -0.91 (-5.64, 3.83) | | -3.74 (-15.24, 7.76) | | -0.74 (-9.11, 7.63) |
| NO2 | -0.88 (-5.60, 3.90) | | -3.69 (-15.20, 7.80) | | -0.73 (-9.10, 7.65) |
| O3 | -0.87 (-5.61, 3.90) | | -3.69 (-15.20, 7.79) | | -0.72 (-9.10, 7.65) |
| NO2 and O3 | -0.90 (-5.62, 3.90) | | -3.70 (-15.21, 7.78) | | -0.71 (-9.08, 7.70) |
| $O_x$ | -0.91 (-5.66, 3.89) | | -3.71 (-15.24, 7.80) | | -0.74 (-9.10, 7.63) |
| $O_x^{wt}$ | -0.90 (-5.63, 3.84) | | -3.72 (-15.22, 7.79) | | -0.73 (-9.10, 7.64) |

Estimates of association are for IQR increases in exposure to $PM_{2.5}$ (2.6 μg/$m^3$), $PM_{2.5}$*$OP^{GSH}$ (1.16% depletion/$m^3$), or $PM_{2.5}$*$OP^{AA}$ (1.42% depletion/$m^3$). Models represent pooled city-specific estimates derived using two-stage random effects meta-analysis and logistic regression (term low birth weight and ORs for preterm birth in association with chronic exposures) or linear regression (term birth weight). Models were adjusted for maternal age at delivery, marital status, maternal cigarette smoking during pregnancy, infant sex, parity, previous caesarean section delivery, maternal comorbidities (i.e. asthma, hypertension, type I and II diabetes mellitus, preeclampsia and gestational diabetes), year of birth, month of birth, census dissemination area median family income, census dissemination area proportion of population who are visible minority and census dissemination area proportion of the adult female population aged 25-64 years old who completed postsecondary education; gestational age was also included in term low birth weight and term birth weight models.

Abbreviations: OR: Odds ratio; β: beta coefficient; $PM_{2.5}$*$OP^{GSH}$: glutathione-related oxidative burden; $PM_{2.5}$ *$OP^{AA}$: ascorbate-related oxidative burden; $O_x$: combined oxidant capacity of $NO_2$ and $O_3$; $O_x^{wt}$: redox-weighted oxidant capacity of $NO_2$ and $O_3$.

**Table S3.** Associations between exposure to $PM_{2.5}$ and $PM_{2.5}$ oxidative burden with additional adjustment for $NO_2$, $O_3$ and their combined oxidant capacity over the second trimester of exposure during pregnancy and birth outcomes in Ontario, Canada (2006 – 2012).

| **Model** | **$PM_{2.5}$** | | **$PM_{2.5}$*$OP^{GSH}$** | | **$PM_{2.5}$*$OP^{AA}$** |
|---|---|---|---|---|---|
| **Term low birth weight OR (95% CI)** | | | | | |
| Base model | 0.96 (0.91, 1.02) | | 0.94 (0.80, 1.10) | | 0.92 (0.82, 1.04) |
| NO2 | 0.95 (0.89, 1.01) | | 0.91 (0.77, 1.08) | | 0.89 (0.78, 1.01) |
| O3 | 0.96 (0.91, 1.03) | | 0.94 (0.80, 1.10) | | 0.93 (0.81, 1.05) |
| NO2 and O3 | 0.95 (0.89, 1.01) | | 0.89 (0.74, 1.07) | | 0.88 (0.76, 1.01) |
| $O_x$ | 0.95 (0.89, 1.02) | | 0.91 (0.77 1.08) | | 0.89 (0.78, 1.02) |
| $O_x^{wt}$ | 0.96 (0.90, 1.02) | | 0.92 (0.78, 1.09) | | 0.91 (0.79, 1.04) |
| **Preterm birth OR (95% CI)** | | | | | |
| Base model | 1.00 (0.91, 1.10) | | 0.99 (0.74, 1.33) | | 1.03 (0.82, 1.30) |
| NO2 | 1.01 (0.94, 1.08) | | 1.05 (0.83, 1.33) | | 1.04 (0.89, 1.23) |
| O3 | 1.01 (0.93, 1.10) | | 1.04 (0.79, 1.36) | | 1.06 (0.85, 1.31) |
| NO2 and O3 | 1.05 (0.95, 1.17) | | 1.20 (0.83, 1.74) | | 1.15 (0.85, 1.57) |
| $O_x$ | 1.06 (0.94, 1.19) | | 1.20 (0.79, 1.83) | | 1.15 (0.85, 1.57) |
| $O_x^{wt}$ | 1.04 (0.93, 1.15) | | 1.12 (0.79, 1.83) | | 1.11 (0.85, 1.45) |
| **Term birth weight β (95% CI)** | | | | | |
| Base model | 0.88 (-3.68, 5.45) | | -2.41 (-13.77, 8.96) | | 3.26 (-4.71, 11.23) |
| NO2 | 0.84 (-3.72, 5.41) | | -2.38 (-13.75, 8.98) | | 3.24 (-4.69, 11.25) |
| O3 | 0.84 (-3.71, 5.40) | | -2.37 (-13.75, 8.97) | | 3.24 (-4.69, 11.25) |
| NO2 and O3 | 0.83(-3.69, 5.40) | | -2.37 (-13.75, 8.98) | | 3.24 (-4.69, 11.25) |
| $O_x$ | 0.88 (-3.67, 5.44) | | -2.40 (-13.78, 8.97) | | 3.26 (-4.71, 11.23) |
| $O_x^{wt}$ | 0.87 (-3.67, 5.46) | | -2.40 (-13.78, 8.97) | | 3.25 (-4.70, 11.24) |

Estimates of association are for IQR increases in exposure to $PM_{2.5}$ (2.6 μg/$m^3$), $PM_{2.5}$*$OP^{GSH}$ (1.16% depletion/$m^3$), or $PM_{2.5}$*$OP^{AA}$ (1.42% depletion/$m^3$). Models represent pooled city-specific estimates derived using two-stage random effects meta-analysis and logistic regression (term low birth weight and ORs for preterm birth in association with chronic exposures) or linear regression (term birth weight). Models were adjusted for maternal age at delivery, marital status, maternal cigarette smoking during pregnancy, infant sex, parity, previous caesarean section delivery, maternal comorbidities (i.e. asthma, hypertension, type I and II diabetes mellitus, preeclampsia and gestational diabetes), year of birth, month of birth, census dissemination area median family income, census dissemination area proportion of population who are visible minority and census dissemination area proportion of the adult female population aged 25-64 years old who completed postsecondary education; gestational age was also included in term low birth weight and term birth weight models.

Abbreviations: OR: Odds ratio; β: beta coefficient; $PM_{2.5}$*$OP^{GSH}$: glutathione-related oxidative burden; $PM_{2.5}$ *$OP^{AA}$: ascorbate-related oxidative burden; $O_x$: combined oxidant capacity of $NO_2$ and $O_3$; $O_x^{wt}$: redox-weighted oxidant capacity of $NO_2$ and $O_3$.

**Table S4.** Associations between exposure to $PM_{2.5}$ and $PM_{2.5}$ oxidative burden with additional adjustment for $NO_2$, $O_3$ and their combined oxidant capacity over the third trimester of exposure during pregnancy and birth outcomes in Ontario, Canada (2006 – 2012).

| **Model** | **$PM_{2.5}$** | | **$PM_{2.5}$*$OP^{GSH}$** | | **$PM_{2.5}$*$OP^{AA}$** |
|---|---|---|---|---|---|
| **Term low birth weight OR (95% CI)** | | | | | |
| Base model | 0.95 (0.90, 1.00) | | 0.92 (0.79, 1.07) | | 0.89 (0.79, 1.00) |
| NO2 | 0.96 (0.90, 1.02) | | 0.94 (0.80, 1.10) | | 0.91 (0.80, 1.04) |
| O3 | 0.96 (0.90, 1.01) | | 0.93 (0.80, 1.09) | | 0.90 (0.80, 1.01) |
| NO2 and O3 | 0.97 (0.91, 1.03) | | 0.95 (0.81, 1.12) | | 0.92 (0.81, 1.05) |
| $O_x$ | 0.97 (0.91, 1.03) | | 0.95 (0.81, 1.12) | | 0.92 (0.81, 1.04) |
| $O_x^{wt}$ | 0.96 (0.90, 1.02) | | 0.94 (0.80, 1.11) | | 0.91 (0.80, 1.03) |
| **Preterm birth OR (95% CI)** | | | | | |
| Base model | 0.98 (0.94, 1.03) | | 0.96 (0.85, 1.09) | | 0.97 (0.87, 1.07) |
| NO2 | 0.98 (0.93, 1.03) | | 0.95 (0.82, 1.09) | | 0.95 (0.85, 1.07) |
| O3 | 1.00 (0.95, 1.06) | | 1.02 (0.89, 1.18) | | 1.02 (0.90, 1.15) |
| NO2 and O3 | 1.00 (0.95, 1.06) | | 1.02 (0.88, 1.18) | | 1.02 (0.90, 1.16) |
| $O_x$ | 1.02 (0.96, 1.09) | | 1.08 (0.91, 1.30) | | 1.06 (0.91, 1.22) |
| $O_x^{wt}$ | 1.02 (0.96, 1.08) | | 1.07 (0.91, 1.26) | | 1.05 (0.91, 1.20) |
| **Term birth weight β (95% CI)** | | | | | |
| Base model | 6.60 (-2.22, 12.98) | | 6.69 (-4.26, 17.63) | | 10.62 (2.89, 18.35) |
| NO2 | 6.57 (-2.19, 13.01) | | 6.67 (-4.24, 17.65) | | 10.59 (2.92, 18.38) |
| O3 | 6.57 (-2.19, 13.01) | | 6.68 (-4.25, 17.64) | | 10.62 (2.89, 18.35) |
| NO2 and O3 | 6.57 (-2.19, 13.01) | | 6.67 (-4.24, 17.65) | | 10.59 (2.86, 18.32) |
| $O_x$ | 6.59 (-2.21, 12.99) | | 6.69 (-4.26, 17.63) | | 10.61 (2.88, 18.34) |
| $O_x^{wt}$ | 6.59 (-2.21, 12.99) | | 6.69 (-4.26, 17.63) | | 10.62 (2.89, 18.35) |

Estimates of association are for IQR increases in exposure to $PM_{2.5}$ (2.6 μg/$m^3$), $PM_{2.5}$*$OP^{GSH}$ (1.16% depletion/$m^3$), or $PM_{2.5}$*$OP^{AA}$ (1.42% depletion/$m^3$). Models represent pooled city-specific estimates derived using two-stage random effects meta-analysis and logistic regression (term low birth weight and ORs for preterm birth in association with chronic exposures) or linear regression (term birth weight). Models were adjusted for maternal age at delivery, marital status, maternal cigarette smoking during pregnancy, infant sex, parity, previous caesarean section delivery, maternal comorbidities (i.e. asthma, hypertension, type I and II diabetes mellitus, preeclampsia and gestational diabetes), year of birth, month of birth, census dissemination area median family income, census dissemination area proportion of population who are visible minority and census dissemination area proportion of the adult female population aged 25-64 years old who completed postsecondary education; gestational age was also included in term low birth weight and term birth weight models.

Abbreviations: OR: Odds ratio; β: beta coefficient; $PM_{2.5}$*$OP^{GSH}$: glutathione-related oxidative burden; $PM_{2.5}$ *$OP^{AA}$: ascorbate-related oxidative burden; $O_x$: combined oxidant capacity of $NO_2$ and $O_3$; $O_x^{wt}$: redox-weighted oxidant capacity of $NO_2$ and $O_3$.

**Table S5.** Associations between exposure to $PM_{2.5}$ and $PM_{2.5}$ oxidative burden with additional adjustment for $NO_2$, $O_3$ and their combined oxidant capacity over the whole pregnancy and birth outcomes in Ontario, Canada (2006 – 2012).

| Model | $PM_{2.5}$ | | $PM_{2.5}$*$OP^{GSH}$ | | $PM_{2.5}$*$OP^{AA}$ |
|---|---|---|---|---|---|
| **Term low birth weight OR (95% CI)** | | | | | |
| Base model | 0.96 (0.86, 1.07) | | 1.15 (0.84, 1.56) | | 0.90 (0.73, 1.11) |
| NO2 | 0.94 (0.83, 1.17) | | 1.02 (0.68, 1.54) | | 0.87 (0.68, 1.13) |
| O3 | 0.98 (0.87, 1.11) | | 1.18 (0.84, 1.66) | | 0.92 (0.73, 1.15) |
| NO2 and O3 | 0.95 (0.83, 1.09) | | 1.01 (0.65, 1.56) | | 0.89 (0.67, 1.18) |
| $O_x$ | 0.96 (0.84, 1.10) | | 1.10 (0.73, 1.66) | | 0.91 (0.70, 1.18) |
| $O_x^{wt}$ | 0.97 (0.85, 1.10) | | 1.14 (0.79, 1.65) | | 0.91 (0.71, 1.17) |
| **Preterm birth OR (95% CI)** | | | | | |
| Base model | 0.94 (0.84, 1.04) | | 0.79 (0.55, 1.12) | | 0.90 (0.67, 1.20) |
| NO2 | 0.96 (0.85, 1.08) | | 0.87 (0.58, 1.29) | | 0.92 (0.70, 1.21) |
| O3 | 0.86 (0.78, 0.95) | | 0.65 (0.43, 0.94) | | 0.72 (0.57, 0.91) |
| NO2 and O3 | 0.96 (0.82, 1.12) | | 0.88 (0.55, 1.43) | | 0.89 (0.62, 1.28) |
| $O_x$ | 0.95 (0.85, 1.07) | | 0.89 (0.65, 1.23) | | 0.89 (0.70, 1.13) |
| $O_x^{wt}$ | 0.89 (0.80, 0.98) | | 0.73 (0.54, 0.99) | | 0.77 (0.62, 0.95) |
| **Term birth weight β (95% CI)** | | | | | |
| Base model | 5.49 (-1.46, 12.33) | | 1.50 (-12.98, 15.98) | | 9.19 (-1.94, 20.32) |
| NO2 | 5.47 (-1.48, 12.31) | | 1.48 (-13.00, 15.96) | | 9.17 (-1.96, 20.30) |
| O3 | 5.49 (-1.46, 12.33) | | 1.50 (-12.98, 15.98) | | 9.18 (-1.95, 20.31) |
| NO2 and O3 | 5.47 (-1.48, 12.31) | | 1.48 (-13.00, 15.96) | | 9.17 (-1.96, 20.30) |
| $O_x$ | 5.49 (-1.46, 12.33) | | 1.50 (-12.98, 15.98) | | 9.19 (-1.94, 20.32) |
| $O_x^{wt}$ | 5.49 (-1.46, 12.33) | | 1.49 (-12.99, 15.97) | | 9.19 (-1.94, 20.32) |

Estimates of association are for IQR increases in exposure to $PM_{2.5}$ (2.6 μg/$m^3$), $PM_{2.5}$*$OP^{GSH}$ (1.16% depletion/$m^3$), or $PM_{2.5}$*$OP^{AA}$ (1.42% depletion/$m^3$). Models represent pooled city-specific estimates derived using two-stage random effects meta-analysis and logistic regression (term low birth weight and ORs for preterm birth in association with chronic exposures) or linear regression (term birth weight). Models were adjusted for maternal age at delivery, marital status, maternal cigarette smoking during pregnancy, infant sex, parity, previous caesarean section delivery, maternal comorbidities (i.e. asthma, hypertension, type I and II diabetes mellitus, preeclampsia and gestational diabetes), year of birth, month of birth, census dissemination area median family income, census dissemination area proportion of population who are visible minority and census dissemination area proportion of the adult female population aged 25-64 years old who completed postsecondary education; gestational age was also included in term low birth weight and term birth weight models.

Abbreviations: OR: Odds ratio; β: beta coefficient; $PM_{2.5}$*$OP^{GSH}$: glutathione-related oxidative burden; $PM_{2.5}$ *$OP^{AA}$: ascorbate-related oxidative burden; $O_x$: combined oxidant capacity of $NO_2$ and $O_3$; $O_x^{wt}$: redox-weighted oxidant capacity of $NO_2$ and $O_3$.

**Table S6.** Associations between exposure to $PM_{2.5}$ and $PM_{2.5}$ oxidative burden with additional adjustment for $NO_2$, $O_3$ and their combined oxidant capacity over acute exposure periods and preterm birth in Ontario, Canada (2006 – 2012).

| Model | $PM_{2.5}$ | | $PM_{2.5}$*$OP^{GSH}$ | | $PM_{2.5}$*$OP^{AA}$ |
|---|---|---|---|---|---|
| | HR (95% CI) | | HR (95% CI) | | HR (95% CI) |
| **Last 4 weeks of pregnancy** | | | | | |
| Base model | 0.94 (0.89, 0.99) | | 0.93 (0.86, 1.08) | | 0.96 (0.88, 1.09) |
| NO2 | 0.95 (0.89, 1.00) | | 0.94 (0.87, 1.08) | | 0.96 (0.88, 1.09) |
| O3 | 0.94 (0.89, 0.99) | | 0.93 (0.86, 1.08) | | 0.96 (0.88, 1.09) |
| NO2 and O3 | 0.94 (0.89, 0.99) | | 0.94 (0.87, 1.09) | | 0.96 (0.88, 1.09) |
| $O_x$ | 0.94 (0.89, 0.99) | | 0.93 (0.86, 1.08) | | 0.96 (0.88, 1.09) |
| $O_x^{wt}$ | 0.94 (0.89, 0.99) | | 0.93 (0.86, 1.08) | | 0.96 (0.88, 1.09) |
| **Same day of delivery** | | | | | |
| Base model | 0.99 (0.98, 1.00) | | 1.01 (0.99, 1.02) | | 0.99 (0.99, 1.00) |
| NO2 | 0.99 (0.97, 1.01) | | 1.01 (0.98, 1.02) | | 0.99 (0.99, 1.00) |
| O3 | 0.99 (0.98, 1.00) | | 1.01 (0.99, 1.02) | | 0.99 (0.99, 1.00) |
| NO2 and O3 | 0.99 (0.98, 1.00) | | 1.01 (0.99, 1.02) | | 0.99 (0.99, 1.00) |
| $O_x$ | 0.99 (0.98, 1.00) | | 1.01 (0.99, 1.02) | | 0.99 (0.99, 1.00) |
| $O_x^{wt}$ | 0.99 (0.98, 1.00) | | 1.01 (0.99, 1.02) | | 0.99 (0.99, 1.00) |

Estimates of association are for IQR increases in exposure to $PM_{2.5}$ (7.1 µg/$m^3$), $PM_{2.5}$*$OP^{GSH}$ (1.16% depletion/$m^3$), or $PM_{2.5}$*$OP^{AA}$ (1.42% depletion/$m^3$). Models represent pooled city-specific estimates derived using two-stage random effects meta-analysis and Cox proportional hazard models (HRs for preterm birth in association with exposures during the last 4 weeks of pregnancy or on the day of delivery). Models were adjusted for maternal age at delivery, marital status, maternal cigarette smoking during pregnancy, infant sex, parity, previous caesarean section delivery, maternal comorbidities (i.e. asthma, hypertension, type I and II diabetes mellitus, preeclampsia and gestational diabetes), year of birth, month of birth, mean temperature and mean relative humidity, census dissemination area median family income, census dissemination area proportion of population who are visible minority and census dissemination area proportion of the adult female population aged 25-64 years old who completed postsecondary education

Abbreviations: HR: Hazard ratio; $PM_{2.5}$*$OP^{GSH}$: glutathione-related oxidative burden; $PM_{2.5}$ *$OP^{AA}$: ascorbate-related oxidative burden; $O_x$: combined oxidant capacity of $NO_2$ and $O_3$; $O_x^{wt}$: redox-weighted oxidant capacity of $NO_2$ and $O_3$.

**Table S7.** Associations (95% CIs) between exposure to $PM_{2.5}$ across quartiles of ascorbic acid-related oxidative potential ($OP^{AA}$) over different periods of exposure during pregnancy and birth outcomes in Ontario, Canada (2006 – 2012).

| **Birth outcome and exposure time period** | **Percentile of $OP^{AA}$** | | | | **P value for effect modification** |
|---|---|---|---|---|---|
| | **<25th** | **25-50th** | **50-75th** | **>75th** | |
| **Term low birth weight** OR (95% CI) | | | | | |
| 1st trimester | 1.23 (0.91, 1.65) | 1.05 (0.89, 1.24) | 1.10 (0.98, 1.25) | 1.04 (0.90, 1.20) | 0.46 |
| 2nd trimester | 0.96 (0.80, 1.17) | 0.93 (0.80, 1.08) | 1.01 (0.91, 1.11) | 0.93 (0.84, 1.03) | 0.82 |
| 3rd trimester | 1.06 (0.80, 1.40) | 1.01 (0.86, 1.18) | 0.88 (0.78, 0.98) | 0.95 (0.86, 1.05) | 0.18 |
| Whole pregnancy | 1.24 (0.72, 2.11) | 0.96 (0.72, 1.27) | 0.99 (0.80, 1.21) | 0.93 (0.79, 1.10) | 0.50 |
| **Preterm birth** | | | | | |
| *Chronic exposure* OR (95% CI) | | | | | |
| 1st trimester | 1.13 (0.98, 1.31) | 0.91 (0.82, 1.01) | 0.68 (0.34, 1.36) | 0.90 (0.85, 0.96) | 0.22 |
| 2nd trimester | 0.87 (0.79, 0.95) | 0.99 (0.93, 1.06) | 1.23 (0.93, 1.63) | 0.93 (0.82, 1.04) | 0.30 |
| 3rd trimester | 0.96 (0.83, 1.11) | 0.92 (0.85, 0.99) | 1.02 (0.96, 1.08) | 0.99 (0.92, 1.07) | 0.06 |
| Whole pregnancy | 0.86 (0.69, 1.06) | 0.87 (0.75, 1.02) | 1.38 (0.85, 2.24) | 0.87 (0.74, 1.01) | 0.74 |
| *Acute exposure* HR (95% CI) | | | | | |
| Last 4 weeks of pregnancy | 0.80 (0.61, 1.02) | 1.07 (0.97, 1.17) | 0.98 (0.87, 1.10) | 0.89 (0.83, 1.02) | 0.75 |
| Same day of delivery | 0.99 (0.96, 1.02) | 0.99 (0.97, 1.01) | 0.99 (0.97, 1.01) | 0.99 (0.97, 1.01) | 0.92 |
| **Term birth weight** β (95% CI) | | | | | |
| 1st trimester | -4.24 (-13.53, 5.06) | -0.27 (-8.20, 7.66) | -2.08 (-13.79, 9.63) | -1.22 (-10.17, 7.74) | 0.49 |
| 2nd trimester | -4.48 (-13.83, 4.88) | -2.75 (-5.07, 10.56) | -5.46 (-16.19, 5.26) | 1.75 (-6.38, 9.90) | 0.53 |
| 3rd trimester | -5.98 (-15.18, 3.22) | 12.70 (5.21, 20.18) | 17.89 (6.89, 28.88) | 0.01 (-7.74, 7.75) | 0.18 |
| Whole pregnancy | -7.38 (-19.19, 7.43) | 12.21 (0.06, 24.36) | 15.54 (-2.07, 33.15) | 0.07 (-12.01, 12.16) | 0.35 |

Estimates of association are for IQR increases in exposure to $PM_{2.5}$ (2.6 $\mu g/m^3$). Models represent pooled city-specific estimates derived using two-stage random effects meta-analysis and logistic regression (term low birth

weight and ORs for preterm birth in association with chronic exposures), Cox proportional hazard models (HRs for preterm birth in association with IQR increases in exposure to $PM_{2.5}$ (7.1 $\mu g/m^3$) during the last 4 weeks of pregnancy or on the day of delivery), or linear regression (term birth weight). Models were adjusted for maternal age at delivery, marital status, maternal cigarette smoking during pregnancy, infant sex, parity, previous caesarean section delivery, maternal comorbidities (i.e. asthma, hypertension, type I and II diabetes mellitus, preeclampsia and gestational diabetes), year of birth, month of birth, census dissemination area median family income, census dissemination area proportion of population who are visible minority and census dissemination area proportion of the adult female population aged 25-64 years old who completed postsecondary education; gestational age was also included in term low birth weight and term birth weight models; mean temperature and mean relative humidity were also included in preterm birth acute exposure models. Random-effects multivariate meta-regression models were used to test potential effect modification by between-city differences in $OP^{AA}$. The outcome variables in the meta-regression models in this study were the pooled estimates and the explanatory variable (i.e. potential effect modifier) was the categorical variable of $OP^{AA}$ at the city level. Effect modification was considered statistically significant if the effect modifier's p-value was less than 0.05.

Abbreviations: OR: Odds ratio; HR: Hazard ratio; β: beta coefficient; $OP^{AA}$: ascorbate-related oxidative potential

**Table S8.** Second-stage random-effects meta-analysis and meta-regression models: multivariate Wald test on significance of each oxidative potential meta-predictor in explaining variation in overall associations, Cochran Q test for heterogeneity, $I^2$ statistics for residual heterogeneity.

| Birth outcome and exposure | Test for effect modification by regional oxidative potential (p value) | Q test (p value) | $I^2$ |
|---|---|---|---|
| **Term low birth weight** | | | |
| 1st trimester | | | |
| Base | | 0.485 | 1.0% |
| $OP^{GSH}$ | 0.021 | 0.721 | 1.0% |
| $OP^{AA}$ | 0.146 | 0.535 | 1.0% |
| 2nd trimester | | | |
| Base | | 0.847 | 1.0% |
| $OP^{GSH}$ | 0.487 | 0.832 | 1.0% |
| $OP^{AA}$ | 0.755 | 0.817 | 1.0% |
| 3rd trimester | | | |
| Base | | 0.510 | 1.0% |
| $OP^{GSH}$ | 0.287 | 0.517 | 1.0% |
| $OP^{AA}$ | 0.399 | 0.496 | 1.0% |
| Whole pregnancy | | | |
| Base | | 0.187 | 18.2% |
| $OP^{GSH}$ | 0.002 | 0.549 | 1.0% |
| $OP^{AA}$ | 0.344 | 0.180 | 18.9% |
| **Term birth weight** | | | |
| 1st trimester | | | |
| Base | | 0.999 | 1.0% |
| $OP^{GSH}$ | 0.55 | 0.999 | 1.0% |
| $OP^{AA}$ | 0.42 | 0.999 | 1.0% |
| 2nd trimester | | | |
| Base | | | |
| $OP^{GSH}$ | 0.82 | 0.453 | 1.0% |
| $OP^{AA}$ | 0.56 | 0.468 | 1.0% |
| 3rd trimester | | | |
| Base | | 0.083 | 27.3% |
| $OP^{GSH}$ | 0.19 | 0.100 | 25.8% |
| $OP^{AA}$ | 0.30 | 0.078 | 28.4% |
| Whole pregnancy | | | |
| Base | | 0.832 | 1.0% |
| $OP^{GSH}$ | 0.31 | 0.839 | 1.0% |
| $OP^{AA}$ | 0.30 | 0.840 | 1.0% |
| **Preterm birth** | | | |
| 1st trimester | | | |
| Base | | < 0.001 | 82.1% |
| $OP^{GSH}$ | 0.861 | < 0.001 | 82.4% |
| $OP^{AA}$ | 0.386 | < 0.001 | 82.3% |
| 2nd trimester | | | |
| Base | | < 0.001 | 74.8% |
| $OP^{GSH}$ | 0.632 | < 0.001 | 75.6% |

| | | | |
|---|---|---|---|
| $OP^{AA}$ | 0.503 | < 0.001 | 75.6% |
| 3rd trimester | | | |
| Base | | 0.002 | 47.0% |
| $OP^{GSH}$ | 0.483 | 0.002 | 48.5% |
| $OP^{AA}$ | 0.238 | 0.003 | 46.5% |
| Whole pregnancy | | | |
| Base | | < 0.001 | 65.3% |
| $OP^{GSH}$ | 0.436 | < 0.001 | 66.0% |
| $OP^{AA}$ | 0.956 | < 0.001 | 66.3% |
| Last 4 weeks of pregnancy | | | |
| Base | | 0.488 | 1.0% |
| $OP^{GSH}$ | 0.711 | 0.651 | 1.0% |
| $OP^{AA}$ | 0.882 | 0.541 | 1.0% |
| Same day of delivery | | | |
| Base | | 0.523 | 1.0% |
| $OP^{GSH}$ | 0.041 | 0.830 | 1.0% |
| $OP^{AA}$ | 0.901 | 0.783 | 1.0% |

For each outcome and exposure period, three meta-regression models are being presented: base model with no predictors (i.e. only including pooled ORs), model with meta-predictor $OP^{GSH}$ and model with meta-predictor $OP^{AA}$. Random-effects multivariate meta-regression models were used to test potential effect modification by between-city differences in $OP^{GSH}$ and $OP^{AA}$. The outcome variables in the meta-regression models in this study were the pooled estimates and the explanatory variable (i.e. potential effect modifier) was the continuous variable of $OP^{GSH}$ or $OP^{AA}$ at the city level. Effect modification was considered statistically significant if the effect modifier's p-value was less than 0.05.

Abbreviations: $OP^{GSH}$: glutathione-related oxidative potential; $OP^{AA}$: ascorbate-related oxidative potential

**Table S9.** Associations between exposure to $PM_{2.5}$ and $PM_{2.5}$ oxidative burden over different periods of exposure during pregnancy and birth outcomes in Ontario, Canada (2006 – 2012).

| **Model** | **$PM_{2.5}$** | | **$PM_{2.5}$*$OP^{GSH}$** | | **$PM_{2.5}$*$OP^{AA}$** |
|---|---|---|---|---|---|
| **Term low birth weight OR (95% CI)** | | | | | |
| 1st trimester | 1.08 (1.01, 1.15) | | 1.31 (1.07, 1.61) | | 1.12 (0.95, 1.32) |
| 2nd trimester | 0.96 (0.92, 1.02) | | 0.94 (0.80, 1.10) | | 0.92 (0.82, 1.04) |
| 3rd trimester | 0.95 (0.90, 1.00) | | 0.92 (0.79, 1.07) | | 0.89 (0.79, 1.00) |
| Whole pregnancy | 0.96 (0.86, 1.07) | | 1.15 (0.84, 1.56) | | 0.90 (0.73, 1.11) |
| **Term birth weight β (95% CI)** | | | | | |
| 1st trimester | -0.91 (-5.64, 3.83) | | -3.74 (-15.24, 7.76) | | -0.74 (-9.11, 7.63) |
| 2nd trimester | 0.88 (-3.68, 5.45) | | -2.41 (-13.77, 8.96) | | 3.26 (-4.71, 11.23) |
| 3rd trimester | 6.60 (-2.22, 12.98) | | 6.69 (-4.26, 17.63) | | 10.62 (2.89, 18.35) |
| Whole pregnancy | 5.49 (-1.46, 12.33) | | 1.50 (-12.98, 15.98) | | 9.19 (-1.94, 20.32) |

Estimates of association are for IQR increases in exposure to $PM_{2.5}$ (2.6 μg/$m^3$), $PM_{2.5}$*$OP^{GSH}$ (1.16% depletion/$m^3$), or $PM_{2.5}$*$OP^{AA}$ (1.42% depletion/$m^3$). Models represent pooled city-specific estimates derived using two-stage random effects meta-analysis and logistic regression (term low birth weight and ORs for preterm birth in association with chronic exposures) or linear regression (term birth weight). Models were adjusted for maternal age at delivery, marital status, maternal cigarette smoking during pregnancy, infant sex, parity, previous caesarean section delivery, maternal comorbidities (i.e. asthma, hypertension, type I and II diabetes mellitus, preeclampsia and gestational diabetes), gestational age, year of birth, month of birth, census dissemination area median family income, census dissemination area proportion of population who are visible minority and census dissemination area proportion of the adult female population aged 25-64 years old who completed postsecondary education, mean temperature and mean relative humidity.

Abbreviations: OR: Odds ratio; β: beta coefficient; $PM_{2.5}$*$OP^{GSH}$: glutathione-related oxidative burden; $PM_{2.5}$ *$OP^{AA}$: ascorbate-related oxidative burden.

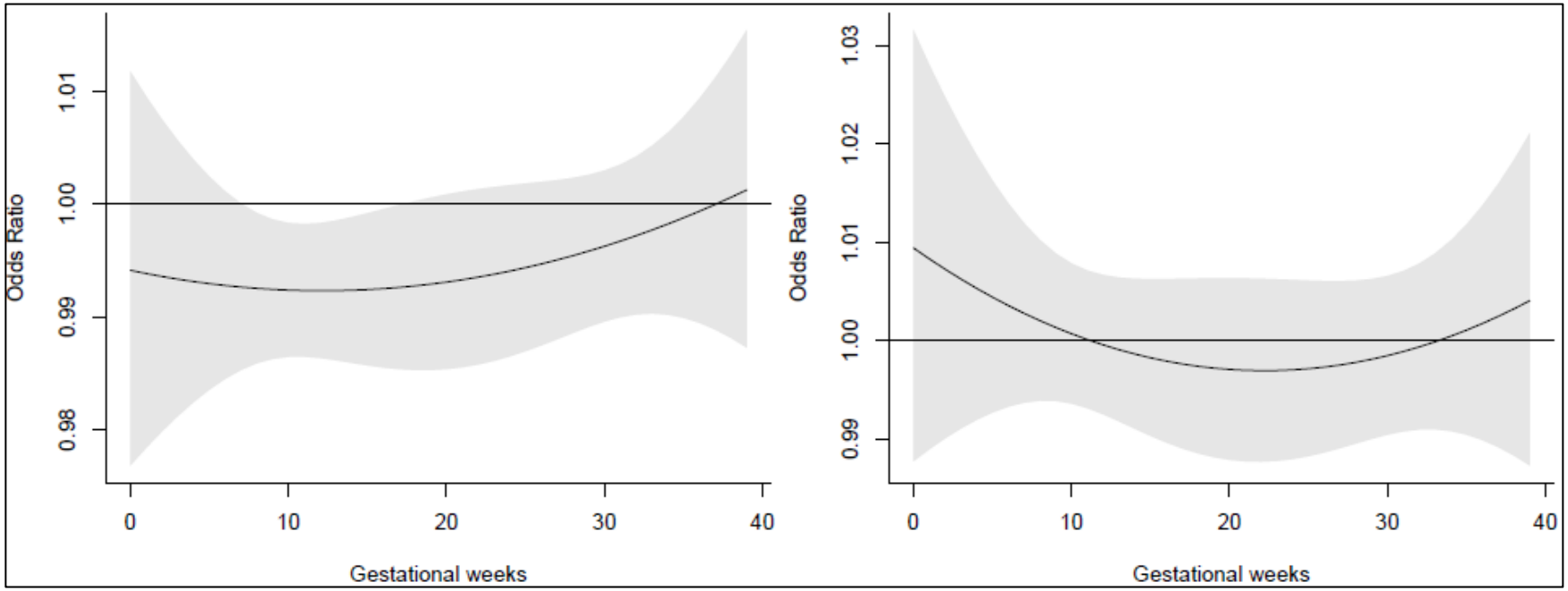


**Figure S1**. Associations between weekly $PM_{2.5}$ levels over gestation and term low birth weight, stratified according to below 25th percentile of $OP^{GSH}$ (left) and above the 75th percentile of $OP^{GSH}$ (right) in Ontario, Canada (2006 – 2012). Solid lines reflect point estimates and gray areas reflect 95% confidence intervals.

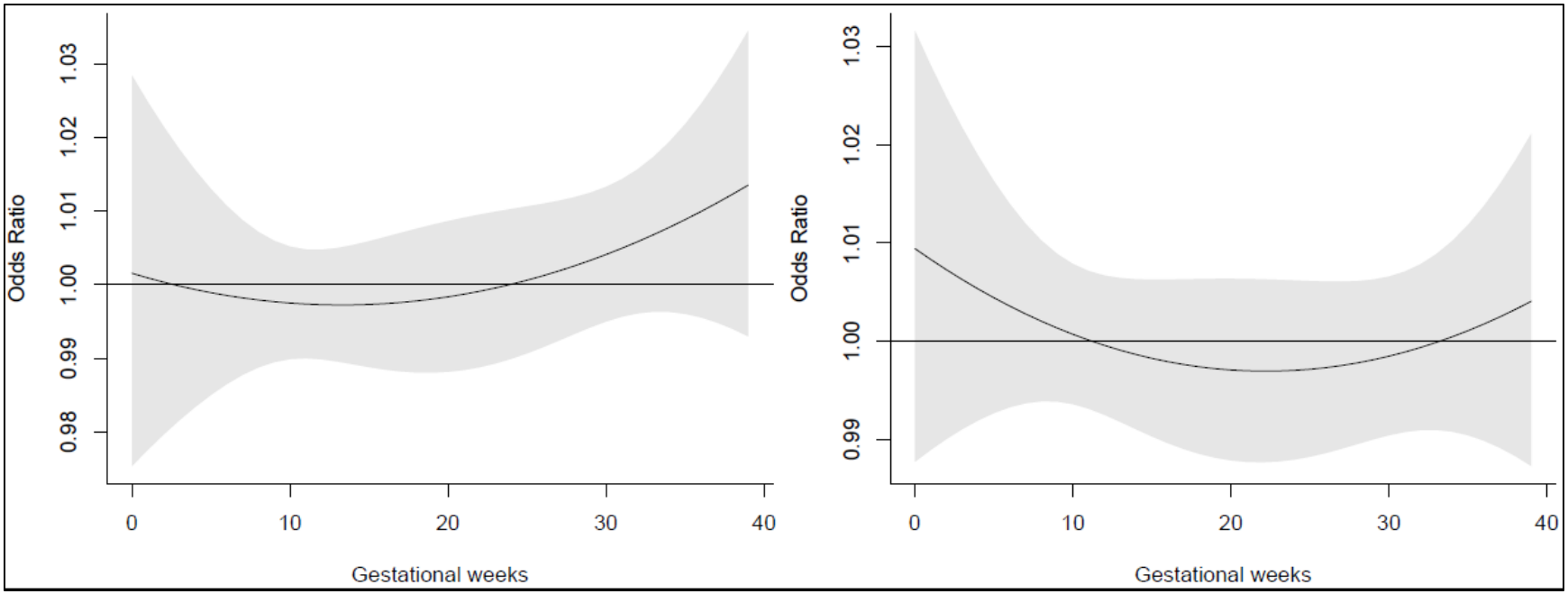


**Figure S2**. Associations between weekly $PM_{2.5}$ levels over gestation and term low birth weight, stratified according to below 25th percentile of $OP^{AA}$ (left) and above the 75th percentile of $OP^{AA}$ (right) in Ontario, Canada (2006 – 2012). Solid lines reflect point estimates and gray areas reflect 95% confidence intervals.

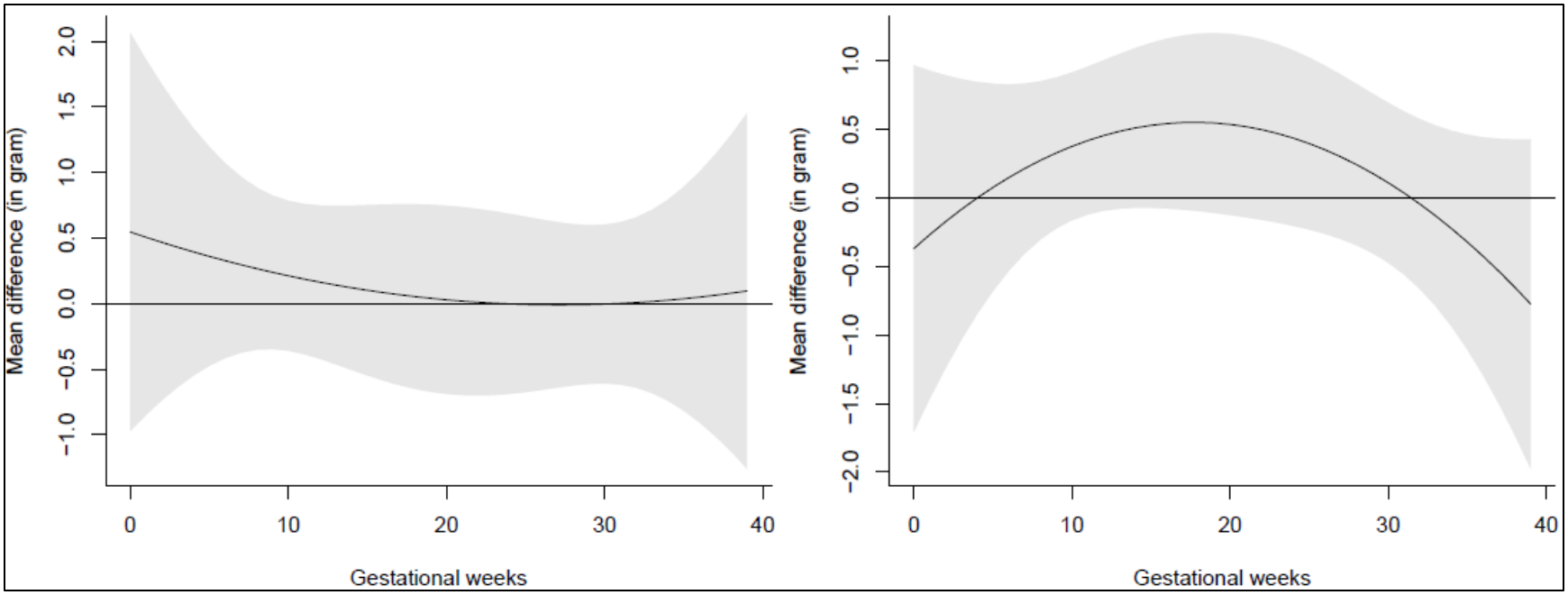


**Figure S3**. Associations between weekly $PM_{2.5}$ levels over gestation and term birth weight, stratified according to below 25th percentile of $OP^{GSH}$ (left) and above the 75th percentile of $OP^{GSH}$ (right) in Ontario, Canada (2006 – 2012). Solid lines reflect point estimates and gray areas reflect 95% confidence intervals.

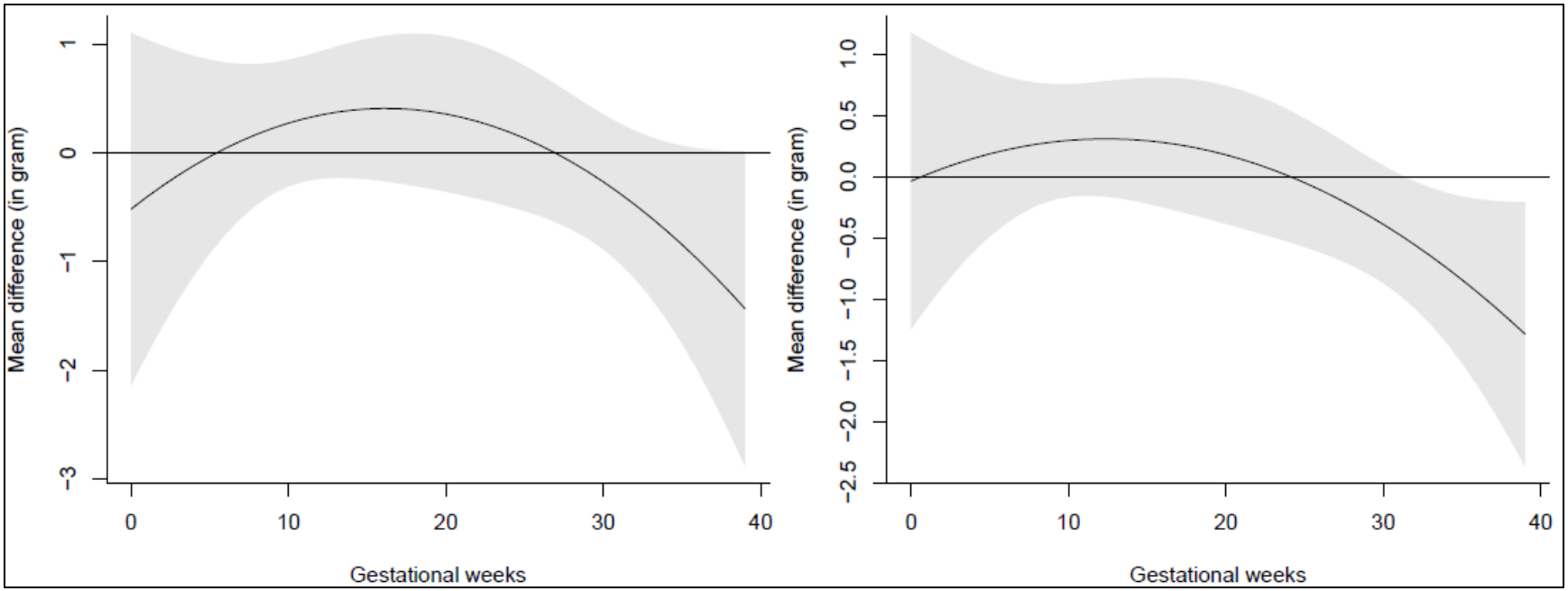


**Figure S4**. Associations between weekly $PM_{2.5}$ levels over gestation and term birth weight, stratified according to below 25th percentile of $OP^{AA}$ (left) and above the 75th percentile of $OP^{AA}$ (right) in Ontario, Canada (2006 – 2012). Solid lines reflect point estimates and gray areas reflect 95% confidence intervals.

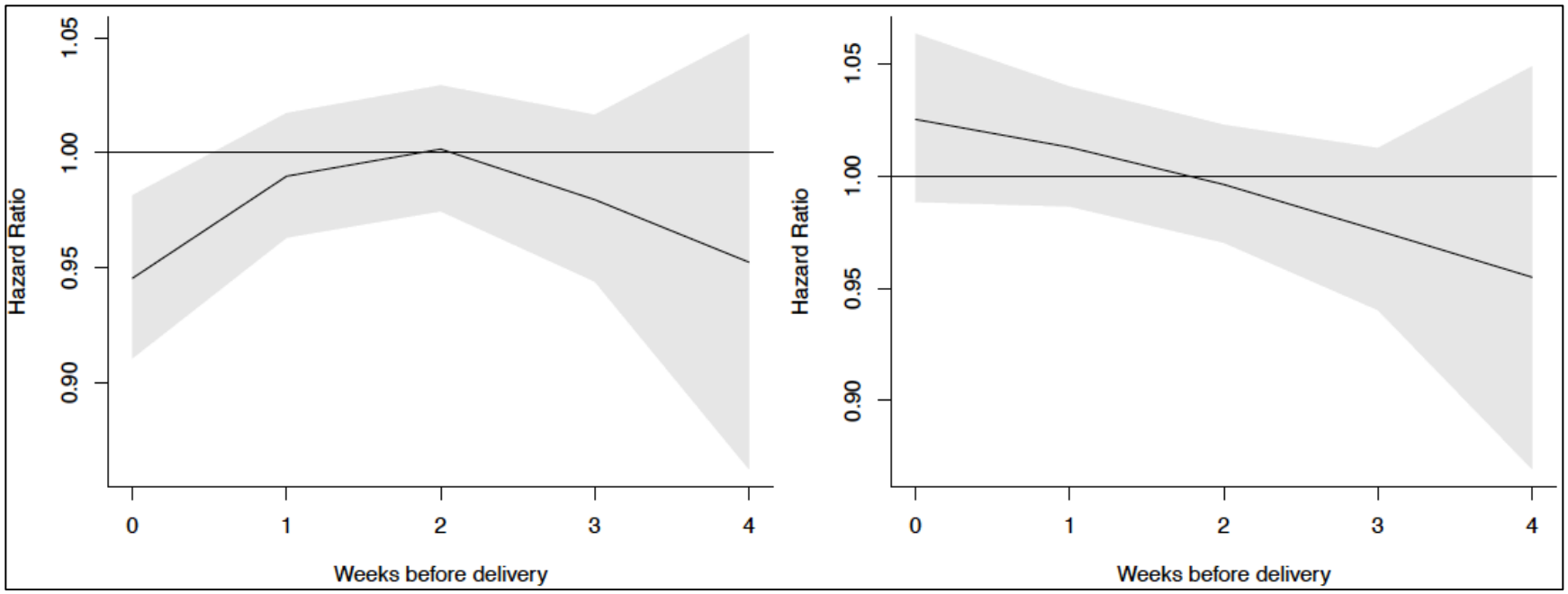


**Figure S5**. Associations between weekly $PM_{2.5}$ levels over the last 4 weeks of pregnancy and preterm birth, stratified according to below 25th percentile of $OP^{GSH}$ (left) and above the 75th percentile of $OP^{GSH}$ (right) in Ontario, Canada (2006 – 2012). Solid lines reflect point estimates and gray areas reflect 95% confidence intervals.

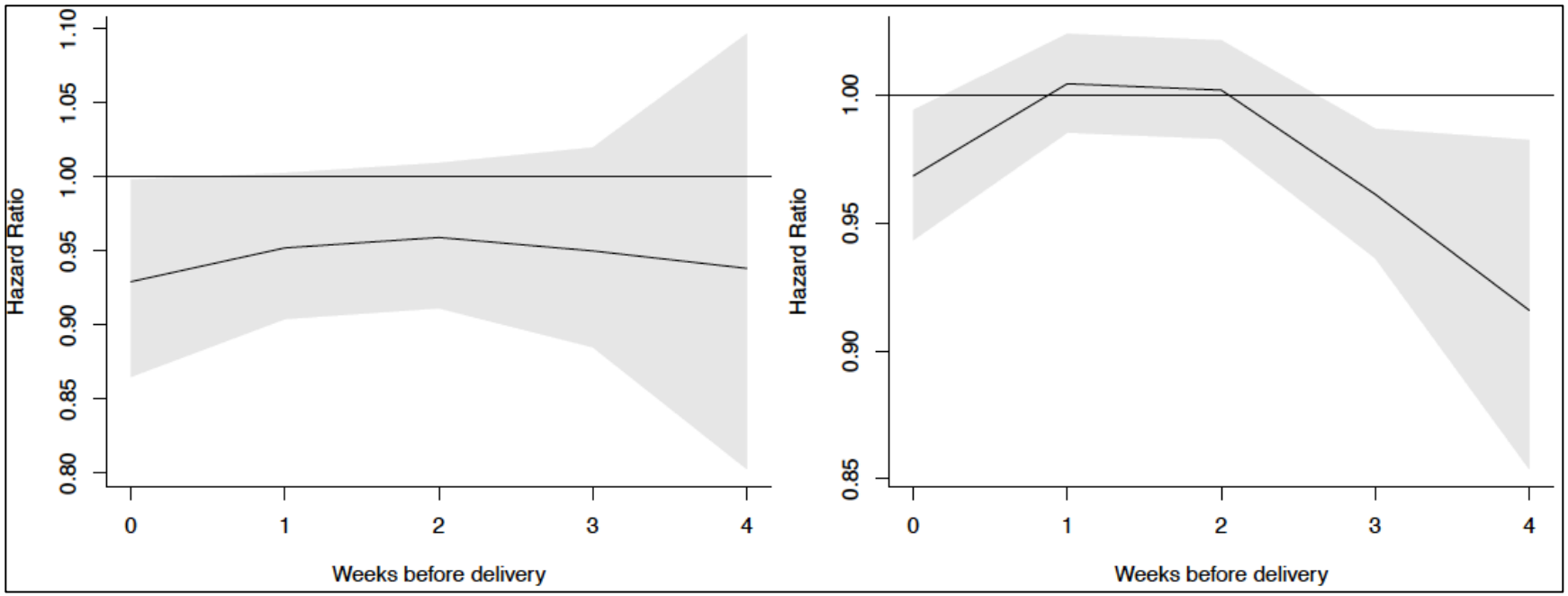


**Figure S6**. Associations between weekly $PM_{2.5}$ levels over the last 4 weeks of pregnancy and preterm birth, stratified according to below 25th percentile of $OP^{AA}$ (left) and above the 75th percentile of $OP^{AA}$ (right) in Ontario, Canada (2006 – 2012). Solid lines reflect point estimates and gray areas reflect 95% confidence intervals.

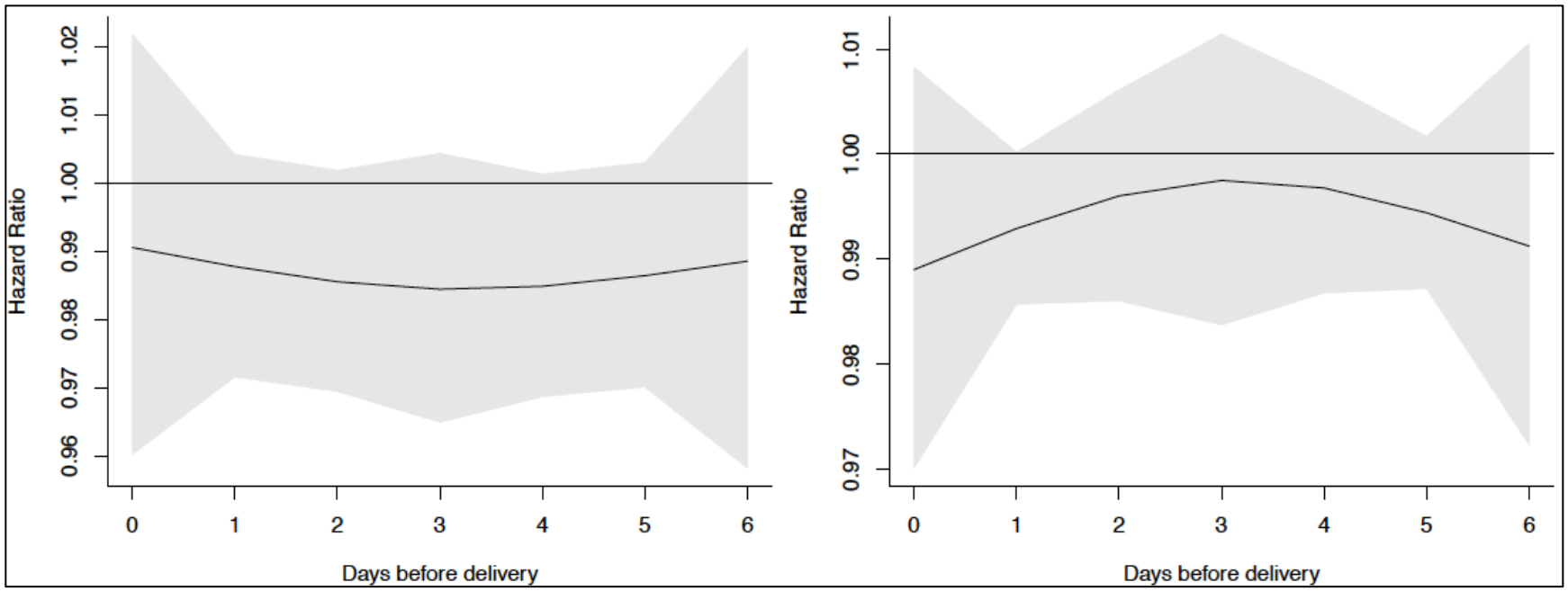


**Figure S7**. Associations between daily $PM_{2.5}$ levels over the last week of pregnancy and preterm birth, stratified according to below 25th percentile of $OP^{AA}$ (left) and above the 75th percentile of $OP^{AA}$ (right) in Ontario, Canada (2006 – 2012). Solid lines reflect point estimates and gray areas reflect 95% confidence intervals.