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Supplemental Material

Exposure to Particulate Matter Air Pollution and Age of Menarche in a Nationwide Cohort of U.S. Girls

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			PM _{2.5}					PM _{2.5-10}				PM ₁₀			
Exposure (µg/m³)	Median (IQR)	Mean (Min, Max)	In utero ^a	1- year	2- year	Cumulative	In utero ^a	1- year	2- year	Cumulative	In utero ^a	1- year	2- year	Cumulative	
PM _{2.5}															
In utero ^a	16.0 (4.6)	16.1 (4.8, 32.2)		0.69	0.71	0.84	0.32	0.21	0.22	0.27	0.71	0.49	0.50	0.61	
1-year	13.6 (4.2)	13.7 (2.3, 32.6)			0.98	0.92	0.20	0.36	0.35	0.32	0.47	0.75	0.73	0.67	
2-year	13.7 (4.2)	13.8 (2.5, 32.2)				0.93	0.20	0.35	0.36	0.32	0.48	0.73	0.74	0.68	
Cumulative	14.2 (4.0)	14.3 (4.0, 31.5)					0.25	0.31	0.32	0.34	0.58	0.67	0.69	0.73	
PM _{2.5-10}															
In utero ^a	10.5 (5.9)	11.6 (1.8, 51.1)						0.78	0.80	0.89	0.89	0.65	0.67	0.77	
1-year	7.9 (5.4)	8.8 (-0.3, 51.1) ^b							0.99	0.94	0.68	0.89	0.88	0.84	
2-year	8.0 (5.3)	8.9 (0.4, 51.1)								0.95	0.70	0.88	0.89	0.85	
Cumulative	8.6 (5.0)	9.6 (1.6, 47.5)									0.79	0.82	0.84	0.89	
PM ₁₀															
In utero ^a	26.7 (7.8)	27.7 (8.8, 83.3)										0.71	0.73	0.86	
1-year	21.6 (7.3)	22.5 (5.6, 83.3)											0.99	0.93	
2-year	21.9 (7.2)	22.7 (5.7, 83.3)												0.94	
Cumulative	23.1 (6.6)	23.8 (8.2, 78.7)													

Table S1. Pearson correlations between particulate matter (PM) exposures among 5,201 girls in the Growing Up Today Study from 1989 to 2008.

^a Correlations for in utero PM exposure were only among a subset of 4906 girls with this available data.

^b PM_{2.5-10} is calculated by subtracting estimated ambient PM_{2.5} exposure from estimated ambient PM₁₀. In rare instances, where PM_{2.5} exposure was predicted to be larger than PM₁₀, this subtraction resulted in negative values for PM_{2.5-10}.

Table S2. Hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations between residential ambient PM_{10} , $PM_{2.5-10}$, and $PM_{2.5}$ exposures and age at menarche using Cox proportional hazard models in the Growing Up Today Study 2, 1988–2008 (n = 5,201).

	HR (95% CI) ^a		
	Unadjusted	Model 1 ^b	Model 2 ^c
In utero exposure, per IQR ^{d,e}			
PM ₁₀	1.04 (1.01, 1.06)	1.06 (1.04, 1.09)	1.02 (1.00, 1.05)
PM _{2.5-10}	1.02 (0.99, 1.04)	1.04 (1.01, 1.07)	1.01 (0.98, 1.04)
PM _{2.5}	1.08 (1.05, 1.11)	1.08 (1.05, 1.11)	1.03 (1.00, 1.06)
1-year average exposure, per IQR ^{<i>d,f</i>}			
PM ₁₀	1.03 (1.00, 1.06)	1.05 (1.01, 1.09)	1.02 (0.99, 1.06)
PM _{2.5-10}	0.99 (0.96, 1.02)	1.00 (0.97, 1.04)	0.99 (0.96, 1.03)
PM _{2.5}	1.09 (1.05, 1.13)	1.09 (1.05, 1.14)	1.06 (1.02, 1.10)
2-year average exposure, per IQR ^{<i>d,f</i>}			
PM ₁₀	1.04 (1.00, 1.07)	1.06 (1.02, 1.10)	1.03 (0.99, 1.07)
PM _{2.5-10}	1.00 (0.97, 1.03)	1.01 (0.98, 1.05)	1.00 (0.96, 1.03)
PM _{2.5}	1.09 (1.05, 1.13)	1.10 (1.06, 1.14)	1.06 (1.02, 1.10)
Cumulative average exposure, per IQR ^{<i>d,f</i>}			
PM ₁₀	1.05 (1.02, 1.09)	1.08 (1.04, 1.12)	1.04 (1.00, 1.08)
PM _{2.5-10}	1.02 (0.99, 1.05)	1.04 (1.01, 1.09)	1.01 (0.97, 1.05)
PM _{2.5}	1.10 (1.06, 1.14)	1.10 (1.06, 1.15)	1.06 (1.02, 1.10)

^a Hazard ratios greater than 1 indicate that the exposure is associated with earlier age at menarche and HRs less than 1 indicate an association with later age at menarche.

^b Adjusted for neighborhood SES, region of residence, race, ethnicity, maternal age at menarche, and birthweight.

^cAdjusted for all covariates in model 1 plus year of birth.

^dHazard ratios are per increase in IQR. For PM_{2.5} the IQR is 4 µg/m³, for PM_{2.5-10} the IQR is 5 µg/m³, and for PM₁₀ the IQR is 7 µg/m³.

^e The in-utero models exclude individuals who were missing PM during in-utero or at birth (n=295).

Table S3. Hazard ratios (HRs) and 95% confidence intervals (Cis) for the association between residential ambient PM_{2.5} exposure and age at menarche using restricted cubic splines in the Growing Up Today Study 2, 1988-2008 (n=5,201).

	In utero		1-Year		2-Year		Cumulative	
Spline ^a	PM _{2.5}	HR (95% CI) ^{b,c}						
	(µg/m3)		(µg/m3)		(µg/ms)		(µg/113)	
Knot 1	11.5	1.00 (0.91, 1.11)	8.8	0.89 (0.81, 0.98)	8.9	0.84 (0.76, 0.93)	10.2	0.95 (0.86, 1.04)
Knot 2	16.0	1.00 (1.00, 1.00)	12.1	1.00 (1.00, 1.00)	12.2	1.00 (1.00, 1.00)	13.4	1.00 (1.00, 1.00)
Knot 3	20.5	1.07 (0.97, 1.18)	15.3	1.28 (1.16, 1.41)	15.4	1.34 (1.22, 1.47)	16.6	1.21 (1.10, 1.33)

^aKnots for restricted cubic spline model

^b Hazard ratios greater than 1 indicate that the exposure is associated with earlier age at menarche and HRs less than 1 indicate an association with later age at menarche.

^c Adjusted for neighborhood SES, region of residence, race, ethnicity, maternal age at menarche, birthweight and year of birth.

			Age										
Exposure		8	9	10	11	12	13	14	15	16	17		
PM _{2.5}	10 th	1.00	0.99	0.95	0.77	0.50	0.27	0.15	0.11	0.10	0.10		
	90 th	1.00	0.99	0.94	0.75	0.46	0.23	0.12	0.08	0.08	0.08		
PM _{2 5-10}	10 th	1.00	0.99	0.95	0.76	0.49	0.26	0.15	0.10	0.10	0.09		
2.5 10	90 th	1.00	0.99	0.95	0.76	0.48	0.25	0.14	0.10	0.09	0.09		
PM ₁₀	10 th	1.00	0.99	0.95	0.76	0.49	0.26	0.15	0.10	0.10	0.10		
	90 th	1.00	0.99	0.94	0.75	0.47	0.24	0.13	0.09	0.08	0.08		

Table S4. Predicted survival time for girls in the Growing Up Today Study 2 (n=5,201) exposed to the 10th and 90th percentile for the cumulative average PM exposure from 1988 to 2008 using Cox proportional hazard model.

Predicted survival curves are modeled from adjusted Cox proportional hazard models using the mean value of continuous covariates and most common level for categorical covariates. These specific curves were estimated for a White, non-Hispanic girls living in the Northeast region in a neighborhood with the lowest socioeconomic status, who had a birthweight between 2500 to 4000 grams, whose mother had an age of menarche between 12 and 15 years, and who was born between 1989 and 1990. The solid red line is the predicted survival curve for the 90th percentile for cumulative average PM exposure (PM_{2.5}: 17.9 μ g/m³; PM_{2.5-10}: 14.9 μ g/m³; PM₁₀: 30.5 μ g/m³). The dashed blue line is the predicted survival curve for the 10th percentile for the cumulative average PM exposure (PM_{2.5}: 10.7 μ g/m³; PM_{2.5-10}: 5.2 μ g/m³; PM₁₀: 17.4 μ g/m³).

			Age										
Exposure		8	9	10	11	12	13	14	15	16	17		
PM25	10 th	1.00	0.99	0.95	0.77	0.50	0.27	0.16	0.11	0.11	0.10		
	90 th	1.00	1.00	0.94	0.75	0.47	0.24	0.14	0.09	0.09	0.09		
PM _{2.5-10}	10 th	1.00	0.99	0.95	0.76	0.48	0.26	0.15	0.10	0.10	0.10		
	90 th	1.00	0.99	0.94	0.75	0.48	0.25	0.14	0.10	0.09	0.09		
PM ₁₀	10 th	1.00	0.99	0.95	0.76	0.49	0.26	0.15	0.11	0.10	0.10		
	90 th	1.00	0.99	0.94	0.75	0.47	0.24	0.14	0.09	0.09	0.09		

Table S5. Predicted survival time for girls in the Growing Up Today Study 2 (n=4,906) exposed to the 10th and 90th percentile for the in utero PM average from 1988 to 2008 using Cox proportional hazard model.

Predicted survival curves are modeled from adjusted Cox proportional hazard models using the mean value of continuous covariates and most common level for categorical covariates. These specific curves were estimated for a White, non-Hispanic girl living in the Northeast region, in a neighborhood with the lowest socioeconomic status, who had a birthweight between 2500 to 4000 grams, whose mother had an age at menarche between 12 and 15 years, and who was born between 1989 and 1990. The dashed red line is the predicted survival curve for the 90th percentile for cumulative average PM exposure (PM_{2.5}: 20.3 μ g/m³; PM_{2.5-10}: 18.3 μ g/m³; PM₁₀: 35.4 μ g/m³). The dotted blue line is the predicted survival curve for the 10th percentile for the cumulative average PM exposure (PM_{2.5}: 11.6 μ g/m³; PM_{2.5-10}: 6.2 μ g/m³; PM₁₀: 20.1 μ g/m³). In utero model excluded 297 individuals and childhood models excluded 2 individuals with missing exposure information.

		Age										
Exposure		8	9	10	11	12	13	14	15	16	17	
PM _{2.5}	10 th	1.00	0.99	0.95	0.77	0.49	0.26	0.15	0.10	0.10	0.10	
	90 th	1.00	0.99	0.94	0.74	0.45	0.23	0.12	0.08	0.08	0.07	
PM _{2.5-10}	10 th	1.00	0.99	0.95	0.76	0.48	0.26	0.15	0.10	0.09	0.09	
	90 th	1.00	0.99	0.95	0.77	0.49	0.26	0.15	0.10	0.10	0.10	
PM ₁₀	10 th	1.00	0.99	0.95	0.76	0.49	0.26	0.15	0.10	0.10	0.09	
	90 th	1.00	0.99	0.94	0.75	0.47	0.24	0.13	0.09	0.09	0.08	

Table S6. Predicted survival time for girls in the Growing Up Today Study 2 (n=5,201) exposed to the 10th and 90th percentile for the 1-year PM average from 1988 to 2008 using Cox proportional hazard model.

Predicted survival curves are modeled from adjusted Cox proportional hazard models using the mean value of continuous covariates and most common level for categorical covariates. These specific curves were estimated for a White, non-Hispanic girl living in the Northeast region, in a neighborhood with the lowest socioeconomic status, who had a birthweight between 2500 to 4000 grams, whose mother had an age at menarche between 12 and 15 years, and who was born between 1989 and 1990. The dashed red line is the predicted survival curve for the 90th percentile for cumulative average PM exposure (PM_{2.5}: 17.7 μ g/m³; PM_{2.5-10}: 14.2 μ g/m³; PM₁₀: 30.0 μ g/m³). The dotted blue line is the predicted survival curve for the 10th percentile for the cumulative average PM exposure (PM_{2.5}: 9.8 μ g/m³; PM_{2.5-10}: 4.1 μ g/m³; PM₁₀: 15.5 μ g/m³). In utero model excluded 297 individuals and childhood models excluded 2 individuals with missing exposure information.

		Age									
Exposure		8	9	10	11	12	13	14	15	16	17
PM _{2.5}	10 th	1.00	0.99	0.95	0.77	0.49	0.26	0.15	0.10	0.10	0.10
	90 th	1.00	0.99	0.94	0.74	0.45	0.23	0.12	0.08	0.08	0.07
PM _{2 5-10}	10 th	1.00	0.99	0.95	0.76	0.49	0.26	0.15	0.10	0.10	0.09
2.0.10	90 th	1.00	0.99	0.95	0.76	0.49	0.26	0.15	0.10	0.10	0.10
PM ₁₀	10 th	1.00	0.99	0.95	0.76	0.49	0.26	0.15	0.10	0.10	0.09
	90 th	1.00	0.99	0.94	0.75	0.47	0.24	0.13	0.09	0.08	0.08

Table S7. Predicted survival time for girls in the Growing Up Today Study 2 (n=5,201) exposed to the 10th and 90th percentile for the 2-year PM average from 1988 to 2008 using Cox proportional hazard model.

Predicted survival curves are modeled from adjusted Cox proportional hazard models using the mean value of continuous covariates and most common level for categorical covariates. These specific curves were estimated for a White, non-Hispanic girl living in the Northeast region, in a neighborhood with the lowest socioeconomic status, who had a birthweight between 2500 to 4000 grams, whose mother had an age at menarche between 12 and 15 years, and who was born between 1989 and 1990. The dashed red line is the predicted survival curve for the 90th percentile for cumulative average PM exposure (PM_{2.5}: 17.7 μ g/m³; PM_{2.5-10}: 14.4 μ g/m³; PM₁₀: 30.2 μ g/m³). The dotted blue line is the predicted survival curve for the 10th percentile for the cumulative average PM exposure (PM_{2.5}: 10.0 μ g/m³; PM_{2.5-10}: 4.3 μ g/m³; PM₁₀: 15.8 μ g/m³). In utero model excluded 297 individuals and childhood models excluded 2 individuals with missing exposure information. **Table S8.** Hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations between residential PM_{10} , $PM_{2.5-10}$, and $PM_{2.5}$ exposures and age at menarche using Cox proportional hazard models in the Growing Up Today Study 2, 1988–2008 who did not move during the study period (n = 1827).

	HR (9	5% CI) ^{1a}
	Unadjusted	Adjusted ^b
In utero exposure, per IQR ^{c,d}		
PM ₁₀	1.01 (0.94, 1.07)	1.03 (0.96, 1.11)
PM _{2.5-10}	0.98 (0.92, 1.03)	1.02 (0.94, 1.10)
PM _{2.5}	1.07 (1.00, 1.15)	1.04 (0.97, 1.12)
1-year average exposure, per IQR ^c		
PM ₁₀	0.97 (0.90, 1.05)	1.02 (0.94, 1.11)
PM _{2.5-10}	0.92 (0.86, 0.99)	0.95 (0.87, 1.04)
PM _{2.5}	1.11 (1.02, 1.21)	1.11 (1.02, 1.21)
2-year average exposure, per IQR ^c		
PM ₁₀	0.98 (0.91, 1.07)	1.04 (0.95, 1.13)
PM _{2.5-10}	0.94 (0.87, 1.01)	0.98 (0.90, 1.06)
PM _{2.5}	1.12 (1.02, 1.22)	1.12 (1.02, 1.22)
Cumulative average exposure, per IQR ^c		
PM ₁₀	1.00 (0.93, 1.08)	1.05 (0.97, 1.14)
PM _{2.5-10}	0.95 (0.89, 1.02)	1.00 (0.92, 1.09)
PM _{2.5}	1.12 (1.02, 1.22)	1.12 (1.01, 1.21)

^a Hazard ratios greater than 1 indicate that the exposure is associated with earlier age at menarche and HRs less than 1 indicate an association with later age at menarche.

^b Adjusted for neighborhood SES, median house value, region of residence, race, ethnicity, maternal age at menarche, birthweight, and year of birth.

^c Hazard ratios are per increase in IQR. For PM_{2.5} the IQR is 4 μ g/m³, for PM_{2.5-10} the IQR is 5 μ g/m³, and for PM₁₀ the IQR is 7 μ g/m³.

^dThe in-utero models exclude individuals who were missing PM during in-utero or at birth (n=81).

Table S9. Hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations between residential $PM_{2.5-10}$, and $PM_{2.5}$ exposures and age at menarche using Cox proportional hazard models in the Growing Up Today Study 2, 1988–2008 (n = 5,201) using multipollutant models.

Time period	In utero ^a HR (95% CI) ^{b,c}		1-Yea HR (95	ar lag % Cl) ^{b,c}	2-Yea HR (95	ar lag % Cl) ^{b,c}	Cumulative HR (95% CI) ^{b,c}		
Exposure	Unadjusted	Adjusted ^d	Unadjusted	Adjusted ^d	Unadjusted	Adjusted ^d	Unadjusted	Adjusted ^d	
PM _{2.5-10}	1.00 (0.97, 1.02)	1.00 (0.97, 1.03)	0.98 (0.95, 1.01)	0.98 (0.94, 1.01)	0.98 (0.95, 1.02)	0.98 (0.95, 1.02)	1.00 (0.97, 1.03)	0.99 (0.95, 1.03)	
PM _{2.5}	1.08 (1.05, 1.11)	1.03 (1.00, 1.07)	1.09 (1.05, 1.13)	1.06 (1.02, 1.10)	1.09 (1.05, 1.14)	1.06 (1.02, 1.10)	1.10 (1.06, 1.14)	1.07 (1.03, 1.11)	

^a The in-utero models exclude individuals who were missing PM during in-utero or at birth (n=295).

^b Hazard ratios greater than 1 indicate that the exposure is associated with earlier age at menarche and HRs less than 1 indicate an association with later age at menarche.

^c Hazard ratios are per increase in IQR. For PM_{2.5} the IQR is 4 μ g/m³ and for PM_{2.5-10} the IQR is 5 μ g/m³.

^{*d*}Adjusted for neighborhood SES, region of residence, race, ethnicity, maternal age at menarche, birthweight, year of birth, and size fraction (PM_{2.5}, PM_{2.5-10}).

Table S10. Hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations between 1-year average residential PM_{10} , $PM_{2.5-10}$, and $PM_{2.5}$ exposures and age at menarche in the Growing Up Today Study 2, 1988–1995 (n = 5,201) further adjusting for cumulative average exposures.

	Adjusted HR (95% CI) further accounting for cumulative average ^a							
Exposure	PM _{2.5}	PM _{2.5-10}	PM ₁₀					
1-year average exposure, per IQR	1.01 (0.96, 1.06)	0.99 (0.95, 1.04)	1.00 (0.96, 1.04)					

^a Hazard ratios greater than 1 indicate that the exposure is associated with earlier age at menarche and HRs less than 1 indicate an association with later age at menarche.

^b Hazard ratios are per increase in IQR. For PM_{2.5} the IQR is 4 µg/m³, for PM_{2.5-10} the IQR is 5 µg/m³, and for PM₁₀ the IQR is 7 µg/m³.

^c Adjusted for neighborhood SES, region of residence, race, ethnicity, maternal age at menarche, birthweight, year of birth, and cumulative average exposure.

Figure S1. Overview of exclusion criteria applied to the Growing Up Today Study 2 participants from 1988 to 2008



Figure S2. Restricted cubic spline models to test the non-linear association between PM_{2.5} and age at menarche in the Growing Up Today Study 2, 1988–2008 (n=5,201) (see Table S3).



Caption. Restricted cubic splines were adjusted for race, ethnicity, region of residence, birth weight, maternal age at menarche, neighborhood socioeconomic status, and year of birth. The p-value for non-linearity were 0.40 for in utero, 0.09 for 1-year average, 0.14 for 2-year average, and 0.09 for cumulative PM_{2.5} exposure. P-values represent the test for curvature with smaller p-values indicating likelihood of a non-linear association between PM exposure and age at menarche. In utero model excluded 295 individuals with missing exposure information.

Figure S3. Predicted survival time for girls in the Growing Up Today Study 2 (n=5,201) exposed to the 10th and 90th percentile for the in utero PM average from 1988 to 2008 using Cox proportional hazard model (see Table S5).



Caption. Predicted survival curves are modeled from adjusted Cox proportional hazard models using the mean value of continuous covariates and most common level for categorical covariates. These specific curves were estimated for a White, non-Hispanic girl living in the Northeast region, in a neighborhood with the lowest socioeconomic status, who had a birthweight between 2500 to 4000 grams, whose mother had an age at menarche between 12 and 15 years, and who was born between 1989 and 1990. The dashed red line is the predicted survival curve for the 90th percentile for cumulative average PM exposure (PM_{2.5}: 20.3 μ g/m³; PM_{2.5-10}: 18.3 μ g/m³; PM₁₀: 35.4 μ g/m³). The dotted blue line is the predicted survival curve for the 10th percentile for the cumulative average PM exposure (PM_{2.5}: 11.6 μ g/m³; PM_{2.5-10}: 6.2 μ g/m³; PM₁₀: 20.1 μ g/m³). In utero model excluded 295 individuals with missing exposure information.

Figure S4. Predicted survival time for girls in the Growing Up Today Study 2 (n=5,201) exposed to the 10th and 90th percentile for the 1-year PM average from 1988 to 2008 using Cox proportional hazard model (see Table S6).



Caption. Predicted survival curves are modeled from adjusted Cox proportional hazard models using the mean value of continuous covariates and most common level for categorical covariates. These specific curves were estimated for a White, non-Hispanic girl living in the Northeast region, in a neighborhood with the lowest socioeconomic status, who had a birthweight between 2500 to 4000 grams, whose mother had an age at menarche between 12 and 15 years and who was born between 1989 and 1990. The dashed red line is the predicted survival curve for the 90th percentile for cumulative average PM exposure (PM_{2.5}: 17.7 μ g/m³; PM_{2.5-10}: 14.2 μ g/m³; PM₁₀: 30.0 μ g/m³). The dotted blue line is the predicted survival curve for the 10th percentile for the cumulative average PM exposure (PM_{2.5}: 9.8 μ g/m³; PM_{2.5-10}: 4.1 μ g/m³; PM₁₀: 15.5 μ g/m³). For PM_{2.5-10} the 10th and 90th percentiles are almost indistinguishable. In utero model excluded 295 individuals with missing exposure information.

Figure S5. Predicted survival time for girls in the Growing Up Today Study 2 (n=5,201) exposed to the 10th and 90th percentile for the 2-year PM average from 1988 to 2008 using Cox proportional hazard model (see Table S7).



Caption. Predicted survival curves are modeled from adjusted Cox proportional hazard models using the mean value of continuous covariates and most common level for categorical covariates. These specific curves were estimated for a White, non-Hispanic girl living in the Northeast region, in a neighborhood with the lowest socioeconomic status, who had a birthweight between 2500 to 4000 grams, whose mother had an age at menarche between 12 and 15 years, and who was born between 1989 and 1990. The dashed red line is the predicted survival curve for the 90th percentile for cumulative average PM exposure (PM_{2.5}: 17.7 μ g/m³; PM_{2.5-10}: 14.4 μ g/m³; PM₁₀: 30.2 μ g/m³). The dotted blue line is the predicted survival curve for the 10th percentile for the cumulative average PM exposure (PM_{2.5}: 10.0 μ g/m³; PM_{2.5-10}: 4.3 μ g/m³; PM₁₀: 15.8 μ g/m³). In utero model excluded 295 individuals with missing exposure information.