Supplementary Materials

Tables

Table S1. Multivariable linear regression analysis between categorized $PM_{2.5}$ and NO_2 exposures in MIREC participants

Exposure	**Biomarker and Percent Difference[a]**	**95% CI**	**p–value**
	CRP[b] (n=1,080)		
$PM_{2.5}$ equidistant (14 day average)			0.01
<5µg/m^3	Ref.		
5–<10µg/m^3	-1.9%	-21.3, 22.1	
10–<15µg/m^3	13.9%	-12.2, 49.2	
>15µg/m^3	50.7%	8.3, 107.5	
Trend			0.01
$PM_{2.5}$ equidistant (30 day average)			0.40
<5µg/m^3			
5–<10µg/m^3	-2.9%	-24.4, 24.6	
10–<15µg/m^3	4.1%	-22.9, 39.1	
15>µg/m^3	22.1%	-14.8, 75.1	
Trend			0.20
NO_2 equidistant (14 day average)			0.57
<10ppb	Ref.		
10–<20ppb	-1.9%	-23.7, 25.9	
20–<30ppb	-1.9%	-26.7, 31.0	
>30ppb	13.9%	-17.3, 60.0	
Trend			0.39
NO_2 equidistant (30 day average)			0.22
<10ppb			
10–<20ppb	8.3%	-16.5, 40.5	
20–<30ppb	2.0%	-4.4, 37.7	
>30ppb	27.1%	-8.6, 78.6	
Trend			0.20
	IL–6[c] (n=1,003)		
$PM_{2.5}$ equidistant (14 day average)			0.25
<5µg/m^3			
5–<10µg/m^3	-11.3%	-26.7, 6.2	
10–<15µg/m^3	-20.6%	-35.6, -1.0	

15>µg/m^3	-17.3%	-36.2, 8.3	
Trend			0.12
$PM_{2.5}$ equidistant (30 day average)			0.08
<5µg/m^3			
5–<10µg/m^3	-19.8%	-34.9, -1.0	
10–<15µg/m^3	-26.7%	-42.9, -5.8	
15>µg/m^3	-17.3%	-38.7, 11.6	
Trend			0.23
NO_2 equidistant (14 day average)			0.97
<10ppb	Ref.		
10–<20ppb	-0.6%	-18.9, 20.9	
20–<30ppb	-3.9%	-24.4, 20.9	
>30ppb	-4.9%	-27.4, 25.9	
Trend			0.67
NO_2 equidistant (30 day average)			0.59
<10ppb	Ref.		
10–<20ppb	-6.8%	-24.4, 15.0	
20–<30ppb	-0.4%	-22.1, 27.1	
>30ppb	7.3%	-18.9, 41.9	
Trend			0.41
	IL–8[d] (n=1,072)		
$PM_{2.5}$ equidistant (14 day average)			0.32
<5µg/m^3	Ref.		
5–<10µg/m^3	-8.6%	-18.1, 3.0	
10–<15µg/m^3	-2.9%	-15.6, 11.6	
15>µg/m^3	-1.9%	-17.3, 17.4	
Trend			0.77
$PM_{2.5}$ equidistant (30 day average)			0.75
<5µg/m^3			
5–<10µg/m^3	-4.9%	-17.3, 8.3	
10–<15µg/m^3	-1.0%	-15.6, 15.0	
15>µg/m^3	-0.3%	-17.3, 20.9	
Trend			0.76
NO_2 equidistant (14 day average)			0.98
<10ppb	Ref.		

10–<20ppb	3.1%	-10.4, 17.4	
20–<30ppb	2.0%	-13.1, 18.5	
>30ppb	2.0%	-3.9, 22.1	
Trend			0.87
NO_2 equidistant (30 day average)			0.98
<10ppb	Ref.		
10–<20ppb	-1.9%	-14.8, 12.7	
20–<30ppb	-1.0%	-15.6, 15.0	
>30ppb	-1.9%	-18.1, 17.4	
Trend			0.89
	TNFα[c] (n=1,083)		
$PM_{2.5}$ equidistant (14 day average)			0.72
<5µg/m^3	Ref.		
5–<10µg/m^3	-4.9%	-13.9, 4.1	
10–<15µg/m^3	-3.9%	-14.8, 8.3	
15>µg/m^3	-1.9%	-15.6, 8.3	
Trend			0.89
$PM_{2.5}$ equidistant (30 day average)			0.10
<5µg/m^3			
5–<10µg/m^3	-10.4%	-19.7, -0.1	
10–<15µg/m^3	-9.5%	-20.5, 3.0	
15>µg/m^3	-1.9%	-16.5, 15.0	
Trend			0.89
NO_2 equidistant (14 day average)			0.39
<10ppb	Ref.		
10–<20ppb	9.4%	-2, 22.1	
20–<30ppb	4.1%	-7.7, 18.5	
>30ppb	3.1%	-10.4, 19.7	
Trend			0.96
NO_2 equidistant (30 day average)			0.65
<10ppb	Ref.		
10–<20ppb	4.1%	-7.7, 16.2	
20–<30ppb	-0.9%	-13.8, 11.6	
>30ppb	-0.4%	-13.9, 16.2	
Trend			0.64

MIREC – Maternal–Infant Research on Environmental Chemicals Study, IQR – Interquartile range,

CRP – C–reactive protein, IL–6 – Interluekin–6, IL–8 – Interleukin–8, TNFα – Tumour necrosis factor–alpha, CI – confidence interval

[a]Percent difference represents the percentage difference in biomarker levels compared to referent group (lowest category of exposure).

[b]Model for CRP controlled for recruitment centre, alcohol, income, activity, body mass index.

[c]Model for IL–6 controlled for recruitment centre, maternal age, outside time, body mass index, folic acid, main heating, furnace.

[d]Model for IL–8 controlled for recruitment centre, maternal age, alcohol, income, activity, body mass index, folic acid.

[e]Model for TNFα controlled for recruitment centre, maternal age, body mass index.

Differing final counts in models due to differing availability of covariates selected for each biomarker.

Table S2. Multivariable linear regression analysis for the relationship between longer–term $PM_{2.5}$ and NO_2 exposure and biomarkers of inflammation in MIREC participants

Exposure	**Biomarker and Percent Change[a]**	**95% CI**	**p–value**
	CRP[b] (n=1,080)		
$PM_{2.5}$ (per IQR increase)			
Trimester 3 average	20.9%	-1.0, 49.2	0.07
Pregnancy average	-5.8%	-27.4, 22.1	0.64
NO_2 (per IQR increase)			
Trimester 3 average	9.4%	-12.2, 36.3	0.44
Pregnancy average	-3.9%	-25.9, 23.4	0.73
	IL–6[c] (n=1,003)		
$PM_{2.5}$ (per IQR increase)			
Trimester 3 average	-0.1%	-16.5, 18.5	0.99
Pregancy average	4.1%	-16.5, 28.4	0.74
NO_2 (per IQR increase)			
Trimester 3 average	7.3%	-10.4, 28.4	0.43
Pregancy average	0.1%	-18.9, 23.4	0.99
	IL–8[d] (n=1,072)		
$PM_{2.5}$ (per IQR increase)			
Trimester 3 average	8.3%	-3.9, 20.9	0.18
Pregancy average	6.2%	-7.7, 22.1	0.38
NO_2 (per IQR increase)			
Trimester 3 average	0.5%	-10.4, 12.7	0.92
Pregancy average	2.0%	-10.4, 17.4	0.73
	TNFα[e] (n=1,083)		
$PM_{2.5}$ (per IQR increase)			
Trimester 3 average	1.0%	-7.7, 11.6	0.79
Pregancy average	4.1%	-7.7, 16.2	0.53
NO_2 (per IQR increase)			
Trimester 3 average	-1.9%	-10.4, 8.3	0.71
Pregnancy average	4.1%	-6.8, 16.2	0.49

MIREC – Maternal–Infant Research on Environmental Chemicals Study, IQR – Interquartile range, CRP – C–reactive protein, IL–6 – Interluekin–6, IL–8 – Interleukin–8, TNFα – Tumour necrosis factor–alpha, CI – confidence interval

[a]Percent difference represents the percentage increase in biomarkers per IQR difference in pollutant.

[b]Model for CRP controlled for recruitment centre, alcohol, income, activity, body mass index.

[c]Model for IL–6 controlled for recruitment centre, maternal age, outside time, body mass index, folic acid, main heating, furnace.

[d]Model for IL–8 controlled for recruitment centre, maternal age, alcohol, income, activity, body mass index, folic acid.
[e]Model for TNFα controlled for recruitment centre, maternal age, body mass index.
Differing final counts in models due to differing availability of covariates selected for each biomarker.

Table S3. Sensitivity analyses for the relationships between short–term $PM_{2.5}$ and NO_2 exposures, excluding women with preeclampsia, IGT, and gestational diabetes in MIREC participants

Exposure	Biomarker and Percent Change[a]	95% CI	p–value
	CRP[b] (n=770)		
$PM_{2.5}$ (per IQR increase)			
14 day average	19.7%	0.1, 39.1	0.02
30 day average	15.0%	0.0, 36.3	0.09
NO_2 (per IQR increase)			
14 day average	18.5%	0.0, 44.8	0.11
30 day average	16.2%	0.0, 44.8	0.17
	IL–6[c] (n=772)		
$PM_{2.5}$ (per IQR increase)			
30 day average	-0.3%	-12.2, 12.7	0.96
14 day average	-0.1%	-13.1, 13.9	0.99
NO_2 (per IQR increase)			
30 day average	5.1%	-12.2, 24.6	0.59
14 day average	10.5%	-7.7, 32.3	0.27
	IL–8[d] (n=763)		
$PM_{2.5}$ (per IQR increase)			
30 day average	3.1%	-3.9, 11.6	0.38
14 day average	-1.9%	-9.5, 7.3	0.70
NO_2 (per IQR increase)			
30 day average	1.0%	-8.6, 12.7	0.81
14 day average	-0.1%	-11.3, 11.6	0.98
	TNFα[e] (n=771)		
$PM_{2.5}$ (per IQR increase)			
30 day average	1.0%	-9.5, 8.3	0.76
14 day average	2.0%	-4.9, 9.4	0.60
NO_2 (per IQR increase)			
30 day average	-1.0%	-10.4, 8.3	0.81
14 day average	-0.9%	-9.5, 9.4	0.86

IGT – Impaired glucose tolerance, MIREC – Maternal–Infant Research on Environmental Chemicals Study, IQR – Interquartile range, CRP – C–reactive protein, IL–6 – Interluekin–6, IL–8 – Interleukin–8, TNFα – Tumour necrosis factor–alpha, CI – confidence interval

[a]Percent difference represents the percentage increase in biomarkers per IQR difference in pollutant.

[b]Model for CRP controlled for recruitment centre, alcohol, income, activity, body mass index.

[c]Model for IL–6 controlled for recruitment centre, maternal age, outside time, body mass index, folic acid, main heating, furnace.

[d]Model for IL–8 controlled for recruitment centre, maternal age, alcohol, income, activity, body mass index, folic acid.
[e]Model for TNFα controlled for recruitment centre, maternal age, body mass index.
Differing final counts in models due to differing availability of covariates selected for each biomarker.

Table S4. Sensitivity analyses for the relationships between short–term $PM_{2.5}$ and NO_2 exposures, excluding CRP levels > 100mg/L in MIREC participants

Exposure	**Biomarker and Beta Coefficient**[a]	**95% CI**	**p–value**
	CRP[b] (n=1,028)		
$PM_{2.5}$ (per IQR increase)			
14 day average	15.0%	1.0, 29.7	0.03
30 day average	8.3%	-4.9, 23.4	0.24
NO_2 (per IQR increase)			
14 day average	3.1%	-12.2, 20.9	0.74
30 day average	3.1%	-13.1, 22.1	0.75

MIREC – Maternal–Infant Research on Environmental Chemicals Study, IQR – Interquartile range, CRP – C–reactive protein, CI – confidence interval

[a]Percent difference represents the percentage increase in biomarkers per IQR difference in pollutant.

[b]Model for CRP controlled for recruitment centre, alcohol, income, activity, body mass index.

Table S5. Sensitivity analyses for the relationships between short–term $PM_{2.5}$ and NO_2 exposures, controlling for blood–lead levels in MIREC participants

Exposure	Biomarker and Percent Change[a]	95% CI	p–value
	CRP[b] (n=1,079)		
$PM_{2.5}$ (per IQR increase)			
14 day average	24.6%	9.4, 43.3	0.0008
30 day average	18.5%	2.0, 36.3	0.02
	IL–6[c] (n=1,001)		
$PM_{2.5}$ (per IQR increase)			
30 day average	-1.9%	-12.2, 9.4	0.77
14 day average	0.4%	-11.3, 12.7	0.94
	IL–8[d] (n=1,070)		
$PM_{2.5}$ (per IQR increase)			
30 day average	3.1%	-3.9, 10.5	0.38
14 day average	0.2%	-6.8, 8.3	0.94
	TNFα[e] (n=1,081)		
$PM_{2.5}$ (per IQR increase)			
30 day average	2.0%	-3.9, 7.3	0.6
14 day average	2.0%	-3.9, 9.4	0.46

MIREC – Maternal–Infant Research on Environmental Chemicals Study, IQR – Interquartile range, CRP – C–reactive protein, IL–6 – Interluekin–6, IL–8 – Interleukin–8, TNFα – Tumour necrosis factor–alpha, CI – confidence interval

[a]Percent difference represents the percentage increase in biomarkers per IQR difference in pollutant.

[b]Model for CRP controlled for recruitment centre, alcohol, income, activity, body mass index, and blood–lead levels.

[c]Model for IL–6 controlled for recruitment centre, maternal age, outside time, body mass index, folic acid, main heating, furnace, and blood–lead levels.

[d]Model for IL–8 controlled for recruitment centre, maternal age, alcohol, income, activity, body mass index, folic acid, and blood–lead levels.

[e]Model for TNFα controlled for recruitment centre, maternal age, body mass index, and blood–lead levels.

Differing final counts in models due to differing availability of covariates selected for each biomarker.

Table S6. Interaction analyses by fetal sex in the relationships between short–term $PM_{2.5}$ and NO_2 exposures in MIREC participants

	Fetal sex male		**Fetal sex female**		
Exposure	**Biomarker and Percent Change[a]**	**95% CI**	**Biomarker and Percent Change[a]**	**95% CI**	**Interaction p-value**
	CRP[b] (n=560)		**CRP[b]** (n=522)		
$PM_{2.5}$ (per IQR increase)					
14 day average	23.4%	3.0, 47.7	25.9%	4.1, 53.7	0.81
30 day average	12.8%	-6.8, 37.7	23.4%	-0.2, 53.7	0.71
NO_2 (per IQR increase)					
14 day average	16.2%	-8.6, 49.2	3.1%	-19.7, 33.6	0.49
30 day average	15.0%	-11.3, 50.7	1.0%	-3.0, 33.6	0.55
	IL–6[c] (527)		**IL–6[c]** (477)		
$PM_{2.5}$ (per IQR increase)					
30 day average	-2.9%	-16.5, 11.6	-2.9%	-18.1, 12.7	0.68
14 day average	-1.9%	8.3, -17.3	-1.9%	-17.3, 17.4	0.73
NO_2 (per IQR increase)					
30 day average	-8.6%	-26.7, 12.7	11.6%	-9.5, 39.1	0.21
14 day average	-5.8%	-24.4, 17.4	22.1%	-2.0, 53.7	0.19
	IL–8[d] (n=558)		**IL–8[d]** (n=515)		
$PM_{2.5}$ (per IQR increase)					
30 day average	2.0%	-7.7, 11.6	4.1%	-5.8, 16.2	0.90
14 day average	0.0%	-9.5, 10.5	-0.3%	-11.3, 11.6	0.96
NO_2 (per IQR increase)					
30 day average	-0.5%	-13.1, 13.9	1.0%	-12.2, 16.2	0.88
14 day average	-0.1%	-13.1, 13.9	2.0%	-12.2, 18.5	0.87
	TNFα[e] (n=559)		**TNFα[e]** (n=516)		
$PM_{2.5}$ (per IQR increase)					
30 day average	0.2%	-6.8, 8.3	5.1%	-3.9, 13.9	0.15
14 day average	2.0%	-5.8, 11.6	4.1%	-4.9, 15.0	0.22
NO_2 (per IQR increase)					
30 day average	-1.9%	-12.2, 8.3	-0.4%	-11.3, 11.6	0.87
14 day average	-1.9%	-13.1, 9.4	0.5%	-11.3, 13.9	0.36

MIREC – Maternal–Infant Research on Environmental Chemicals Study, IQR – Interquartile range, CRP – C–reactive protein, IL–6 – Interluekin–6, IL–8 – Interleukin–8, TNFα – Tumour necrosis factor–alpha, CI – confidence interval

[a]Percent difference represents the percentage increase in biomarkers per IQR difference in pollutant.

[b]Model for CRP controlled for recruitment centre, alcohol, income, activity, body mass index, and blood–lead levels.

[c]Model for IL–6 controlled for recruitment centre, maternal age, outside time, body mass index, folic acid, main heating, furnace, and blood–lead levels.
[d]Model for IL–8 controlled for recruitment centre, maternal age, alcohol, income, activity, body mass index, folic acid, and blood–lead levels.
[e]Model for TNFα controlled for recruitment centre, maternal age, body mass index, and blood–lead levels.
Differing final counts in models due to differing availability of covariates selected for each biomarker.

Figures

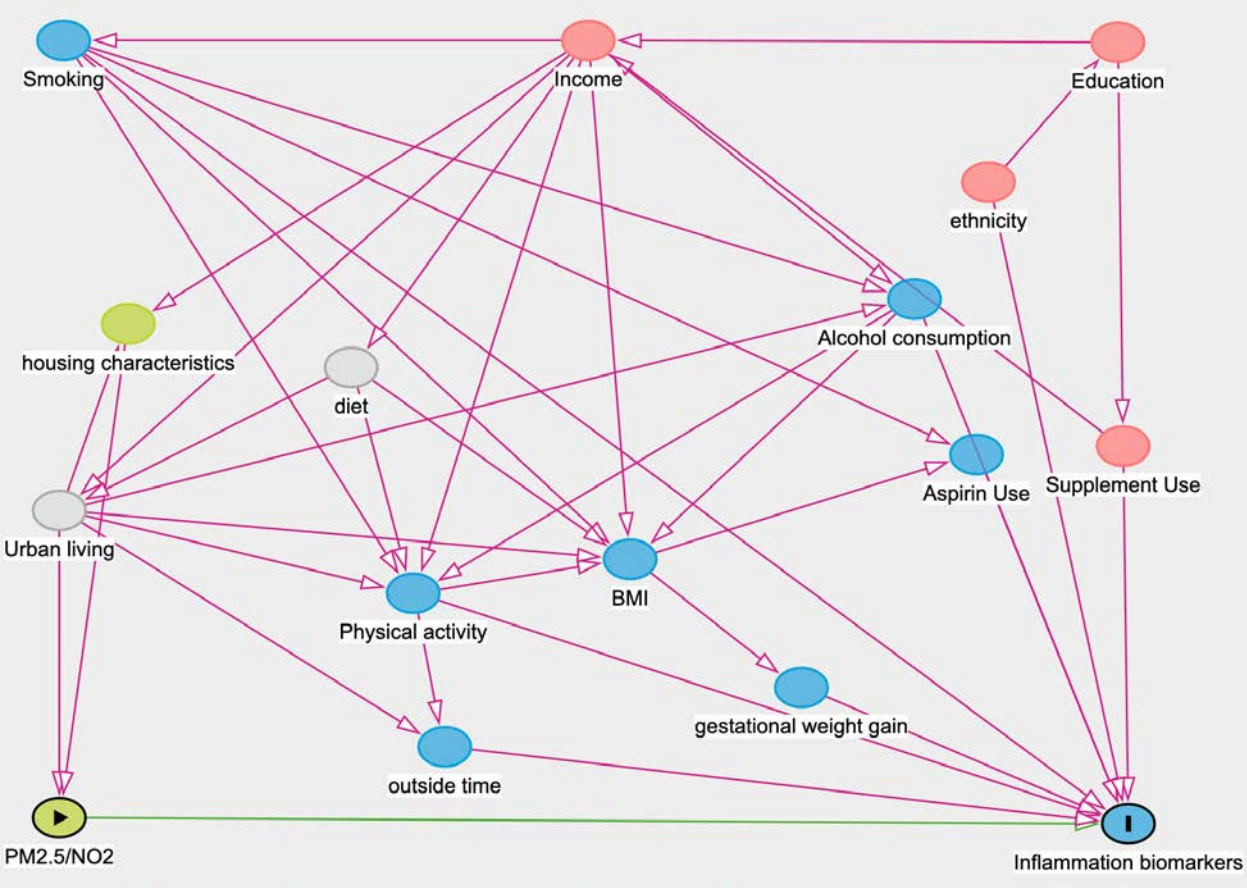

Figure S1. DAG used to identify important covariates in relationships of interest.

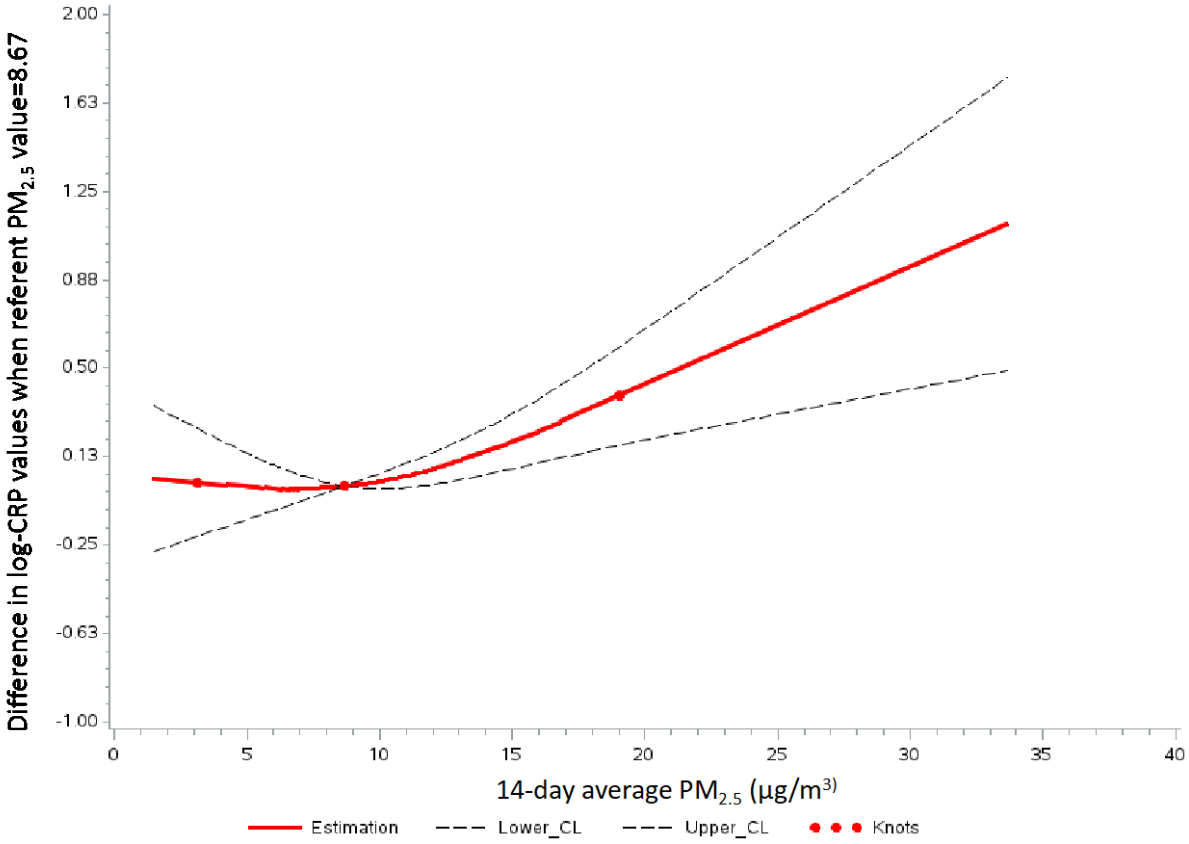

Figure S2. Restricted cubic spline plot for relationship between average 14-day $PM_{2.5}$ and C-reactive protein, adjusted for for recruitment centre, alcohol, income, activity, body mass index (3 knot placements at 5, 50, 95th percentiles).

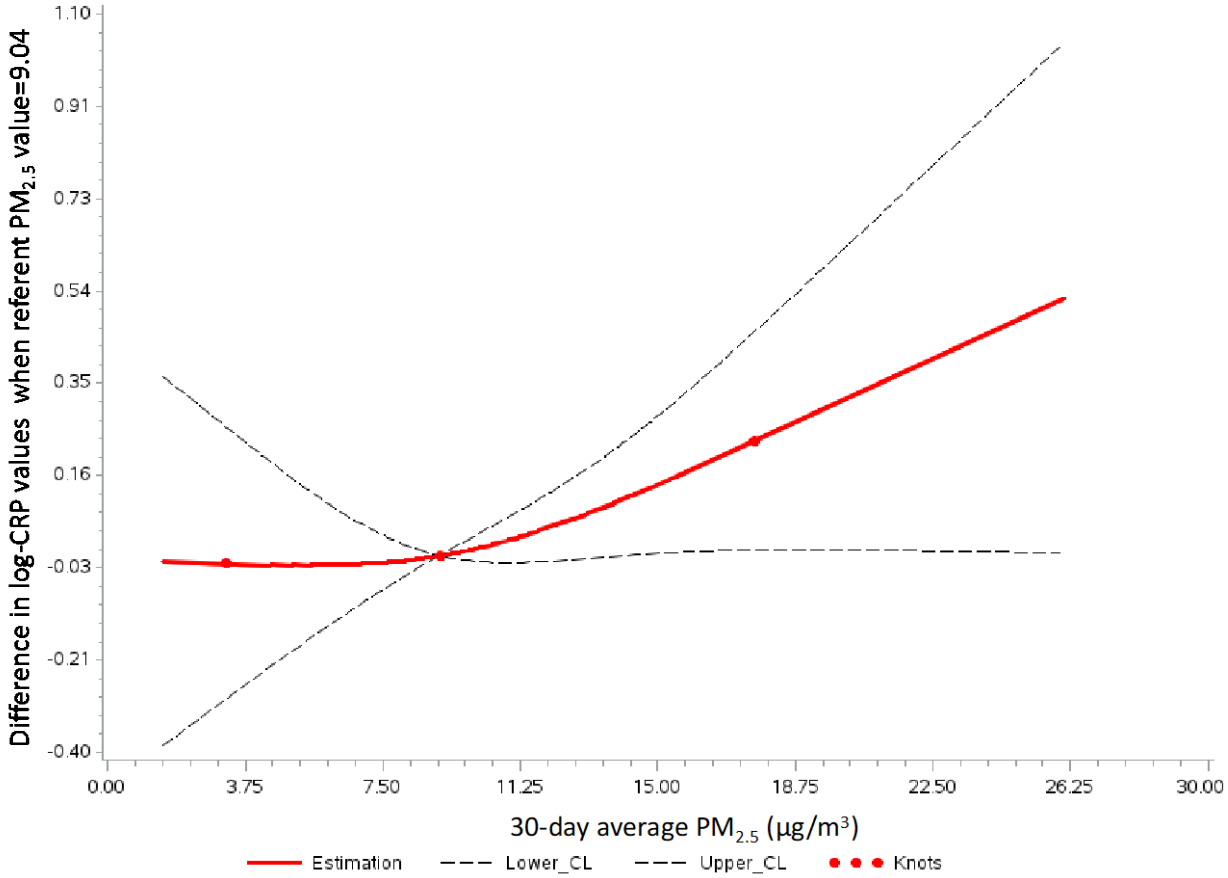

Figure S3. Restricted cubic spline plot for relationship between average 30-day $PM_{2.5}$ and C-reactive protein, adjusted for for recruitment centre, alcohol, income, activity, body mass index (3 knot placements at 5, 50, 95th percentiles).