Supplementary Material

Detail on Methods for prenatal CO measurement

Lascar EL-CO-USB Data Logger (Erie, PA) monitors were deployed in the breathing zone of GRAPHS women (i.e. pinned to clothing) for four 72-hour deployments during pregnancy. Like other portable, real time CO sensors, Lascar CO sensors were designed primarily for industrial hygiene applications, with a stated measurement range of 3-1000 ppm, and a 2 sigma uncertainty of about $\pm$ 7 ppm, for single measurements every 10 seconds. However, by averaging 17,280 such readings over 48 hours, random uncertainty reduces substantially, yielding a standard error of the mean of under 0.03 ppm for each 48-hour measurement. While a lower concentration limit of 3 ppm for the 10-second measurements may seem problematic at first, the problem is mitigated by the fact that in Ghana, CO concentrations vary between zero (most of the time) and very high (during cooking). When one averages those measurements over 48 hours, one gets a reasonable estimate of the mean exposure level over that period.

To estimate the Lascar monitors' limit of detection in a laboratory setting, we diluted a NIST traceable carbon monoxide gas of a known concentration with "zero air" gas until several Lascar monitors no longer provided a reading other than 0 ppm. Based on multiple such procedures, we concluded that 3 ppm CO was the true level where the Lascar units recorded non-zero concentrations (i.e., as a minimum response level of the Lascar), which is consistent with their report of the Lascars responding between 3 -1000 ppm. However, this information was obtained one time in the USA and it was impractical to reproduce this data in Ghana given the lack of calibration diluter equipment and the high cost of shipping reference gas and zero air gas tanks to Ghana. Instead we based our adjustments on the unit providing zero values when not exposed to the span gas and then post-adjusted readings to the one the NIST traceable tank of 50 ppm CO in Air every 6 weeks (i.e. we did one-point calibrations). We used all values after adjustment provided by the Lascar units (i.e. we did not replace any values below an LOD threshold). Our rationale is that in the settings were the women predominantly cooked and spent the vast majority of their time (many of which were outdoors or had ample ventilation to the outdoors), it was very likely that the zero values were reflective of true

concentrations. To confirm this interpretation, we also did a mobile survey during non-cooking times of CO levels in one community using a more sensitive CO meter (TSI IAQ) co-located with Lascar units and saw values were zero or occasionally the 0.1-0.2 ppm range on the TSI unit while the Lascars read 0; based on this survey we interpreted zero values as much more likely to be zero than to be as high as replacement values, e.g., LOD/sqrt(2) or 2.1ppm. As such we just averaged all values provided into 1-minute averages, adjusted those based on the bracketed span gas readings, and then truncated runtimes to be able to average the 1-minute readings into 48-hour averages.

Methods for prenatal $PM_{2.5}$ measurement

In a subset of GRAPHS participants (N=769), personal exposure to $PM_{2.5}$ was collected during a single exposure monitoring session after intervention, using the RTI MicroPEM V3.2 monitor (Research Triangle Park, NC). Data found lacking following quality assurance/quality control checks – see (Chillrud et al. 2021) – were considered missing. Because only a single $PM_{2.5}$ monitoring occurred during pregnancy, the 48-hour personal exposure average from this session was used as an estimate of PM exposure during the prenatal period. No PM measurements were removed based on model diagnostics.

Table S1. Baseline Characteristics of GRAPHS mothers, all births and analytic dataset for $PM_{2.5}$ analyses

	All live births (n = 1306)	Live births with available $PM_{2.5}$ data (N = 750)	Live births with available $PM_{2.5}$ data and Placental Malaria Status (N = 667)	
	Total (N=1306)	FALSE (N=750)	Negative (N=515)	Positive (N=152)
Age				
Mean (SD)	27.6 (7.1)	27.7 (7.1)	29.1 (6.7)	23.4 (6.3)
Range	14.0 - 48.0	14.0 - 45.0	15.0 - 45.0	14.0 - 41.0
Missing	3	1	1	0
BMI				
Mean (SD)	23.3 (3.2)	23.5 (3.2)	23.6 (3.2)	23.1 (3.0)
Range	14.1 - 38.5	15.4 - 37.3	15.4 - 37.3	17.2 - 35.2
Missing	2	1	0	0
Parity				
Mean (SD)	2.7 (2.2)	2.7 (2.2)	3.2 (2.1)	1.2 (1.5)
Range	0.0 - 13.0	0.0 - 11.0	0.0 - 11.0	0.0 - 9.0
Missing	0	0	0	0
Asset Index				
Mean (SD)	0.0 (2.0)	0.1 (2.1)	0.1 (2.1)	0.1 (2.1)
Range	-3.0 - 13.1	-2.8 - 13.1	-2.8 - 13.1	-2.8 - 11.4
Missing	0	0	0	0
Gestational Age at Enrollment (weeks)				
Mean (SD)	15.8 (4.3)	15.7 (4.4)	15.7 (4.4)	16.0 (4.4)
Range	6.0 - 26.0	6.0 - 26.0	6.0 - 24.0	6.0 - 24.0
Missing	3	2	1	1
Smoker in Household or Compound				
Yes	272 (20.8%)	159 (21.2%)	100 (19.4%)	34 (22.4%)
Missing	0	0	0	0
History of Anaemia				
Yes	29 (2.2%)	11 (1.5%)	7 (1.4%)	3 (2.0%)
Missing	0	0	0	0
History of Hypertension				
Yes	18 (1.4%)	14 (1.9%)	12 (2.3%)	1 (0.7%)
Missing	0	0	0	0
History of Diabetes				
Yes	2 (0.2%)	1 (0.1%)	0 (0.0%)	0 (0.0%)
Missing	0	0	0	0
History of HIV				
Yes	1 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Missing	0	0	0	0
Completed Primary Education				

Yes	774 (59.3%)	453 (60.4%)	280 (54.4%)	114 (75.0%)
Missing	0	0	0	0
Is Married				
Yes	730 (55.9%)	436 (58.1%)	332 (64.5%)	62 (40.8%)
Missing	0	0	0	0
4+ ANC Visits				
Yes	907 (69.8%)	527 (70.5%)	349 (68.0%)	116 (76.8%)
Missing	7	3	2	1
Ethnicity				
Akan	221 (16.9%)	143 (19.1%)	100 (19.4%)	26 (17.1%)
Mo	170 (13.0%)	104 (13.9%)	67 (13.0%)	23 (15.1%)
Northern Tribes	858 (65.7%)	470 (62.7%)	323 (62.7%)	97 (63.8%)
Other	57 (4.4%)	33 (4.4%)	25 (4.9%)	6 (3.9%)
Missing	0	0	0	0
Prenatal CO exposure (ppm)				
Mean (SD)	1.3 (0.9)	1.3 (0.9)	1.3 (0.9)	1.3 (1.0)
Median	1.1	1.0	1.1	1.0
Range	0.0 - 6.7	0.0 - 6.7	0.0 - 6.6	0.1 - 6.7
Missing	18	6	3	1
Prenatal PM exposure ($\mu g/m^3$)				
Mean (SD)	85.2 (58.7)	85.2 (58.7)	84.1 (56.5)	87.5 (63.0)
Median	69.0	69.0	67.6	74.8
Range	6.4 - 414.2	6.4 - 414.2	6.4 - 328.2	14.0 - 414.2
Missing	556	0	0	0

Table S2. Birth Outcomes, all births and analytic dataset for $PM_{2.5}$ analyses

	All live births (n = 1306)	Live births with available $PM_{2.5}$ data (n = 750)	Live births with available $PM_{2.5}$ data and Placental Malaria Status (N = 667)	
			Placental Malaria Negative (N=515)	Placental Malaria Positive (N=152)
Birthweight (grams)				
Mean (SD)	2890.9 (459.6)	2903.4 (449.8)	2939.3 (438.7)	2794.4 (468.5)
IQR	560.0	565.0	510.0	592.5
Missing	39	24	0	0
Birth Length (cm)				
Mean (SD)	46.6 (3.6)	46.8 (3.4)	46.9 (3.3)	46.3 (3.7)
IQR	4.3	4.0	4.0	4.7
Missing	24	9	4	1
Head Circumference (cm)				
Mean (SD)	33.5 (2.5)	33.5 (2.5)	33.5 (2.5)	33.1 (2.1)
IQR	3.0	3.0	3.0	2.4
Missing	37	15	6	5
Gestational Age at Delivery (weeks)				
Mean (SD)	39.6 (1.6)	39.7 (1.5)	39.8 (1.5)	39.4 (1.7)
IQR	1.7	1.7	1.6	1.9
Missing	15	9	5	3
Weight-for-age Z Score (standard deviations)				
Mean (SD)	-0.9 (1.0)	-0.9 (1.0)	-0.9 (1.0)	-1.1 (1.1)
IQR	1.3	1.3	1.2	1.4
Missing	66	40	11	4
Pre-Term Birth				
Yes	52 (4.0%)	25 (3.3%)	14 (2.7%)	7 (4.6%)
Missing	0	0	0	0
Low Birth Weight				
Yes	216 (17.0%)	117 (16.1%)	69 (13.4%)	36 (23.7%)
Missing	39	24	0	0
Small for Gestational Age				
Yes	283 (22.6%)	162 (22.6%)	102 (20.0%)	40 (26.8%)
Missing	54	33	5	3
Delivery during high malaria transmission season				
Yes	568 (43.5%)	312 (41.6%)	207 (40.2%)	70 (46.1%)
Missing	0	0	0	0
Male Sex				
Yes	664 (50.8%)	379 (50.5%)	266 (51.7%)	69 (45.4%)
Missing	0	0	0	0

Results for $PM_{2.5}$ analyses

Prenatal $PM_{2.5}$ and Birth Outcomes

In the smaller subset of women with $PM_{2.5}$ data (N = 667 with both $PM_{2.5}$ and placental malaria status, see Tables S1 and S2), no evidence was seen for interaction between $PM_{2.5}$ exposure and placental malaria for any birth outcome (all p-values for interaction > 0.05), but we did observe evidence of interaction between $PM_{2.5}$ and infant sex for the outcome of gestational age (p-value for interaction 0.008). We therefore present results stratified by infant sex for the $PM_{2.5}$-gestational age association, and unstratified results for all other outcomes.

We did not observe associations between prenatal $PM_{2.5}$ exposure and birth weight, birth length, head circumference, or Weight-for-age Z score (Table S3). Among all infants, the odds of LBW and SGA were associated with increases in $PM_{2.5}$ exposure, with a 3% [95% CI: 1%, 6%] increased odds for LBW and 2% [95% CI: 0%, 5%] increased odds for SGA per 10 $\mu g/m^3$ increase in $PM_{2.5}$ exposure. As with CO, we did not observe an association between $PM_{2.5}$ exposure and PTB (OR [95% CI] of 0.99 [0.94, 1.05]). There was a small observed association with reduced gestational age of -0.3 days [95% CI: -0.4, -0.1] per 10 $\mu g/m^3$ increase in $PM_{2.5}$ among boys only, with no association among girls. As sex-stratified results did not suggest similar trends by infant sex for the effect of $PM_{2.5}$ on other outcomes (results not reported), we suggest this finding be interpreted with caution.

Table S3. Associations of prenatal $PM_{2.5}$ exposure with birth outcomes.

	Adjusted Models[a]			
	Coefficient per 10 $\mu g/m^3$ $PM_{2.5}$	**95% CI**	**Stratified by infant sex: OR (95% CI)**	**N**
Birth Weight (g)	-3.3	(-9.38, 2.68)		663
Birth Length (cm)	0.01	(-0.05, 0.06)		658
Head Circumference (cm)	-0.01	(-0.05, 0.03)		652
Gestational age (days)[b]	-0.1	(-0.24, 0.00)	Girls: 0.1 (-0.2, 0.3) **Boys: -0.3 (-0.4, -0.1)**	655
Weight-for-age Z score (standard deviations)	0.002	(-0.01, 0.02)	Girls: 0.006 (-0.01, 0.03) Boys: -0.0004 (-0.02, 0.02)	648
	OR per 10 $\mu g/m^3$ $PM_{2.5}$	**95% CI**		**N**
Low Birth Weight	1.03	(1.01, 1.06)		663
Small for Gestational Age	1.02	(1.00, 1.05)		655
Preterm Birth	0.99	(0.94, 1.05)		663

[a]Covariates included in adjusted models: maternal BMI, maternal age, parity, infant sex, ANC visits, ethnicity, asset index, and placental malaria.

[b]Stratified gestational age models additionally include a term for the interaction between CO and infant sex.

Figure S1. Birth Weight exposure-response curve

Exposure-response curve for $PM_{2.5}$ – birth weight association from a generalized additive model (GAM) using thin plate regression splines with 3 degrees of freedom, adjusted for maternal BMI, age, parity, asset index, ANC visits, ethnicity, placental malaria, and infant sex. Boxplots demonstrate the distribution of exposure, while gray boxes demarcate the exposure range covering 95% of the data.

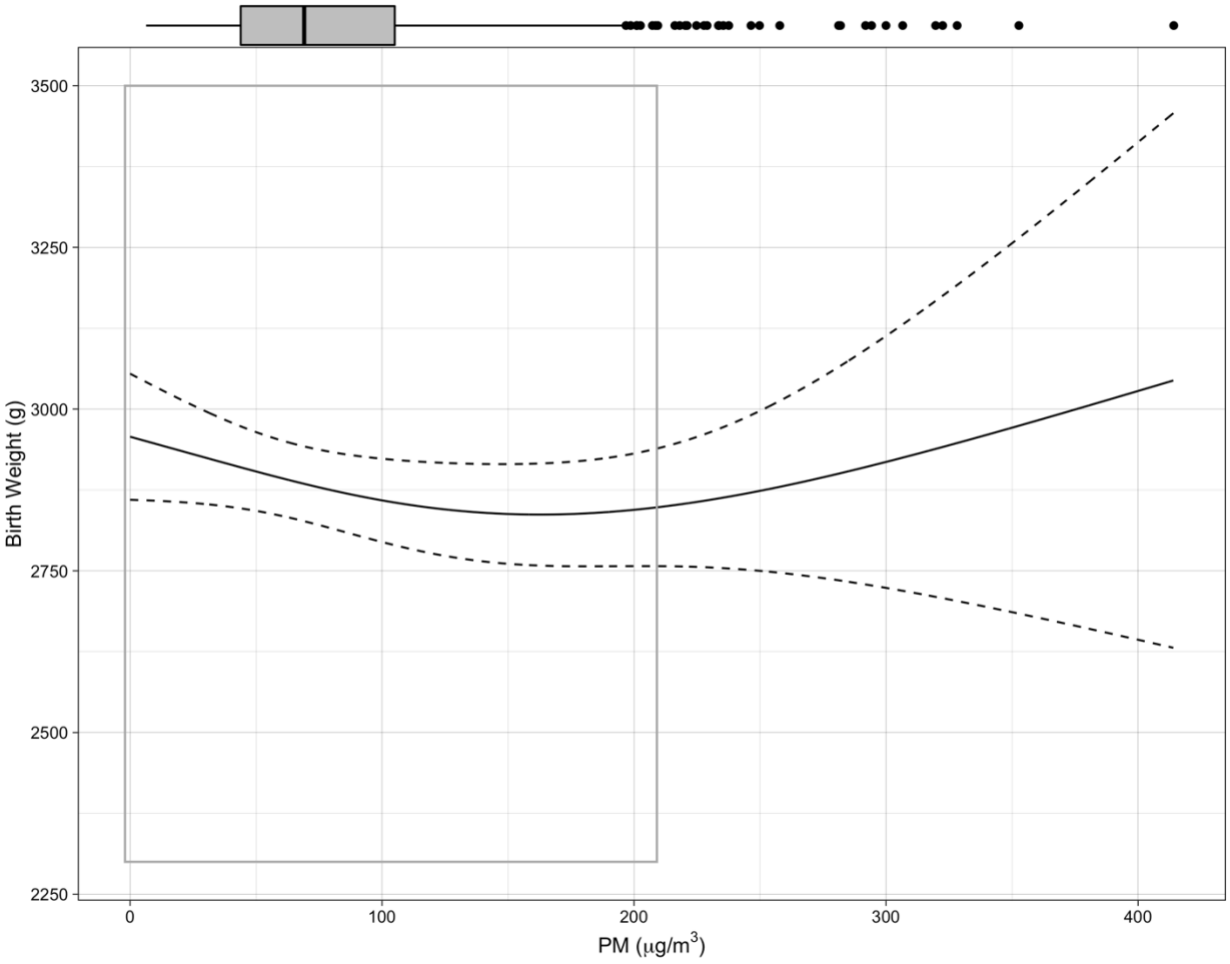


Figure S2. Birth Length exposure-response curve

Exposure-response curve for $PM_{2.5}$ – birth length association from a generalized additive model (GAM) using thin plate regression splines with 3 degrees of freedom, adjusted for maternal BMI, age, parity, asset index, ANC visits, ethnicity, placental malaria, and infant sex. Boxplots demonstrate the distribution of exposure, while gray boxes demarcate the exposure range covering 95% of the data.

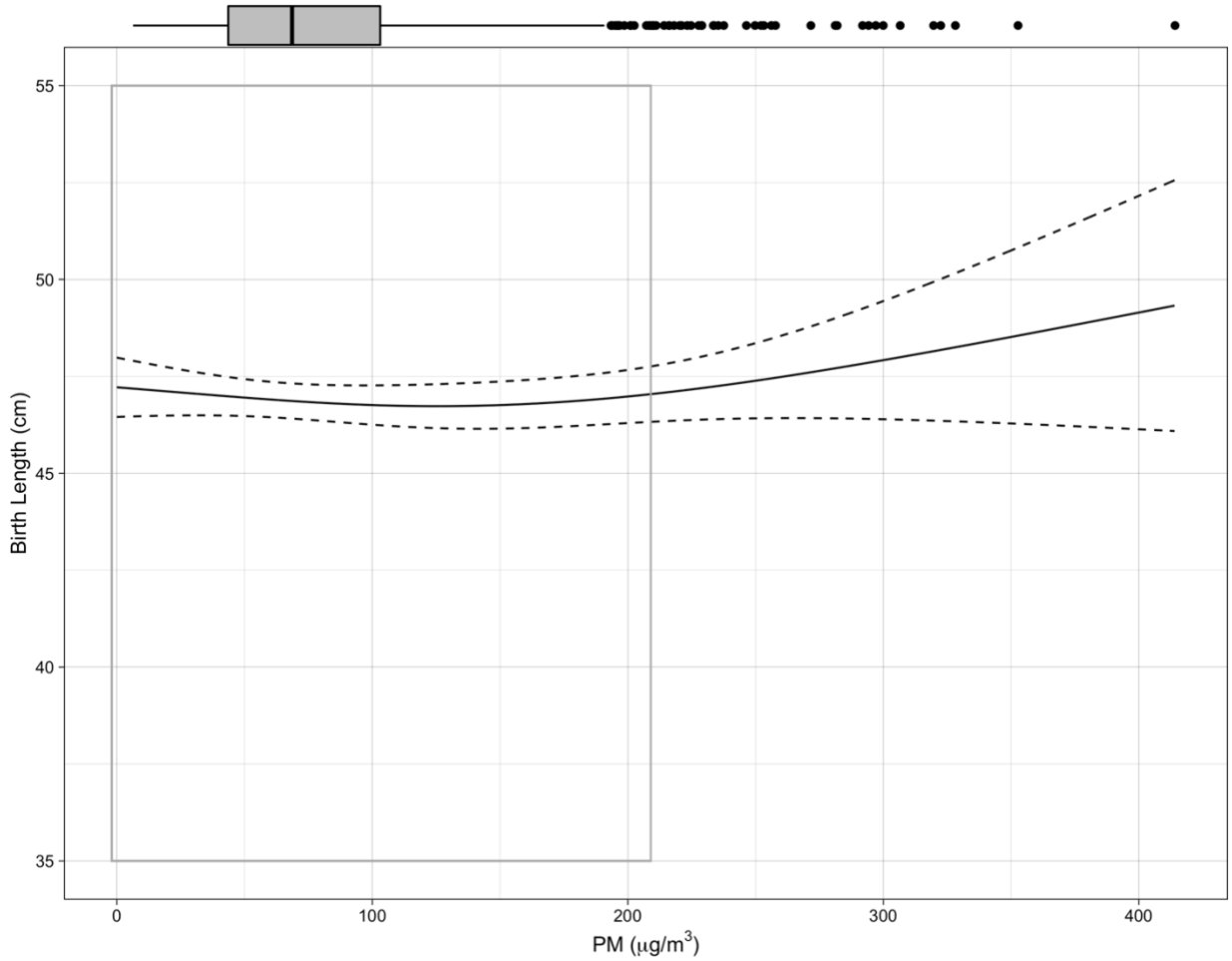


Figure S3. Head Circumference exposure-response curve

Exposure-response curve for $PM_{2.5}$ – head circumference association from a generalized additive model (GAM) using thin plate regression splines with 3 degrees of freedom, adjusted for maternal BMI, age, parity, asset index, ANC visits, ethnicity, placental malaria, and infant sex. Boxplots demonstrate the distribution of exposure, while gray boxes demarcate the exposure range covering 95% of the data.

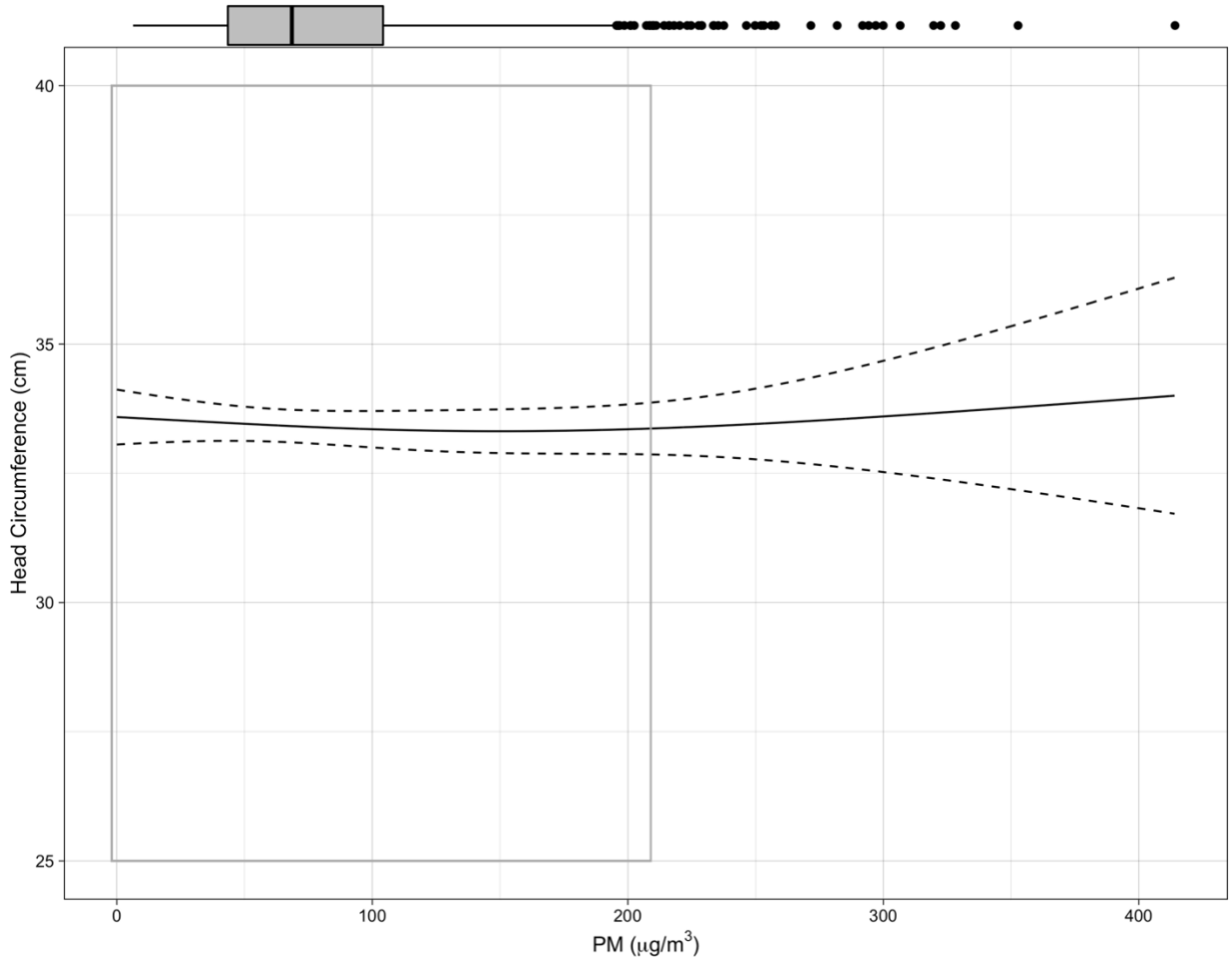
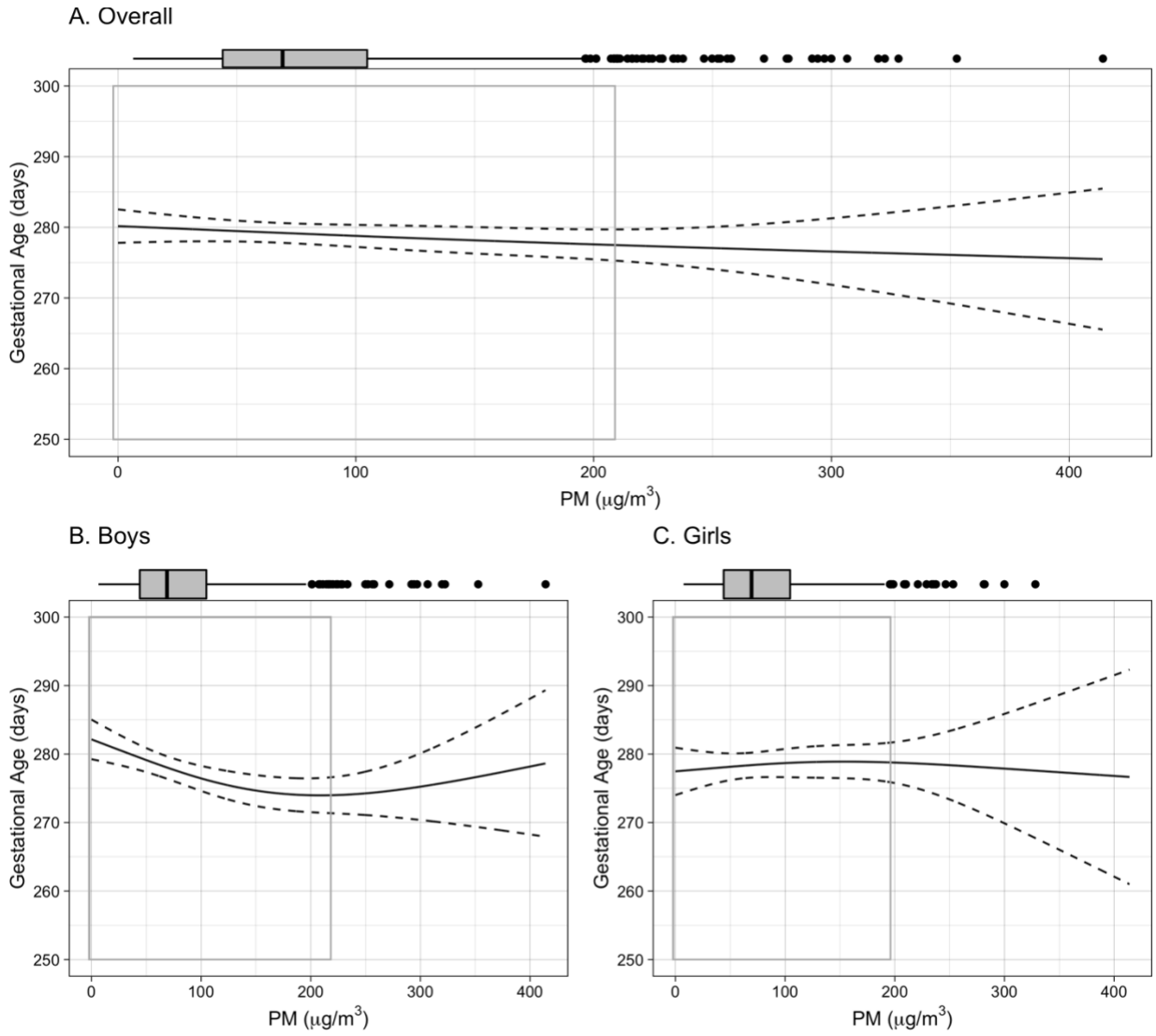


Figure S4. Gestational Age exposure-response curves

Exposure-response curve for $PM_{2.5}$ – gestational age association among A. all live births, B. Boys, and C. Girls; from a generalized additive model (GAM) using thin plate regression splines with 3 degrees of freedom, adjusted for maternal BMI, age, parity, asset index, ANC visits, ethnicity, and placental malaria. Plots are stratified by infant sex due to the presence of a significant interaction term between $PM_{2.5}$ and infant sex in regression models for this outcome. Boxplots demonstrate the distribution of exposure, while gray boxes demarcate the exposure range covering 95% of the data.



Multiple imputation using MICE

Methods:

The Multivariate Imputation by Chained Equations ("mice") package in R (van Buuren and Groothuis-Oudshoorn 2011) was employed to create 10 multiple imputation datasets to estimate the values of missing data in our analytic dataset. MICE is based on Fully Conditional Specification, where separate models are used to impute each incomplete variable. Missingness

of the original variables can be found in Table 1. Variables used for imputation were: age; BMI; parity; community name; history of: anemia, hypertension, diabetes, and HIV; education; marital status; presence of smoker in household or compound; asset index; ANC visits, gestational age at enrollment; gestational age at delivery; birth weight, head circumference; birth length; infant sex; placental malarial status; season of delivery; prenatal CO; and prenatal PM2.5. Each of the 10 imputed datasets contained 1306 complete observations, and analysis of the imputed data was conducted by pooling across the 10 multiply imputed datasets.

Results:

Table S4. Associations of prenatal CO exposure with birth outcomes, imputed data

	Overall Adjusted Model[a]		**Stratified by Placental Malaria Status**			
	Coefficient per 1ppm CO	**95% CI**	**Placental Malaria Status**	**Coefficient per 1ppm CO**	**95% CI**	**N**
Birth Weight (g)	-38.6	(-64.2, -13.8)	Negative	-51.5	(-82.7, -20.2)	1306
			Positive	-1.6	(-57.4, 54.2)	
Birth Length (cm)	-0.3	(-0.5, -0.02)	Negative	-0.4	(-0.6, -0.1)	1306
			Positive	-0.02	(-0.5, 0.4)	
Head Circumference (cm)	-0.1	(-0.2, 0.1)	Negative	-0.1	(-0.3, 0.1)	1306
			Positive	0.01	(-0.3, 0.3)	
Gestational age (days)	-0.5	(-1.2, 0.1)	Negative	-1.0	(-1.8, -0.2)	1306
			Positive	0.7	(-0.7, 2.1)	
Weight-for-age Z score (standard deviations)	-0.06	(-0.12, 0.001)	Negative	-0.07	(-0.15, 0.004)	1306
			Positive	-0.02	(-0.16, 0.12)	
	OR per 1ppm CO	**95% CI**		**OR per 1ppm CO**	**95% CI**	**N**
Low Birth Weight	1.13	0.98, 1.30	Negative	1.14	(0.95, 1.38)	1306
			Positive	1.10	(0.82, 1.48)	
Small for Gestational Age	1.14	(0.99, 1.31)	Negative	1.08	(0.91, 1.29)	1306
			Positive	1.28	(0.97, 1.68)	
Preterm Birth	0.98	(0.77, 1.24)	Negative	1.15	(0.80, 1.66)	1306
			Positive	0.65	(0.30, 1.39)	

[a] Covariates included in adjusted models: maternal BMI, maternal age, parity, infant sex, ANC visits, ethnicity, asset index, and placental malaria.

References

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