



APPENDIX AVAILABLE ON THE HEI WEBSITE

Research Report 213

Ambient Air Pollution and All-Cause and Cause-Specific Mortality in an Analysis of Asian Cohorts

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Appendix: Supplementary Tables and Figures

This Appendix was reviewed solely for spelling, grammar, and cross-references to the main text.
It has not been formatted or fully edited by HEI. This document was part of the HEI Review
Committee's review process.

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Appendix: Supplementary Tables and Figures

Ambient Air Pollution and All-Cause and Cause-Specific Mortality in an Analysis of Asian Cohorts

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Supplementary Tables and Figures: Community-based Cancer Screening Program (CBCSCP)

Table A1. Demographic features of the Community-based Cancer Screening Program (CBCSCP)

Variable	Mean (sd) or n (%)	n. missing values
Number participants	23,759	
Age at recruitment	47 (10)	
Sex		
Male	11,939 (50%)	
Female	11,820 (50%)	
Recruitment year		
1991	12,037 (51%)	
1992	11,722 (49%)	
Follow-up (years)	23 (6)	
Smoking		40
Ever	6,861 (29%)	
Never	16,858 (71%)	
Pack-years (ever smokers only)	24 (20)	330
BMI	24 (3.4)	56
<20	2,423 (10%)	
20-25	12,761 (54%)	
25-30	7,374 (31%)	
>30	1,145 (5%)	
Education		
Illiterate	5,081 (21%)	
Elementary	9,884 (42%)	
Junior high school	3,267 (14%)	
Senior high school	3,546 (15%)	
Junior college	1,310 (6%)	
University	617 (3%)	
Graduate school or higher	44 (<1%)	
No answer	10 (<1%)	
Alcohol history		56
Ever drinker	2,518 (11%)	
Never drinker	21,185 (89%)	
Mortality		
All-cause	6,295	
Nonaccidental	5,281	
All cancer	2,189	
Lung cancer	466	
Cardiovascular disease	1,089	
Nonmalignant lung disease	587	

Table A2. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ in the Community-based Cancer Screening Program (CBCSCP)

	Model 1		Model 2		Model 3	
	n. events (total = 23,390)	HR (95% CI)	n. events (total = 23,390)	HR (95% CI)	n. events (total = 22,952)	HR (95% CI)
All-cause	6,185	0.96 (0.94, 0.98)	6,185	0.98 (0.96, 1.00)	6,016	1.00 (0.98, 1.02)
Nonaccidental	5,720	0.97 (0.95, 0.99)	5,720	0.98 (0.96, 1.00)	5,564	1.00 (0.98, 1.02)
All cancer	2,144	0.97 (0.94, 1.01)	2,144	0.99 (0.95, 1.02)	2,089	1.00 (0.97, 1.04)
Lung cancer	460	0.96 (0.89, 1.04)	460	0.98 (0.91, 1.06)	449	1.01 (0.93, 1.09)
Cardiovascular disease	1,071	1.02 (0.98, 1.07)	1,071	1.03 (0.99, 1.09)	1,049	1.05 (1.00, 1.10)
Nonmalignant lung disease	579	0.94 (0.87, 1.01)	579	0.95 (0.89, 1.03)	551	0.98 (0.91, 1.05)

Model 1: Unadjusted.

Model 2: Adjusted for recruitment year and sex.

Model 3: Adjusted for recruitment year, sex, smoking status and intensity, BMI, education, and alcohol intake.

Table A3. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to a 10-ppb increase in NO_2 in the in the Community-based Cancer Screening Program (CBCSCP)

	Model 1		Model 2		Model 3	
	n. events (total = 13,035)	HR (95% CI)	n. events (total = 13,035)	HR (95% CI)	n. events (total = 12,844)	HR (95% CI)
All-cause	3,396	0.66 (0.56, 0.78)	3,396	0.67 (0.57, 0.79)	3,321	0.76 (0.65, 0.90)
Nonaccidental	3,111	0.65 (0.55, 0.77)	3,111	0.66 (0.55, 0.78)	3,041	0.74 (0.62, 0.88)
All cancer	1,058	1.02 (0.78, 1.33)	1,058	1.03 (0.78, 1.35)	1,035	1.15 (0.87, 1.51)
Lung cancer	226	1.15 (0.64, 2.06)	226	1.18 (0.66, 2.10)	218	1.44 (0.79, 2.60)
Cardiovascular disease	593	0.64 (0.43, 0.95)	593	0.63 (0.43, 0.94)	581	0.74 (0.49, 1.10)
Nonmalignant lung disease	372	0.45 (0.27, 0.76)	372	0.45 (0.27, 0.76)	360	0.58 (0.34, 1.00)

Model 1: Unadjusted.

Model 2: Adjusted for recruitment year and sex.

Model 3: Adjusted for recruitment year, sex, smoking status and intensity, BMI, education, and alcohol intake.

Table A4. Hazard ratios (and 95% confidence intervals) for specific causes of death for a two-pollutant model in the Community-based Cancer Screening Program (CBCSCP) (Model 3)

	n. events (total = 12,843)	PM _{2.5} HR (95% CI)	NO ₂ HR (95% CI)
All-cause	3,321	1.01 (0.98, 1.03)	0.76 (0.65, 0.90)
Nonaccidental	3,041	1.01 (0.98, 1.03)	0.74 (0.62, 0.88)
All cancer	1,035	1.00 (0.96, 1.04)	1.14 (0.87, 1.51)
Lung cancer	218	1.01 (0.92, 1.10)	1.43 (0.79, 2.60)
Cardiovascular disease	581	1.05 (1.00, 1.11)	0.71 (0.48, 1.07)
Nonmalignant lung disease	360	1.03 (0.96, 1.10)	0.58 (0.34, 0.99)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂.

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, education, and alcohol intake.

Table A5. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ in the Community-based Cancer Screening Program (CBCSCP), stratified by smoking status (Model 3)

	Ever-smokers		Never-smokers	
	n. events (total = 6,414)	HR (95% CI)	n. events (total = 16,538)	HR (95% CI)
All-cause	2,472	1.01 (0.97, 1.04)	3,544	0.99 (0.96, 1.02)
Nonaccidental	2,285	1.01 (0.97, 1.04)	3,279	1.00 (0.97, 1.03)
All cancer	885	1.01 (0.96, 1.07)	1,204	1.00 (0.95, 1.04)
Lung cancer	219	1.05 (0.93, 1.17)	230	0.98 (0.87, 1.09)
Cardiovascular disease	442	1.05 (0.97, 1.14)	607	1.06 (0.99, 1.13)
Nonmalignant lung disease	259	0.92 (0.81, 1.03)	292	1.03 (0.94, 1.14)

Models adjusted for recruitment year, sex, smoking intensity (ever smokers only), BMI, education, and alcohol intake.

Table A6. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 10-ppb increase in NO_2 in the Community-based Cancer Screening Program (CBCSCP), stratified by smoking status (Model 3)

	Ever-smokers		Never-smokers	
	n. events (total = 3,698)	HR (95% CI)	n. events (total = 9,146)	HR (95% CI)
All-cause	1,357	0.86 (0.66, 1.11)	1,964	0.71 (0.57, 0.88)
Nonaccidental	1,240	0.84 (0.64, 1.10)	1,801	0.68 (0.54, 0.86)
All cancer	446	1.52 (1.01, 2.28)	589	0.91 (0.62, 1.33)
Lung cancer	115	1.57 (0.70, 3.52)	103	1.31 (0.54, 3.16)
Cardiovascular disease	248	0.65 (0.35, 1.21)	333	0.81 (0.48, 1.38)
Nonmalignant lung disease	168	0.53 (0.23, 1.20)	192	0.62 (0.30, 1.28)

Models adjusted for recruitment year, sex, smoking intensity (ever smokers only), BMI, education, and alcohol intake.

Table A7. Hazard ratios (and 95% confidence intervals) for specific causes of death among nonsmoking women within the Community-based Cancer Screening Program (CBCSCP) (Model 3)

	PM _{2.5}		NO ₂	
	n. events (total = 11,452)	HR (95% CI)	n. events (total = 6,358)	HR (95% CI)
All-cause	2,229	0.99 (0.96, 1.03)	1,221	0.69 (0.52, 0.91)
Nonaccidental	2,076	1.00 (0.96, 1.03)	1,132	0.67 (0.50, 0.90)
All cancer	745	1.00 (0.94, 1.06)	376	0.91 (0.57, 1.46)
Lung cancer	154	0.96 (0.84, 1.10)	74	1.31 (0.46, 3.76)
Cardiovascular disease	403	1.06 (0.98, 1.14)	212	0.78 (0.40, 1.51)
Nonmalignant lung disease	174	1.06 (0.95, 1.19)	114	0.75 (0.29, 1.90)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Models adjusted for recruitment year, BMI, education, and alcohol intake.

Table A8. Hazard ratios (and 95% confidence intervals) for specific causes of death among those of the Community-based Cancer Screening Program (CBCSCP) who were alive in 1998 (Model 3)

	PM _{2.5}		NO ₂	
	n. events (total = 22,286)	HR (95% CI)	n. events (total = 12,499)	HR (95% CI)
All-cause	5,350	0.99 (0.97, 1.01)	2,976	0.73 (0.61, 0.87)
Nonaccidental	5,007	0.99 (0.97, 1.01)	2,761	0.71 (0.59, 0.86)
All cancer	1,853	0.99 (0.95, 1.03)	929	1.09 (0.82, 1.47)
Lung cancer	412	1.00 (0.92, 1.09)	197	1.44 (0.78, 2.68)
Cardiovascular disease	924	1.05 (0.99, 1.11)	513	0.64 (0.42, 0.99)
Nonmalignant lung disease	520	0.98 (0.90, 1.06)	342	0.49 (0.28, 0.86)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Models adjusted for recruitment year, sex, smoking intensity (ever smokers only), BMI, education status, and alcohol intake.

Table A9. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to a 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ after additional adjustment for specific urban scenarios within the Community-based Cancer Screening Program (CBCSCP) (Model 3)

	Within Urban Center (Y/N)*		Degree of Urbanicity† in 2000		Degree of Urbanicity in 2010	
	n. events (total = 22,952)	HR (95% CI)	n. events (total = 22,612)	HR (95% CI)	n. events (total = 22,612)	HR (95% CI)
All-cause	6,016	0.99 (0.95, 1.02)	5,909	1.02 (0.99, 1.05)	5,909	1.02 (0.99, 1.04)
Nonaccidental	5,564	0.99 (0.96, 1.02)	5,458	1.03 (1.00, 1.06)	5,458	1.02 (0.99, 1.05)
All cancer	2,089	1.09 (1.03, 1.15)	2,049	1.05 (1.01, 1.10)	2,049	1.05 (1.00, 1.10)
Lung cancer	449	1.16 (1.03, 1.31)	445	1.05 (0.95, 1.16)	445	1.05 (0.95, 1.15)
Cardiovascular disease	1,049	1.01 (0.93, 1.08)	1,034	1.07 (1.00, 1.14)	1,034	1.06 (1.00, 1.13)
Nonmalignant lung disease	551	0.86 (0.77, 0.96)	542	0.99 (0.90, 1.09)	542	0.98 (0.90, 1.07)

*: Refers to a participant being within an urban center as defined by the Global Human Settlement Layer.

†: Refers to gradient values for urbanicity as described by Gao & O'Neill (2020).

Models additionally adjusted for recruitment year, sex, smoking status and intensity, BMI, education, and alcohol intake.

Table A10. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to a 10-ppb increase in NO₂ after additional adjustment for specific urban scenarios within the Community-based Cancer Screening Program (CBCSCP) (Model 3)

	Within Urban Center (Y/N)*		Degree of Urbanicity† in 2000		Degree of Urbanicity in 2010	
	n. events (total = 12,844)	HR (95% CI)	n. events (total = 12,844)	HR (95% CI)	n. events (total = 12,844)	HR (95% CI)
All-cause	3,321	0.76 (0.65, 0.90)	3,321	0.78 (0.65, 0.93)	3,321	0.78 (0.65, 0.94)
Nonaccidental	3,041	0.74 (0.62, 0.88)	3,041	0.76 (0.63, 0.91)	3,041	0.76 (0.63, 0.92)
All cancer	1,035	1.15 (0.87, 1.52)	1,035	1.23 (0.91, 1.67)	1,035	1.22 (0.9, 1.65)
Lung cancer	218	1.46 (0.80, 2.66)	218	1.51 (0.78, 2.90)	218	1.52 (0.79, 2.92)
Cardiovascular disease	581	0.72 (0.48, 1.08)	581	0.66 (0.43, 1.01)	581	0.65 (0.42, 1.01)
Nonmalignant lung disease	360	0.58 (0.34, 1.00)	360	0.61 (0.34, 1.10)	360	0.63 (0.35, 1.13)

*: Refers to a participant being within an urban center as defined by the Global Human Settlement Layer

†: Refers to gradient values for urbanicity as described by Gao & O'Neill (2020).

Models additionally adjusted for recruitment year, sex, smoking status and intensity, BMI, education, and alcohol intake.

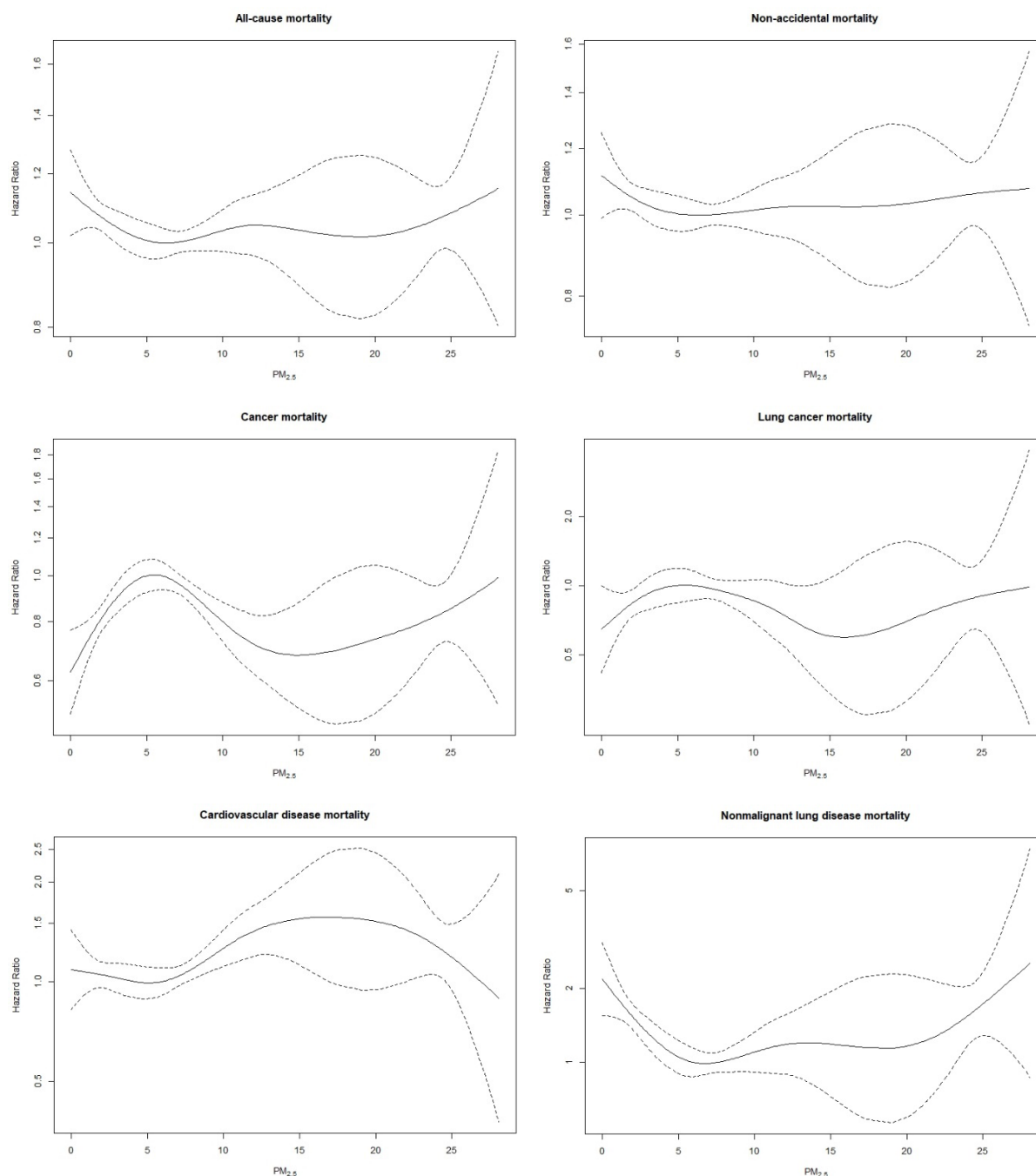


Figure A1: Penalized spline analysis (with 4 degrees of freedom) examining relationship between $PM_{2.5}$ exposure and all-cause and cause-specific mortality within the Community-based Cancer Screening Program (CBCSCP) (Model 3).

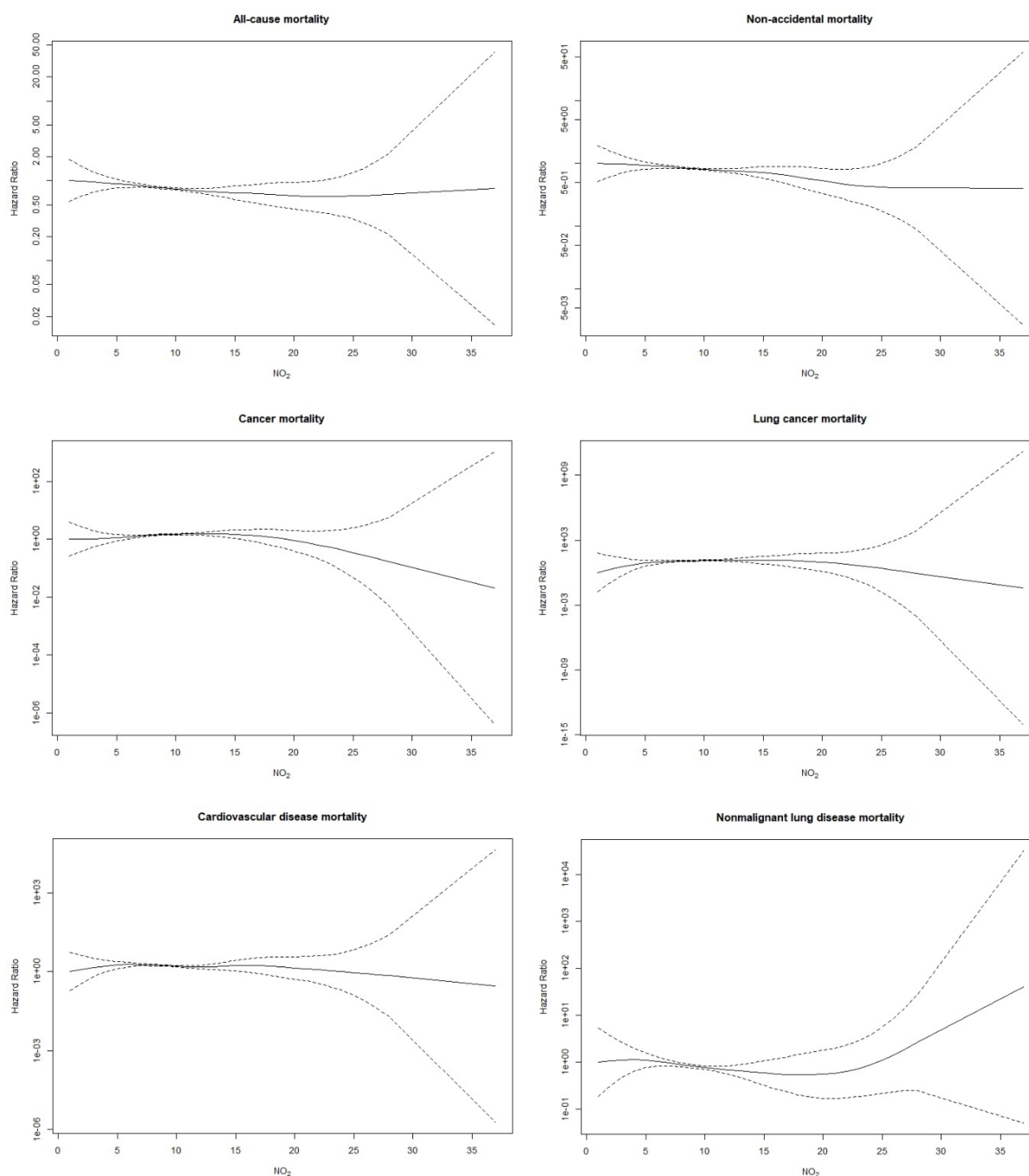


Figure A2: Penalized spline analysis (with 4 degrees of freedom) examining relationship between NO₂ exposure and all-cause and cause-specific mortality within the Community-based Cancer Screening Program (CBCSCP) (Model 3).

Table A11. Hazard ratios (and 95% confidence intervals) for specific causes of death among the Community-based Cancer Screening Program (CBCSCP) by quartile of PM_{2.5} (Model 3)

	n. events (total = 22,952)	Q1 (< 2.5 μg/m ³)	Q2 (2.5–7.0 μg/m ³)	Q3 (7.0–8.8 μg/m ³)	Q4 (>8.8 μg/m ³)
All-cause	6,016	1.00 (ref)	0.97 (0.91, 1.03)	0.92 (0.86, 0.99)	1.01 (0.93, 1.09)
Nonaccidental	5,564	1.00 (ref)	0.98 (0.92, 1.05)	0.94 (0.87, 1.01)	1.01 (0.93, 1.09)
All cancer	2,089	1.00 (ref)	1.34 (1.19, 1.50)	1.13 (1.00, 1.28)	1.01 (0.88, 1.16)
Lung cancer	449	1.00 (ref)	1.23 (0.97, 1.57)	1.05 (0.81, 1.37)	1.06 (0.79, 1.43)
Cardiovascular disease	1,049	1.00 (ref)	0.99 (0.84, 1.16)	1.03 (0.87, 1.21)	1.28 (1.07, 1.54)
Nonmalignant lung disease	551	1.00 (ref)	0.66 (0.53, 0.82)	0.66 (0.52, 0.83)	0.91 (0.71, 1.17)

Models adjusted for recruitment year, sex, smoking intensity (ever smokers only), BMI, education, and alcohol intake.

Table A12. Hazard ratios (and 95% confidence intervals) for specific causes of death among the Community-based Cancer Screening Program (CBCSCP) by quartile of NO₂ (Model 3)

	n. events (total = 12,844)	Q1 (<8 ppb)	Q2 (8–9 ppb)	Q3 (9–10 ppb)	Q4 (>10 ppb)
All-cause	3,321	1.00 (ref)	0.95 (0.87, 1.04)	0.90 (0.82, 0.99)	0.87 (0.79, 0.96)
Nonaccidental	3,041	1.00 (ref)	0.94 (0.85, 1.03)	0.91 (0.82, 1.01)	0.87 (0.79, 0.96)
All cancer	1,035	1.00 (ref)	1.01 (0.86, 1.2)	1.02 (0.86, 1.22)	1.12 (0.95, 1.31)
Lung cancer	218	1.00 (ref)	0.90 (0.61, 1.31)	1.13 (0.78, 1.64)	1.25 (0.88, 1.78)
Cardiovascular disease	581	1.00 (ref)	1.06 (0.85, 1.31)	0.84 (0.67, 1.07)	0.84 (0.67, 1.05)
Nonmalignant lung disease	360	1.00 (ref)	0.93 (0.71, 1.22)	0.90 (0.67, 1.21)	0.76 (0.56, 1.02)

Models adjusted for recruitment year, sex, smoking intensity (ever smokers only), BMI, education, and alcohol intake.

Table A13. Hazard ratios (and 95% confidence intervals) for specific causes of death within the Community-based Cancer Screening Program (CBCSCP) after adapting variables that potentially violated the proportional hazards assumption

	PM _{2.5}		NO ₂	
	n. events (total = 22,952)	HR (95% CI)	n. events (total = 12,844)	HR (95% CI)
All-cause	6,016	1.00 (0.97, 1.03)	3,321	0.78 (0.66, 0.92)
Nonaccidental	5,564	1.00 (0.97, 1.04)	3,041	0.76 (0.64, 0.9)
All cancer	2,089	1.00 (0.95, 1.05)	1,035	1.15 (0.87, 1.51)
Lung cancer	449	1.00 (0.9, 1.11)	218	1.51 (0.84, 2.7)
Cardiovascular disease	1,049	1.08 (1.01, 1.15)	581	0.74 (0.49, 1.11)
Nonmalignant lung disease	551	0.98 (0.89, 1.09)	360	0.57 (0.34, 0.98)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Potential assumption violators were pack-years (removed from analysis), sex, smoking status, and alcohol intake (stratified).

Supplementary Tables and Figures: Golestan Cohort Study

Table A14. Demographic features of the Golestan cohort

		Mean (sd) or n (%)	n. missing values
Number of participants		49,982	
Age at recruitment		52 (9)	
Sex			
	Male	21,213(42%)	
	Female	28,769 (58%)	
Recruitment year			
	2004	5,129 (10%)	
	2005	9,035 (18%)	
	2006	16,000 (32%)	
	2007	14,748 (29%)	
	2008	5,070(10%)	
Follow-up time (years)		11 (2.4)	63
Smoking status			
	Never	39,141 (78%)	
	Former	3,318 (7%)	
	Current	7,523 (15%)	
Pack-years (current/ former smokers only)		17 (18)	
BMI		27 (5)	8
	<20	5,229 (10%)	
	20-25	15,117 (30%)	
	25-30	16,917 (34%)	
	>30	12,711 (25%)	
Education			
	Illiterate:	35,079 (70%)	
	5 years or less	8,451 (17%)	
	6 to 8 years	2,238 (4%)	
	9 to 12 years	3,151 (6%)	
	University	1,063 (2%)	
Diet (g/day)			868
	Protein intake	77 (67)	
	Lipid intake	77 (49)	
	Carbohydrate intake	309 (177)	
Alcohol status			
	Never drinker	48,274 (97%)	
	Former drinker	1,373 (3%)	
	Current drinker	335 (1%)	
Mortality			
	All-cause	7,060	
	Nonaccidental	5,966 (12%)	
	All cancer	1,401 (3%)	
	Lung cancer	94 (<1%)	
	Cardiovascular disease	3,022 (6%)	
	Nonmalignant lung disease	403 (1%)	

Table A15. Domestic fuel usage in the Golestan cohort

Fuel type	n (%)
Firewood	971 (2%)
Organic fuel	100 (<1%)
Kerosene	31,548 (63%)

Represents population reporting “yes” to using one of the three fuel types.

Table A16. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ in the Golestan cohort

	Model 1		Model 2		Model 3	
	n. events (total = 49,982)	HR (95% CI)	n. events (total = 49,982)	HR (95% CI)	n. events (total = 49,106)	HR (95% CI)
All-cause	7,060	0.88 (0.86, 0.91)	7,060	0.91 (0.87, 0.94)	6,878	0.98 (0.94, 1.03)
Nonaccidental	5,966	0.89 (0.86, 0.92)	5,966	0.92 (0.88, 0.96)	5,807	1.00 (0.95, 1.05)
All cancer	1,401	0.84 (0.78, 0.90)	1,401	0.86 (0.79, 0.93)	1,366	1.02 (0.92, 1.13)
Lung cancer	94	0.91 (0.69, 1.20)	94	0.86 (0.62, 1.18)	93	0.84 (0.57, 1.25)
Cardiovascular disease	3,022	0.90 (0.86, 0.95)	3,022	0.95 (0.90, 1.00)	2,941	0.98 (0.91, 1.05)
Nonmalignant lung disease	403	0.92 (0.80, 1.05)	403	0.96 (0.82, 1.12)	394	1.10 (0.91, 1.34)

Model 1: Unadjusted.

Model 2: Adjusted for recruitment year and sex.

Model 3: Adjusted for recruitment year, sex, smoking status and intensity, BMI, education, diet, alcohol intake, and domestic fuel use.

Table A17. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 10-ppb increase in NO_2 in the Golestan cohort

	Model 1		Model 2		Model 3	
	n. events (total = 49,982)	HR (95% CI)	n. events (total = 49,982)	HR (95% CI)	n. events (total = 49,106)	HR (95% CI)
All-cause	7,060	0.69 (0.58, 0.81)	7,060	0.66 (0.54, 0.79)	6,878	1.05 (0.83, 1.33)
Nonaccidental	5,966	0.75 (0.62, 0.9)	5,966	0.67 (0.55, 0.83)	5,807	1.05 (0.81, 1.35)
All cancer	1,401	0.48 (0.32, 0.71)	1,401	0.50 (0.32, 0.77)	1,366	1.19 (0.70, 2.03)
Lung cancer	94	0.38 (0.08, 1.80)	94	0.59 (0.11, 3.29)	93	0.71 (0.10, 5.33)
Cardiovascular disease	3,022	0.88 (0.68, 1.14)	3,022	0.79 (0.59, 1.04)	2,941	0.93 (0.65, 1.33)
Nonmalignant lung disease	403	0.56 (0.27, 1.15)	403	0.65 (0.29, 1.43)	394	1.22 (0.46, 3.21)

Model 1: Unadjusted.

Model 2: Adjusted for recruitment year and sex.

Model 3: Adjusted for recruitment year, sex, smoking status and intensity, BMI, education, diet, alcohol intake, and domestic fuel use.

Table A18. Hazard ratios (and 95% confidence intervals) for specific causes of death for a two-pollutant model in the Golestan cohort

	n. events (total =49,106)	PM _{2.5} HR (95% CI)	NO ₂ HR (95% CI)
All-cause	6,878	0.96 (0.91, 1.02)	1.17 (0.88, 1.56)
Nonaccidental	5,807	0.99 (0.93, 1.05)	1.08 (0.80, 1.48)
All cancer	1,366	1.00 (0.88, 1.13)	1.20 (0.63, 2.27)
Lung cancer	93	0.81 (0.49, 1.33)	1.37 (0.11, 16.66)
Cardiovascular disease	2,941	0.98 (0.90, 1.06)	1.00 (0.65, 1.54)
Nonmalignant lung disease	394	1.13 (0.88, 1.43)	0.85 (0.25, 2.89)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂.

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, education, diet, alcohol intake, and domestic fuel use.

Table A19. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to fuel use in the Golestan cohort

	n. events (total =49,106)	Solid fuel (n = 995) HR (95% CI)	Kerosene (n = 31,548) HR (95% CI)
All-cause	6,878	1.25 (1.09, 1.44)	1.14 (1.08, 1.20)
Nonaccidental	5,807	1.19 (1.02, 1.39)	1.11 (1.05, 1.18)
All cancer	1,366	1.08 (0.78, 1.50)	1.26 (1.12, 1.43)
Lung cancer	93	0.86 (0.21, 3.55)	0.91 (0.58, 1.43)
Cardiovascular disease	2,941	1.18 (0.94, 1.47)	1.06 (0.97, 1.15)
Lung disease	394	1.71 (1.03, 2.85)	0.92 (0.74, 1.14)
Metabolic disease	59	1.55 (0.37, 6.47)	0.75 (0.43, 1.30)

Solid fuel: either firewood or other organic material.

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, education, diet, and alcohol intake.

Table A20. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ in the Golestan cohort, stratified by smoking status (Model 3)

	Never smokers		Former smokers		Current smokers	
	n. events (total = 40,591)	HR (95% CI)	n. events (total = 3,932)	HR (95% CI)	n. events (total = 4,583)	HR (95% CI)
All-cause	5,055	0.98 (0.93, 1.03)	919	1.01 (0.88, 1.15)	904	0.94 (0.82, 1.07)
Nonaccidental	4,271	0.99 (0.94, 1.05)	785	1.04 (0.90, 1.20)	751	0.96 (0.83, 1.11)
All cancer	998	1.09 (0.96, 1.22)	171	0.80 (0.59, 1.08)	197	0.89 (0.67, 1.17)
Lung cancer	36	0.94 (0.49, 1.79)	19	0.56 (0.22, 1.45)	38	0.91 (0.50, 1.67)
Cardiovascular disease	2,197	0.95 (0.88, 1.03)	393	1.14 (0.93, 1.39)	351	0.97 (0.78, 1.20)
Nonmalignant lung disease	245	1.02 (0.80, 1.30)	82	1.06 (0.69, 1.64)	67	1.41 (0.89, 2.23)

Models adjusted for recruitment year, sex, smoking intensity (current/former smokers only), BMI, education, diet, alcohol intake, and domestic fuel use.

Table A21. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 10-ppb increase in NO_2 in the Golestan cohort, stratified by smoking status (Model 3)

	Never smokers		Former smokers		Current smokers	
	n. events (total = 40,591)	HR (95% CI)	n. events (total = 3,932)	HR (95% CI)	n. events (total = 4,583)	HR (95% CI)
All-cause	5,055	1.06 (0.81, 1.40)	919	0.89 (0.46, 1.72)	904	1.10 (0.58, 2.08)
Nonaccidental	4,271	1.07 (0.79, 1.44)	785	0.81 (0.40, 1.65)	751	1.10 (0.55, 2.21)
All cancer	998	1.58 (0.84, 2.96)	171	0.35 (0.08, 1.62)	197	0.86 (0.22, 3.42)
Lung cancer	36	0.34 (0.01, 10.93)	19	0.28 (<0.01 , 30.67)	38	1.85 (0.10, 33.48)
Cardiovascular disease	2,197	0.84 (0.56, 1.27)	393	1.37 (0.50, 3.74)	351	1.14 (0.42, 3.13)
Nonmalignant lung disease	245	1.53 (0.44, 5.34)	82	0.44 (0.05, 3.75)	67	1.27 (0.13, 12.07)

Models adjusted for recruitment year, sex, smoking intensity (current/former smokers only), BMI, education, diet, alcohol intake, and domestic fuel use.

Table A22. Hazard ratios (and 95% confidence intervals) for specific causes of death among nonsmoking women within the for specific causes of death among nonsmoking women within the Golestan cohort (Model 3)

	n. events (total = 28,716)	PM _{2.5} HR (95% CI)	NO ₂ HR (95% CI)
All-cause	2,953	0.98 (0.91, 1.05)	0.98 (0.69, 1.41)
Nonaccidental	2,510	1.00 (0.93, 1.08)	1.06 (0.72, 1.57)
All cancer	567	1.22 (1.04, 1.43)	2.13 (0.93, 4.89)
Lung cancer	17	1.06 (0.42, 2.64)	1.34 (0.01, 219.95)
Cardiovascular disease	1,287	0.89 (0.80, 0.99)	0.67 (0.39, 1.15)
Nonmalignant lung disease	148	0.87 (0.63, 1.19)	0.46 (0.09, 2.34)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Models adjusted for recruitment year, BMI, education, diet, alcohol intake, and domestic fuel use.

Table A23. Hazard ratios (and 95% confidence intervals) for specific causes of death among those of the Golestan cohort with no prevalent disease at recruitment (Model 3)

	n. events (total = 32,469)	PM _{2.5} HR (95% CI)	NO ₂ HR (95% CI)
All-cause	3,276	0.95 (0.89, 1.02)	0.92 (0.65, 1.30)
Nonaccidental	2,679	0.98 (0.91, 1.05)	0.94 (0.64, 1.37)
All cancer	851	0.96 (0.84, 1.09)	1.20 (0.61, 2.37)
Lung cancer	52	0.72 (0.41, 1.24)	0.75 (0.05, 10.68)
Cardiovascular disease	1,158	0.95 (0.85, 1.06)	0.60 (0.34, 1.05)
Nonmalignant lung disease	171	1.13 (0.85, 1.51)	2.05 (0.49, 8.54)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, education, diet, alcohol intake, and domestic fuel use.

Table A24. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to a 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ after additional adjustment for specific urban scenarios within the Golestan Cohort (Model 3)

	Within Urban Center (Y/N)*		Degree of Urbanicity† in 2000		Degree of Urbanicity in 2010	
	n. events (total = 49,106)	HR (95% CI)	n. events (total = 49,106)	HR (95% CI)	n. events (total = 49,106)	HR (95% CI)
All-cause	6,878	0.99 (0.93, 1.04)	6,878	1.00 (0.95, 1.05)	6,878	1.00 (0.95, 1.05)
Nonaccidental	5,807	1.00 (0.95, 1.07)	5,807	1.01 (0.96, 1.07)	5,807	1.01 (0.96, 1.07)
All cancer	1,366	1.05 (0.93, 1.19)	1,366	0.99 (0.89, 1.12)	1,366	0.99 (0.88, 1.12)
Lung cancer	93	0.82 (0.49, 1.38)	93	0.66 (0.40, 1.09)	93	0.65 (0.40, 1.08)
Cardiovascular disease	2,941	0.95 (0.87, 1.04)	2,941	1.00 (0.92, 1.08)	2,941	1.00 (0.93, 1.08)
Nonmalignant lung disease	394	1.16 (0.91, 1.47)	394	1.20 (0.97, 1.49)	394	1.21 (0.97, 1.50)

*: Refers to a participant being within an urban center as defined by the Global Human Settlement Layer.

†: Refers to gradient values for urbanicity as described by Gao & O'Neill (2020).

Models additionally adjusted for recruitment year, sex, smoking status and intensity, BMI, education, domestic fuel use, and alcohol intake.

Table A25. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to a 10-ppb increase in NO_2 after additional adjustment for specific urban scenarios within the Golestan Cohort (Model 3)

	Within Urban Center (Y/N)*		Degree of Urbanicity† in 2000		Degree of Urbanicity in 2010	
	n. events (total = 49,106)	HR (95% CI)	n. events (total = 49,106)	HR (95% CI)	n. events (total = 49,106)	HR (95% CI)
All-cause	6,878	1.15 (0.87, 1.52)	6,878	1.26 (0.94, 1.67)	6,878	1.27 (0.95, 1.69)
Nonaccidental	5,807	1.11 (0.82, 1.51)	5,807	1.20 (0.88, 1.63)	5,807	1.20 (0.88, 1.64)
All cancer	1,366	1.45 (0.77, 2.71)	1,366	1.06 (0.55, 2.01)	1,366	1.05 (0.55, 2.01)
Lung cancer	93	0.91 (0.07, 11.41)	93	0.20 (0.01, 2.97)	93	0.18 (0.01, 2.82)
Cardiovascular disease	2,941	0.85 (0.55, 1.29)	2,941	1.13 (0.73, 1.74)	2,941	1.14 (0.74, 1.76)
Nonmalignant lung disease	394	1.30 (0.39, 4.27)	394	1.97 (0.60, 6.55)	394	2.00 (0.60, 6.66)

*: Refers to a participant being within an urban center as defined by the Global Human Settlement Layer.

†: Refers to gradient values for urbanicity as described by Gao & O'Neill (2020).

Models additionally adjusted for recruitment year, sex, smoking status and intensity, BMI, education, domestic fuel use, and alcohol intake.

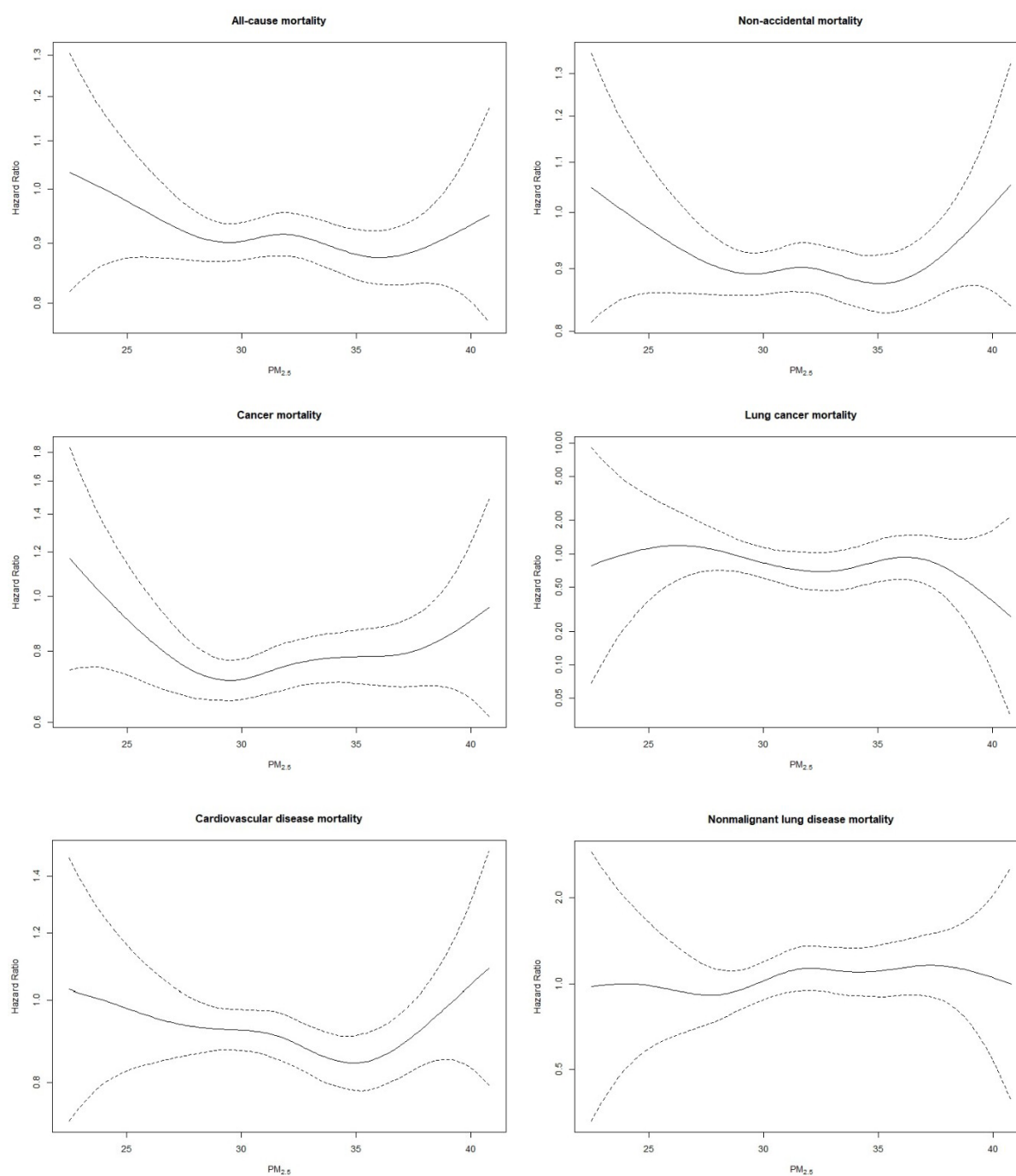


Figure A3: Penalized spline analysis (with 4 degrees of freedom) examining relationship between $PM_{2.5}$ exposure and all-cause and cause-specific mortality within the Golestan cohort (Model 3).

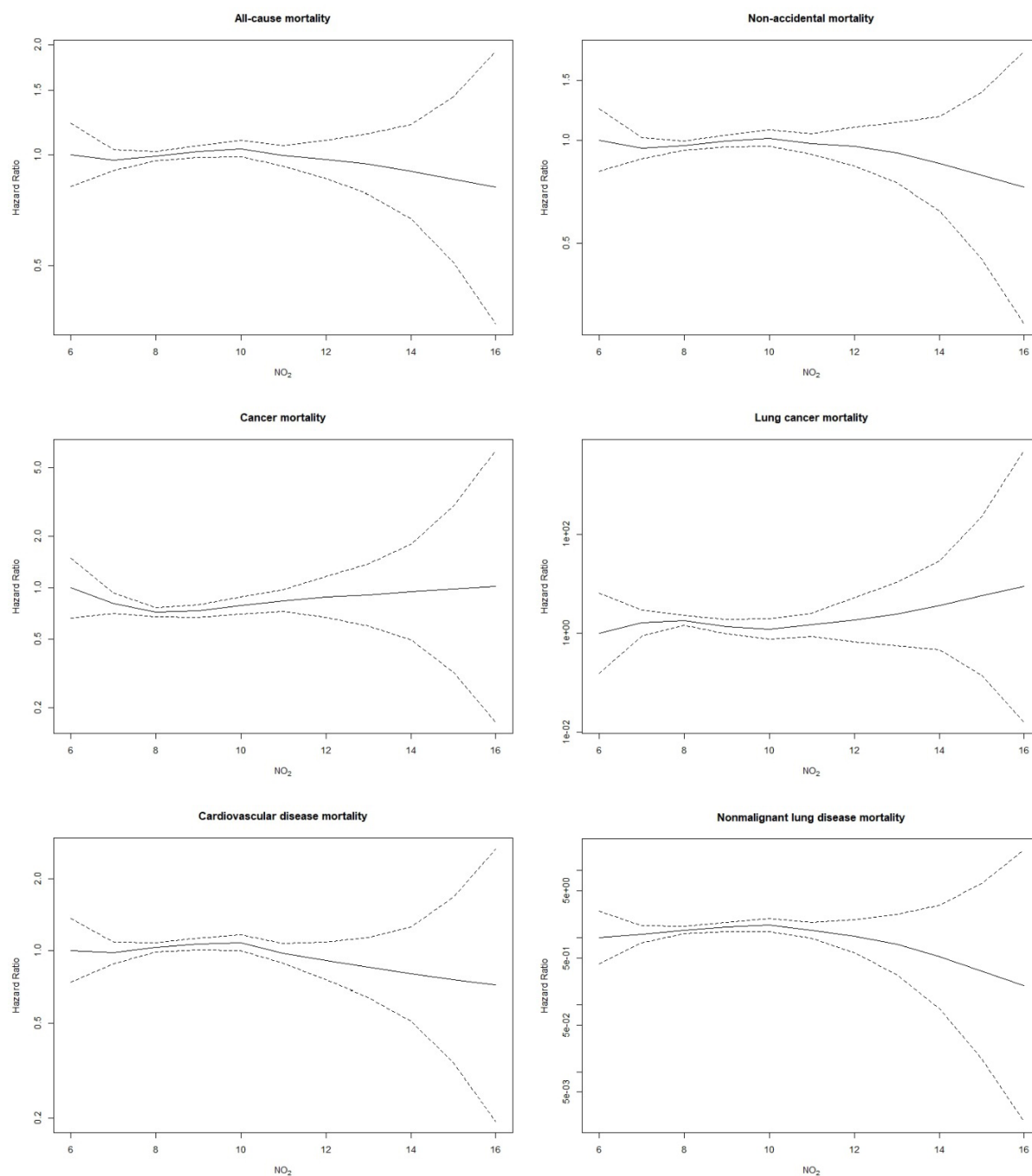


Figure A4: Penalized spline analysis (with 4 degrees of freedom) examining relationship between NO_2 exposure and all-cause and cause-specific mortality within the Golestan cohort (Model 3).

Table A26. Hazard ratios (and 95% confidence intervals) for specific causes of death among the Golestan cohort by quartile of PM_{2.5} (Model 3)

	n. events (total = 49,106)	Q1 (<29.3 µg/m ³)	Q2 (29.3–31.4 µg/m ³)	Q3 (31.4–35.6 µg/m ³)	Q4 (>35.6 µg/m ³)
All-cause	6,878	1.00 (ref)	0.97 (0.91, 1.04)	1.00 (0.93, 1.07)	0.95 (0.87, 1.05)
Nonaccidental	5,807	1.00 (ref)	0.98 (0.91, 1.05)	1.00 (0.92, 1.08)	0.99 (0.89, 1.10)
All cancer	1,366	1.00 (ref)	0.95 (0.81, 1.10)	1.03 (0.88, 1.21)	0.99 (0.80, 1.24)
Lung cancer	93	1.00 (ref)	0.77 (0.43, 1.38)	0.66 (0.34, 1.27)	0.94 (0.43, 2.05)
Cardiovascular disease	2,941	1.00 (ref)	1.02 (0.92, 1.13)	0.96 (0.86, 1.07)	1.00 (0.86, 1.15)
Nonmalignant lung disease	394	1.00 (ref)	1.29 (0.98, 1.71)	1.19 (0.87, 1.63)	1.31 (0.88, 1.96)

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, education, diet, alcohol intake, and domestic fuel use.

Table A27. Hazard ratios (and 95% confidence intervals) for specific causes of death among the Golestan cohort by tertile* of NO₂ (Model 3)

	n. events (total = 49,106)	T1 (<8 ppb)	T2 (8–9 ppb)	T3 (>9 ppb)
All-cause	6,878	1.00 (ref)	1.01 (0.95, 1.08)	1.04 (0.97, 1.13)
Nonaccidental	5,807	1.00 (ref)	1.01 (0.94, 1.08)	1.05 (0.96, 1.14)
All cancer	1,366	1.00 (ref)	0.99 (0.86, 1.14)	1.11 (0.94, 1.32)
Lung cancer	93	1.00 (ref)	0.69 (0.36, 1.29)	0.77 (0.40, 1.47)
Cardiovascular disease	2,941	1.00 (ref)	0.99 (0.89, 1.09)	1.03 (0.92, 1.15)
Nonmalignant lung disease	394	1.00 (ref)	1.11 (0.85, 1.45)	1.14 (0.83, 1.56)

*: Owing to limited contrast, only tertiles of NO₂ were available for analysis.

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, education, diet, alcohol intake, and domestic fuel use.

Table A28. Hazard ratios (and 95% confidence intervals) for specific causes of death within the Golestan cohort after adapting variables which potentially violated the proportional hazards assumption

	PM _{2.5}		NO ₂	
	n. events (total =49,106)	HR (95% CI)	n. events (total =49,106)	HR (95% CI)
All-cause	6,878	0.98 (0.94, 1.03)	6,878	1.07 (0.84, 1.35)
Nonaccidental	5,807	1.00 (0.95, 1.05)	5,807	1.06 (0.82, 1.37)
All cancer	1,366	1.02 (0.92, 1.13)	1,366	1.19 (0.70, 2.04)
Lung cancer	93	0.84 (0.57, 1.25)	93	0.83 (0.11, 6.33)
Cardiovascular disease	2,941	0.98 (0.91, 1.05)	2,941	0.95 (0.66, 1.36)
Nonmalignant lung disease	394	1.10 (0.91, 1.34)	394	1.12 (0.42, 2.94)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Potential assumption violators were pack-years (removed from analysis), sex, smoking status, and alcohol intake (stratified).

Supplementary Tables and Figures: Health Effects for Arsenic Longitudinal Study (HEALS)

Table A29. Demographic features of the Health Effects for Arsenic Longitudinal Study (HEALS)

		Mean (sd) or n (%)	n. missing values
Number of participants		19,990	
Age at recruitment		37 (10)	
Sex			
	Male	8,144 (41%)	
	Female	11,846 (59%)	
Recruitment year			
	2000	748 (4%)	
	2001	8,879 (44%)	
	2002	2,091 (10%)	
	2006	1,086 (5%)	
	2007	5,027 (25%)	
	2008	2,159 (11%)	
Follow-up (years)		10(3)	
Smoking status			8
	Never	13,486 (67%)	
	Former	1,249 (6%)	
	Current	5,250 (26%)	
Pack-years (current or former smokers)		15 (15)	1,934
BMI		20 (3)	280
	<20	11,870 (60%)	
	20-25	6,442 (33%)	
	25-30	1,266 (6%)	
	>30	132 (1%)	
Education			11
	None	8,703 (44%)	
	Primary	6,101 (31%)	
	Secondary	4,411 (22%)	
	Trade/Technical	764 (5%)	
Mortality			
	All-cause	1,532	
	Nonaccidental	1,467	
	All cancer	268	
	Lung cancer	63	
	Cardiovascular disease	513	
	Nonmalignant lung disease	219	

Table A30. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ in the Health Effects for Arsenic Longitudinal Study (HEALS)

	Model 1		Model 2		Model 3	
	n. events (total = 19,990)	HR (95% CI)	n. events (total = 19,990)	HR (95% CI)	n. events (total = 17,361)	HR (95% CI)
All-cause	1,532	0.91 (0.80, 1.03)	1,532	0.57 (0.27, 1.23)	1,300	0.79 (0.35, 1.80)
Nonaccidental	1,467	0.90 (0.79, 1.03)	1,467	0.62 (0.28, 1.34)	1,249	0.84 (0.36, 1.94)
All cancer	268	0.77 (0.57, 1.05)	268	0.28 (0.05, 1.64)	228	0.38 (0.05, 2.63)
Lung cancer	63	0.31 (0.14, 0.70)	63	0.18 (0.01, 5.54)	51	0.14 (<0.01, 6.57)
Cardiovascular disease	513	0.85 (0.68, 1.06)	513	0.59 (0.16, 2.21)	440	0.60 (0.15, 2.43)
Nonmalignant lung disease	219	1.23 (0.88, 1.72)	219	0.30 (0.04, 2.16)	180	0.80 (0.09, 7.37)

Model 1: Unadjusted.

Model 2: Adjusted for recruitment year and sex.

Model 3: Adjusted for recruitment year, sex, smoking status and intensity, BMI, and education.

Table A31. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 10-ppb increase in NO_2 in the Health Effects for Arsenic Longitudinal Study (HEALS)

	Model 1		Model 2		Model 3	
	n. events (total = 19,983)	HR (95% CI)	n. events (total = 19,983)	HR (95% CI)	n. events (total = 17,355)	HR (95% CI)
All-cause	1,530	1.91 (0.97, 3.78)	1,530	2.49 (1.17, 5.31)	1,298	2.80 (1.25, 6.26)
Nonaccidental	1,465	1.71 (0.85, 3.44)	1,465	2.22 (1.02, 4.85)	1,124	2.70 (1.18, 6.16)
All cancer	268	0.50 (0.09, 2.87)	268	0.67 (0.09, 4.85)	228	0.93 (0.12, 7.40)
Lung cancer	63	1.19 (0.04, 37.3)	63	3.89 (0.11, >100)	51	7.34 (0.19, >100)
Cardiovascular disease	512	2.89 (0.91, 9.19)	512	5.67 (1.65, 19.5)	439	9.47 (2.63, 34.1)
Nonmalignant lung disease	219	3.42 (0.58, 20.0)	219	2.55 (0.33, 19.5)	180	2.16 (0.23, 20.0)

Model 1: Unadjusted.

Model 2: Adjusted for recruitment year and sex.

Model 3: Adjusted for recruitment year, sex, smoking status and intensity, BMI, and education.

Table A32. Hazard ratios (and 95% confidence intervals) for specific causes of death for a two-pollutant model in the Health Effects for Arsenic Longitudinal Study (HEALS) (Model 3)

	n. events (total = 17,355)	PM _{2.5} HR (95% CI)	NO ₂ HR (95% CI)
All-cause	1,298	0.87 (0.38, 1.98)	2.76 (1.23, 6.20)
Nonaccidental	1,247	0.92 (0.40, 2.14)	2.68 (1.17, 6.14)
All cancer	228	0.37 (0.05, 2.61)	0.84 (0.10, 6.81)
Lung cancer	51	0.17 (<0.01, 7.99)	6.21 (0.15, >100)
Cardiovascular disease	439	0.73 (0.18, 2.99)	9.24 (2.55, 33.5)
Nonmalignant lung disease	180	0.88 (0.09, 8.17)	2.13 (0.23, 20.1)

Hazard ratios provided for a 5-μg/m³ increase in PM_{2.5} and a 10-ppb increase in NO₂.

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, and education.

Table A33. Hazard ratios (and 95% confidence intervals) for all-cause and nonaccidental mortality in relation to 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ in the Health Effects for Arsenic Longitudinal Study (HEALS), stratified by smoking status (Model 3)

	Never smokers		Former smokers		Current smokers	
	n. events (total = 13,022)	HR (95% CI)	n. events (total = 1,144)	HR (95% CI)	n. events (total = 3,195)	HR (95% CI)
All-cause	479	1.32 (0.32, 5.41)	229	2.76 (0.33, 22.8)	592	0.37 (0.11, 1.19)
Nonaccidental	461	1.39 (0.33, 5.84)	220	3.28 (0.38, 28.5)	568	0.38 (0.11, 1.26)

Models adjusted for recruitment year, sex, smoking intensity (current/former smokers only), BMI, and education.

Table A34. Hazard ratios (and 95% confidence intervals) for all-cause and nonaccidental mortality in relation to 10-ppb increase in NO_2 in the Health Effects for Arsenic Longitudinal Study (HEALS), stratified by smoking status (Model 3)

	Never smokers		Former smokers		Current smokers	
	n. events (total = 13, 018)	HR (95% CI)	n. events (total = 1,144)	HR (95% CI)	n. events (total = 3,193)	HR (95% CI)
All-cause	478	4.83 (1.29, 18.10)	229	1.09 (0.13, 8.98)	591	2.15 (0.66, 6.99)
Nonaccidental	460	4.80 (1.24, 18.50)	220	0.78 (0.09, 6.82)	567	2.16 (0.65, 7.23)

Models adjusted for recruitment year, sex, smoking intensity (current/former smokers only), BMI, and education.

Table A35. Hazard ratios (and 95% confidence intervals) for all-cause and nonaccidental mortality among nonsmoking women within the Health Effects for Arsenic Longitudinal Study (HEALS) (Model 3)

	$\text{PM}_{2.5}$		NO_2	
	n. events (total = 10,768)	HR (95% CI)	n. events (total = 10,764)	HR (95% CI)
All-cause	364	0.55 (0.11, 2.80)	363	6.96 (1.55, 31.3)
Nonaccidental	351	0.59 (0.11, 3.09)	350	6.24 (1.33, 29.3)

Models adjusted for recruitment year, sex, BMI, and education.

Table A36. Hazard ratios for specific causes of death in relation to a 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ after additional adjustment for specific urban scenarios within the Health Effects for Arsenic Longitudinal Study (HEALS)

	Degree of Urbanicity* in 2000		Degree of Urbanicity in 2010	
	n. events (total = 17,361)	HR (95% CI)	n. events (total = 17,361)	HR (95% CI)
All-cause	1,300	0.84 (0.33, 2.12)	1,300	0.81 (0.33, 2.00)
Nonaccidental	1,249	0.92 (0.36, 2.37)	1,249	0.89 (0.36, 2.23)
All cancer	228	0.36 (0.04, 3.33)	228	0.33 (0.04, 2.80)
Lung cancer	51	0.15 (<0.01, 14.0)	51	0.13 (<0.01, 9.61)
Cardiovascular disease	440	0.70 (0.14, 3.37)	440	0.68 (0.15, 3.16)
Nonmalignant lung disease	180	1.30 (0.11, 15.5)	180	1.33 (0.12, 14.6)

Refers to gradient values for urbanicity as described by Gao & O'Neill (2020).

Models additionally adjusted for recruitment year, sex, smoking status and intensity, BMI, and education.

Table A37. Hazard ratios for specific causes of death in relation to a 10-ppb increase in NO_2 after additional adjustment for specific urban scenarios within the Health Effects for Arsenic Longitudinal Study (HEALS)

	Degree of Urbanicity* in 2000		Degree of Urbanicity in 2010	
	n. events (total = 17,355)	HR (95% CI)	n. events (total = 17,355)	HR (95% CI)
All-cause	1,298	2.91 (1.29, 6.54)	1,298	2.92 (1.29, 6.59)
Nonaccidental	1,247	2.82 (1.23, 6.46)	1,247	2.84 (1.23, 6.52)
All cancer	228	0.97 (0.12, 7.82)	228	0.95 (0.12, 7.66)
Lung cancer	51	8.39 (0.21, 340)	51	8.40 (0.20, 346)
Cardiovascular disease	439	10.4 (2.86, 37.9)	439	10.7 (2.93, 39.3)
Nonmalignant lung disease	180	2.40 (0.26, 22.5)	180	2.56 (0.27, 24.2)

Refers to gradient values for urbanicity as described by Gao & O'Neill (2020).

Models additionally adjusted for recruitment year, sex, smoking status and intensity, BMI, and education.

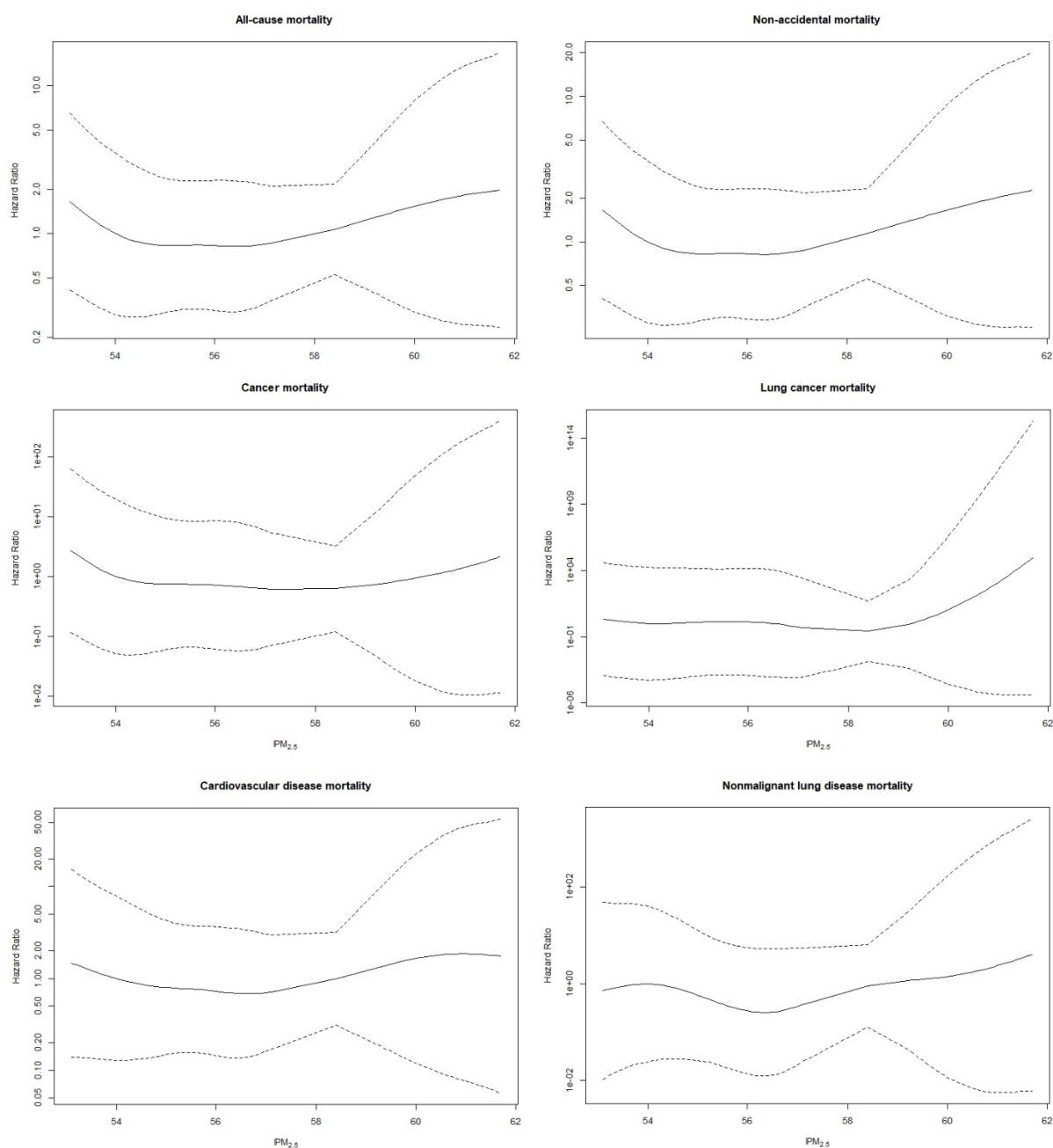


Figure A5: Penalized spline analysis (with 4 degrees of freedom) examining relationship between $PM_{2.5}$ exposure and all-cause and cause-specific mortality within the Health Effects for Arsenic Longitudinal Study (HEALS) (Model 3).

Table A38. Hazard ratios (and 95% confidence intervals) for specific causes of death among the Health Effects for Arsenic Longitudinal Study (HEALS) by quartile of PM_{2.5} (Model 3)

	n. events (total = 49,106)	Q1 (<55.9 µg/m ³)	Q2 (55.9–56.7 µg/m ³)	Q3 (56.7–60.7 µg/m ³)	Q4 (>60.7 µg/m ³)
All-cause	6,878	Ref	0.97 (0.83, 1.13)	0.92 (0.68, 1.24)	0.88 (0.53, 1.48)
Nonaccidental	5,807	Ref	0.97 (0.83, 1.13)	0.96 (0.71, 1.29)	0.92 (0.55, 1.54)
All cancer	1,366	Ref	0.92 (0.63, 1.33)	0.84 (0.41, 1.75)	0.88 (0.25, 3.10)
Lung cancer*	93	Ref	NA	NA	NA
Cardiovascular disease	2,941	Ref	0.89 (0.69, 1.16)	0.92 (0.57, 1.50)	0.84 (0.35, 2.01)
Nonmalignant lung disease	394	Ref	0.86 (0.58, 1.28)	1.23 (0.62, 2.44)	1.20 (0.28, 5.21)

*: Analysis unable to be completed secondary to insufficient sample size.

Models adjusted recruitment year, sex, smoking status and intensity, BMI, and education.

Table A39. Hazard ratios (and 95% confidence intervals) for specific causes of death within the Health Effects for Arsenic Longitudinal Study (HEALS) after adapting variables which potentially violated the proportional hazards assumption

	PM _{2.5}		NO ₂	
	n. events (total = 17,361)	HR (95% CI)	n. events (total = 17,355)	HR (95% CI)
All-cause	1,300	0.65 (0.29, 1.44)	1,298	2.33 (1.07, 5.07)
Nonaccidental	1,249	1.69 (0.30, 0.155)	1,1247	2.13 (0.96, 4.74)
All cancer	228	0.34 (0.05, 2.22)	228	0.90 (0.12, 6.65)
Lung cancer	51	0.11 (<0.01, 4.32)	51	5.35 (0.15, >100)
Cardiovascular disease	440	0.52 (0.13, 2.04)	439	5.98 (1.69, 21.13)
Nonmalignant lung disease	180	0.39 (0.05, 3.14)	180	1.89 (0.23, 15.30)

Hazard ratios provided for a 5-µg/m³ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Potential assumption violator was pack-years (removed from analysis).

Supplementary Tables and Figures: Japan Public Health Center-based Prospective Study (JPHC)

Table A40. Demographic features of the Japan Public Health Center-based Prospective Study (JPHC)

		Mean (sd) or n (%)	n. missing values
Number of participants		87,653	
Age at recruitment		52 (8)	
Sex			
	Male	41,495 (47)	
	Female	46,158 (53)	
Recruitment year			
	1990	36,048 (41%)	
	1991	1,726 (2%)	
	1992	691 (1%)	
	1993	37,663 (43%)	
	1994	11,219 (13%)	
	1995	306 (<1%)	
Follow-up (years)		20 (5)	
Vital status			
Smoking status			317
	Never	51,994 (60%)	
	Former	10,791 (12%)	
	Current	24,551 (28%)	
Pack-years (current or former smokers)		30 (21)	1,355
BMI		23.4 (3)	1,012
	<20	9,915 (11%)	
	20-25	53,440 (62%)	
	25-30	21,150 (24%)	
	>30	2,136 (2%)	
Employment status at recruitment			4,652
	Professional/Office worker	12,482 (19%)	
	Sales clerk/other	15,056 (23%)	
	Agriculture/Fishery/Forestry	18,515 (28%)	
	Manual laborer	16,008 (24%)	
	Unemployed	4,652 (7%)	
Diet:			
	Nutrition (kcal/day)	1587 (636)	
	Vegetables (g/day)	114 (100)	
	Fruit(g/day)	90 (90)	
Alcohol (g/week)		104 (229)	2,995
Mortality			
	All-cause	17,931	
	All cancer	7,331	
	Lung cancer	1,462	
	Cardiovascular	2,349	
	Cerebrovascular	1,819	
	Nonmalignant lung disease	1,196	
	"Other" deaths	5,236	

Table A41. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ in the Japan Public Health Center-based Prospective Study (JPHC)

	Model 1		Model 2		Model 3	
	n. events (total = 87,600)	HR (95% CI)	n. events (total = 87,600)	HR (95% CI)	n. events (total = 78,142)	HR (95% CI)
All-cause	17,916	1.09 (1.07, 1.12)	17,916	1.11 (1.08, 1.14)	15,700	1.06 (1.03, 1.09)
All cancer	7,319	1.16 (1.12, 1.2)	7,319	1.16 (1.12, 1.21)	6,417	1.10 (1.06, 1.16)
Lung cancer	1,458	1.15 (1.06, 1.24)	1,458	1.16 (1.06, 1.27)	1,246	1.02 (0.92, 1.13)
Cardiac disease	2,348	1.04 (0.98, 1.11)	2,348	1.04 (0.97, 1.12)	2,045	1.02 (0.95, 1.10)
Cerebrovascular disease	1,819	1.09 (1.01, 1.17)	1,819	1.17 (1.07, 1.26)	1,599	1.13 (1.03, 1.24)
Combined cardiovascular	4,167	1.06 (1.01, 1.11)	4,167	1.09 (1.04, 1.15)	3,644	1.07 (1.01, 1.13)
Nonmalignant lung disease	1,195	0.98 (0.9, 1.07)	1,195	0.94 (0.86, 1.03)	1,030	0.85 (0.76, 0.94)
“Other” deaths	5,235	1.05 (1.01, 1.10)	5,235	1.10 (1.05, 1.15)	4,609	1.05 (1.00, 1.10)

Model 1: Unadjusted.

Model 2: Adjusted for recruitment year and sex.

Model 3: Adjusted for recruitment year, sex, smoking status and intensity, BMI, occupation, diet, and alcohol intake.

Table A42. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 10-ppb increase in NO₂ in the Japan Public Health Center-based Prospective Study (JPHC)

	Model 1		Model 2		Model 3	
	n. events (total = 85,177)	HR (95% CI)	n. events (total = 85,177)	HR (95% CI)	n. events (total = 76,075)	HR (95% CI)
All-cause	15,455	1.16 (1.13, 1.18)	15,455	1.19 (1.16, 1.23)	13,597	1.16 (1.12, 1.19)
All cancer	6,416	1.18 (1.14, 1.23)	6,416	1.23 (1.18, 1.28)	5,664	1.18 (1.13, 1.23)
Lung cancer	1,236	1.19 (1.10, 1.3)	1,236	1.22 (1.11, 1.34)	1,059	1.13 (1.01, 1.27)
Cardiac disease	1,977	1.11 (1.04, 1.19)	1,977	1.13 (1.05, 1.23)	1,727	1.12 (1.03, 1.23)
Cerebrovascular disease	1,607	1.03 (0.96, 1.11)	1,607	1.05 (0.96, 1.14)	1,411	1.03 (0.93, 1.14)
Combined cardiovascular	3,584	1.08 (1.02, 1.13)	3,584	1.10 (1.03, 1.16)	3,138	1.08 (1.01, 1.16)
Nonmalignant lung disease	949	1.03 (0.96, 1.11)	949	1.26 (1.12, 1.41)	822	1.11 (0.97, 1.26)
“Other” deaths	4,506	1.16 (1.12, 1.21)	4,506	1.21 (1.15, 1.27)	3,973	1.19 (1.13, 1.26)

Model 1: Unadjusted.

Model 2: Adjusted for recruitment year and sex.

Model 3: Adjusted for recruitment year, sex, smoking status and intensity, BMI, occupation, diet, and alcohol intake.

Table A42. Hazard ratios (and 95% confidence intervals) for specific causes of death for a two-pollutant model in the Japan Public Health Center-based Prospective Study (JPHC) (Model 3)

	n. events (total = 76,029)	PM _{2.5} HR (95% CI)	NO ₂ HR (95% CI)
All-cause	13,587	1.23 (1.19, 1.28)	1.06 (1.02, 1.10)
All cancer	5,656	1.27 (1.20, 1.35)	1.07 (1.01, 1.12)
Lung cancer	1,056	1.15 (1.00, 1.32)	1.07 (0.94, 1.21)
Cardiac disease	1,727	1.28 (1.16, 1.42)	1.01 (0.92, 1.11)
Cerebrovascular disease	1,411	1.28 (1.14, 1.43)	0.93 (0.84, 1.04)
Combined cardiovascular	3,138	1.28 (1.19, 1.38)	0.98 (0.91, 1.05)
Nonmalignant lung disease	821	1.10 (0.95, 1.28)	1.06 (0.92, 1.23)
“Other” deaths	3,972	1.17 (1.09, 1.26)	1.11 (1.04, 1.18)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂.

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, occupation, diet, and alcohol intake.

Table A43. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ in the Japan Public Health Center-based Prospective Study (JPHC), stratified by smoking status (Model 3)

	Never smokers		Former smokers		Current smokers	
	n. events (total = 47,969)	HR (95% CI)	n. events (total = 9,637)	HR (95% CI)	n. events (total = 21,580)	HR (95% CI)
All-cause	7,047	1.09 (1.05, 1.13)	2,591	1.04 (0.97, 1.11)	6,394	1.04 (0.99, 1.09)
All cancer	2,794	1.11 (1.04, 1.18)	1,064	1.09 (0.98, 1.21)	2,695	1.15 (1.07, 1.24)
Lung cancer	295	1.01 (0.84, 1.22)	178	0.91 (0.72, 1.16)	803	1.12 (0.97, 1.29)
Cardiac disease	942	1.07 (0.96, 1.19)	321	1.06 (0.88, 1.28)	832	0.94 (0.82, 1.07)
Cerebrovascular disease	794	1.16 (1.02, 1.31)	256	1.10 (0.88, 1.37)	587	1.10 (0.94, 1.30)
Combined cardiovascular	1,736	1.10 (1.02, 1.20)	577	1.07 (0.93, 1.24)	1,419	1.00 (0.90, 1.11)
Nonmalignant lung disease	390	0.90 (0.76, 1.06)	238	0.77 (0.63, 0.95)	428	0.82 (0.69, 0.97)
“Other” deaths	2,127	1.09 (1.02, 1.18)	712	1.06 (0.93, 1.20)	1,852	0.98 (0.90, 1.07)

Models adjusted for recruitment year, sex, smoking intensity (current/former smokers only), BMI, occupation, diet, and alcohol intake.

Table A44. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 10-ppb increase in NO₂ in the Japan Public Health Center-based Prospective Study (JPHC), stratified by smoking status (Model 3)

	Never smokers		Former smokers		Current smokers	
	n. events (total = 46,856)	HR (95% CI)	n. events (total = 9,304)	HR (95% CI)	n. events (total = 20,909)	HR (95% CI)
All-cause	5,906	1.26 (1.20, 1.32)	2,555	1.14 (1.06, 1.22)	5,718	1.06 (1.01, 1.11)
All cancer	2,418	1.29 (1.21, 1.39)	937	1.05 (0.94, 1.18)	2,432	1.13 (1.05, 1.21)
Lung cancer	238	1.18 (0.94, 1.48)	147	1.21 (0.92, 1.59)	701	1.13 (0.98, 1.31)
Cardiac disease	747	1.16 (1.01, 1.33)	285	1.19 (0.98, 1.45)	736	1.01 (0.88, 1.16)
Cerebrovascular disease	673	1.15 (0.99, 1.33)	230	1.11 (0.88, 1.42)	543	0.86 (0.72, 1.02)
Combined cardiovascular	1,420	1.15 (1.04, 1.28)	515	1.16 (1.00, 1.35)	1,279	0.95 (0.85, 1.05)
Nonmalignant lung disease	299	1.18 (0.95, 1.48)	195	1.11 (0.87, 1.41)	347	1.01 (0.82, 1.25)
“Other” deaths	1,769	1.30 (1.19, 1.41)	608	1.26 (1.10, 1.44)	1,660	1.06 (0.97, 1.16)

Models adjusted for recruitment year, sex, smoking intensity (current/former smokers only), BMI, occupation, diet, and alcohol intake.

Table A45. Hazard ratios (and 95% confidence intervals) for specific causes of death among nonsmoking women within the Japan Public Health Center-based Prospective Study (JPHC) (Model 3)

	PM _{2.5}		NO ₂	
	n. events (total = 39,510)	HR (95% CI)	n. events (total = 38,712)	HR (95% CI)
All-cause	5,303	1.08 (1.03, 1.14)	4,482	1.27 (1.2, 1.33)
All cancer	2,158	1.13 (1.05, 1.22)	1,891	1.27 (1.17, 1.37)
Lung cancer	230	1.07 (0.86, 1.33)	184	1.25 (0.97, 1.63)
Cardiac disease	697	1.01 (0.89, 1.14)	551	1.14 (0.97, 1.34)
Cerebrovascular disease	588	1.13 (0.98, 1.31)	502	1.16 (0.98, 1.37)
Combined cardiovascular	1,285	1.06 (0.97, 1.17)	1,053	1.15 (1.02, 1.29)
Nonmalignant lung disease	270	0.96 (0.79, 1.17)	208	1.45 (1.13, 1.86)
“Other” deaths	1,590	1.08 (0.99, 1.17)	1,330	1.34 (1.21, 1.48)

Hazard ratios provided for a 5-μg/m³ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Models adjusted for recruitment year, BMI, occupation, diet, and alcohol intake.

Table A46. Hazard ratios (and 95% confidence intervals) for specific causes of death among participants of the Japan Public Health Center-based Prospective Study (JPHC) with no prevalent disease at recruitment (Model 3)

	PM _{2.5}		NO ₂	
	n. events (total = 37,352)	HR (95% CI)	n. events (total = 37,014)	HR (95% CI)
All-cause	6,198	1.07 (1.01, 1.13)	5,844	0.94 (0.89, 0.99)
All cancer	2,818	1.15 (1.05, 1.24)	2,668	1.00 (0.92, 1.07)
Lung cancer	559	1.01 (0.83, 1.22)	529	0.98 (0.81, 1.18)
Cardiac disease	655	1.11 (0.93, 1.32)	620	0.77 (0.64, 0.94)
Cerebrovascular disease	533	1.02 (0.84, 1.24)	504	0.75 (0.6, 0.93)
Combined cardiovascular	1,188	1.07 (0.94, 1.22)	1,124	0.76 (0.66, 0.88)
Nonmalignant lung disease	367	0.89 (0.72, 1.10)	336	0.85 (0.67, 1.07)
“Other” deaths	1,825	1.00 (0.90, 1.10)	1,716	0.95 (0.86, 1.05)

Hazard ratios provided for a 5-μg/m³ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, occupation, diet, and alcohol intake.

Table A47. Hazard ratios (and 95% confidence intervals) for specific causes of death among participants of the Japan Public Health Center-based Prospective Study (JPHC) who were alive in 1998 (Model 3)

	PM _{2.5}		NO ₂	
	n. events (total = 75,855)	HR (95% CI)	n. events (total = 73,789)	HR (95% CI)
All-cause	13,426	1.04 (1.02, 1.07)	11,324	1.01 (0.97, 1.05)
All cancer	5,419	1.10 (1.05, 1.15)	4,666	1.05 (0.99, 1.11)
Lung cancer	1,080	1.03 (0.93, 1.14)	893	1.07 (0.93, 1.22)
Cardiac disease	1,772	1.02 (0.95, 1.10)	1,454	0.98 (0.87, 1.09)
Cerebrovascular disease	1,345	1.08 (1.00, 1.18)	1,157	0.85 (0.74, 0.96)
Combined cardiovascular	3,117	1.05 (0.99, 1.11)	2,611	0.92 (0.84, 1.00)
Nonmalignant lung disease	930	0.89 (0.80, 0.99)	722	0.92 (0.78, 1.09)
“Other” deaths	3,960	1.01 (0.96, 1.06)	3,325	1.03 (0.96, 1.11)

Hazard ratios provided for a 5-μg/m³ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, occupation, diet, and alcohol intake.

Table A48. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to a 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ after additional adjustment for specific urban scenarios within the Japan Public Health Center-based Prospective Study (JPHC)

	Within Urban Center (Y/N)*		Degree of Urbanicity† in 2000		Degree of Urbanicity in 2010	
	n. events (total = 78,142)	HR (95% CI)	n. events (total = 78,112)	HR (95% CI)	n. events (total = 78,112)	HR (95% CI)
All-cause	15,700	1.06 (1.03, 1.09)	15,689	1.07 (1.04, 1.10)	15,689	1.07 (1.04, 1.10)
All cancer	6,417	1.10 (1.05, 1.15)	6,412	1.11 (1.06, 1.16)	6,412	1.12 (1.06, 1.17)
Lung cancer	1,246	1.01 (0.90, 1.12)	1,246	1.02 (0.92, 1.14)	1,246	1.03 (0.93, 1.15)
Cardiac disease	2,045	1.04 (0.96, 1.12)	2,044	1.04 (0.96, 1.13)	2,044	1.04 (0.96, 1.13)
Cerebrovascular disease	1,599	1.19 (1.08, 1.31)	1,599	1.19 (1.08, 1.31)	1,599	1.19 (1.08, 1.30)
Combined cardiovascular	3,644	1.10 (1.04, 1.17)	3,643	1.10 (1.04, 1.17)	3,643	1.10 (1.04, 1.17)
Nonmalignant lung disease	1,030	0.84 (0.76, 0.94)	1,028	0.84 (0.76, 0.94)	1,028	0.85 (0.76, 0.94)
“Other” deaths	4,609	1.03 (0.98, 1.09)	4,606	1.05 (0.99, 1.10)	4,606	1.05 (0.99, 1.11)

*: Refers to a participant being within an urban center as defined by the Global Human Settlement Layer.

†: Refers to gradient values for urbanicity as described by Gao & O'Neill (2020).

Models additionally adjusted for recruitment year, sex, smoking status and intensity, BMI, occupation, diet, and alcohol intake.

Table A49. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to a 10-ppb increase in NO₂ after additional adjustment for specific urban scenarios within the Japan Public Health Center-based Prospective Study (JPHC)

	Within Urban Center (Y/N)*		Degree of Urbanicity† in 2000		Degree of Urbanicity in 2010	
	n. events (total = 76,075)	HR (95% CI)	n. events (total = 76,045)	HR (95% CI)	n. events (total = 76,045)	HR (95% CI)
All-cause	13,597	1.17 (1.12, 1.21)	13,586	1.21 (1.17, 1.26)	13,586	1.21 (1.17, 1.25)
All cancer	5,664	1.18 (1.12, 1.25)	5,659	1.22 (1.15, 1.29)	5,659	1.22 (1.16, 1.29)
Lung cancer	1,059	1.07 (0.94, 1.23)	1,059	1.15 (1.01, 1.31)	1,059	1.16 (1.02, 1.32)
Cardiac disease	1,727	1.17 (1.06, 1.31)	1,726	1.19 (1.07, 1.32)	1,726	1.19 (1.07, 1.31)
Cerebrovascular disease	1,411	1.18 (1.04, 1.34)	1,411	1.17 (1.04, 1.32)	1,411	1.15 (1.02, 1.3)
Combined cardiovascular	3,138	1.18 (1.09, 1.28)	3,137	1.18 (1.10, 1.28)	3,137	1.17 (1.09, 1.27)
Nonmalignant lung disease	822	1.10 (0.94, 1.29)	820	1.18 (1.01, 1.37)	820	1.16 (1.00, 1.35)
“Other” deaths	3,973	1.14 (1.06, 1.22)	3,970	1.23 (1.15, 1.31)	3,970	1.22 (1.15, 1.31)

*: Refers to a participant being within an urban center as defined by the Global Human Settlement Layer.

†: Refers to gradient values for urbanicity as described by Gao & O’Neill (2020).

Models additionally adjusted for recruitment year, sex, smoking status and intensity, BMI, occupation, diet, and alcohol intake.

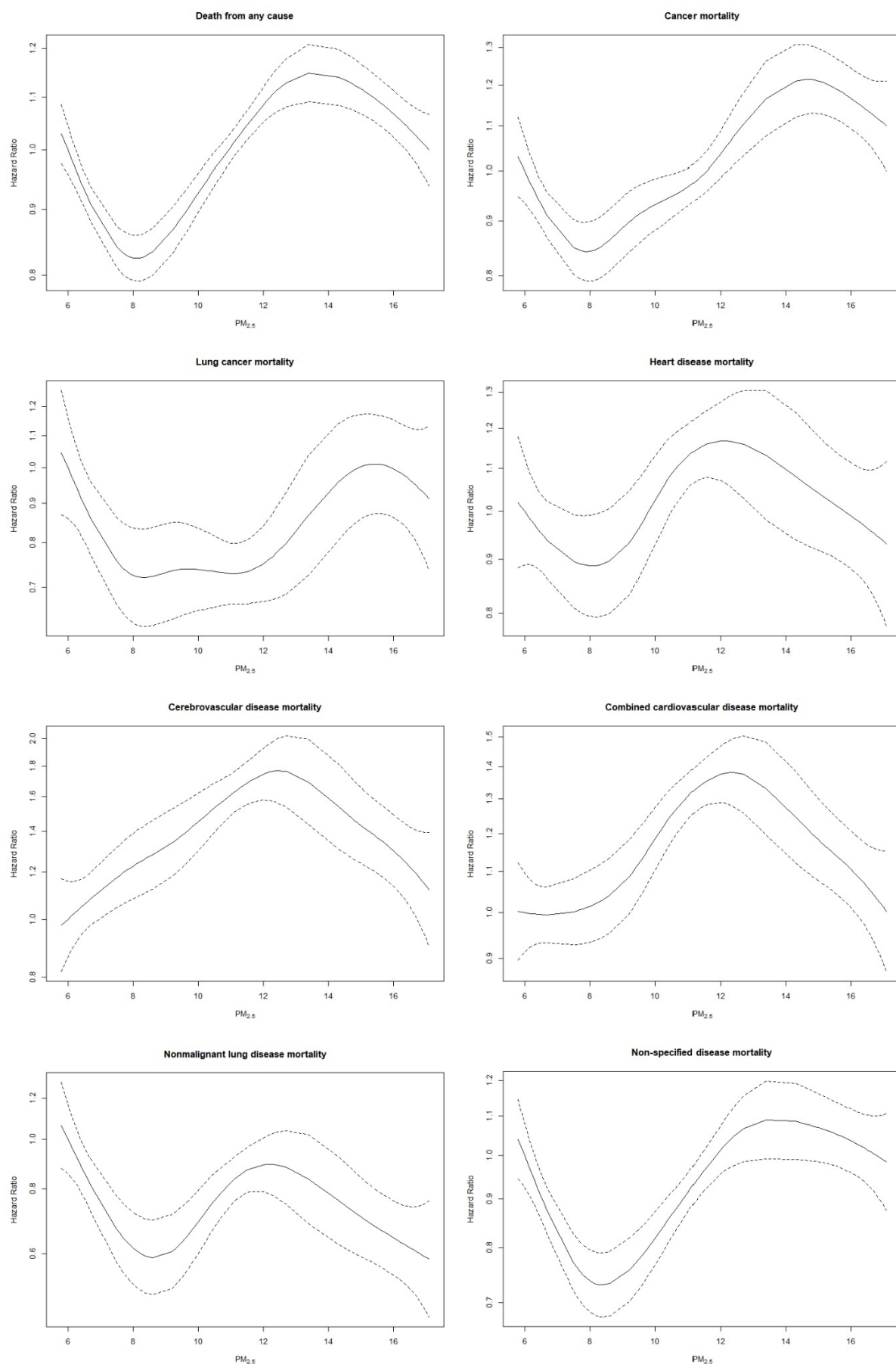


Figure A6: Penalized spline analysis (with 4 degrees of freedom) examining relationship between $PM_{2.5}$ exposure and all-cause and cause-specific mortality within the Japan Public Health Center-based Prospective Study (JPHC) (Model 3).

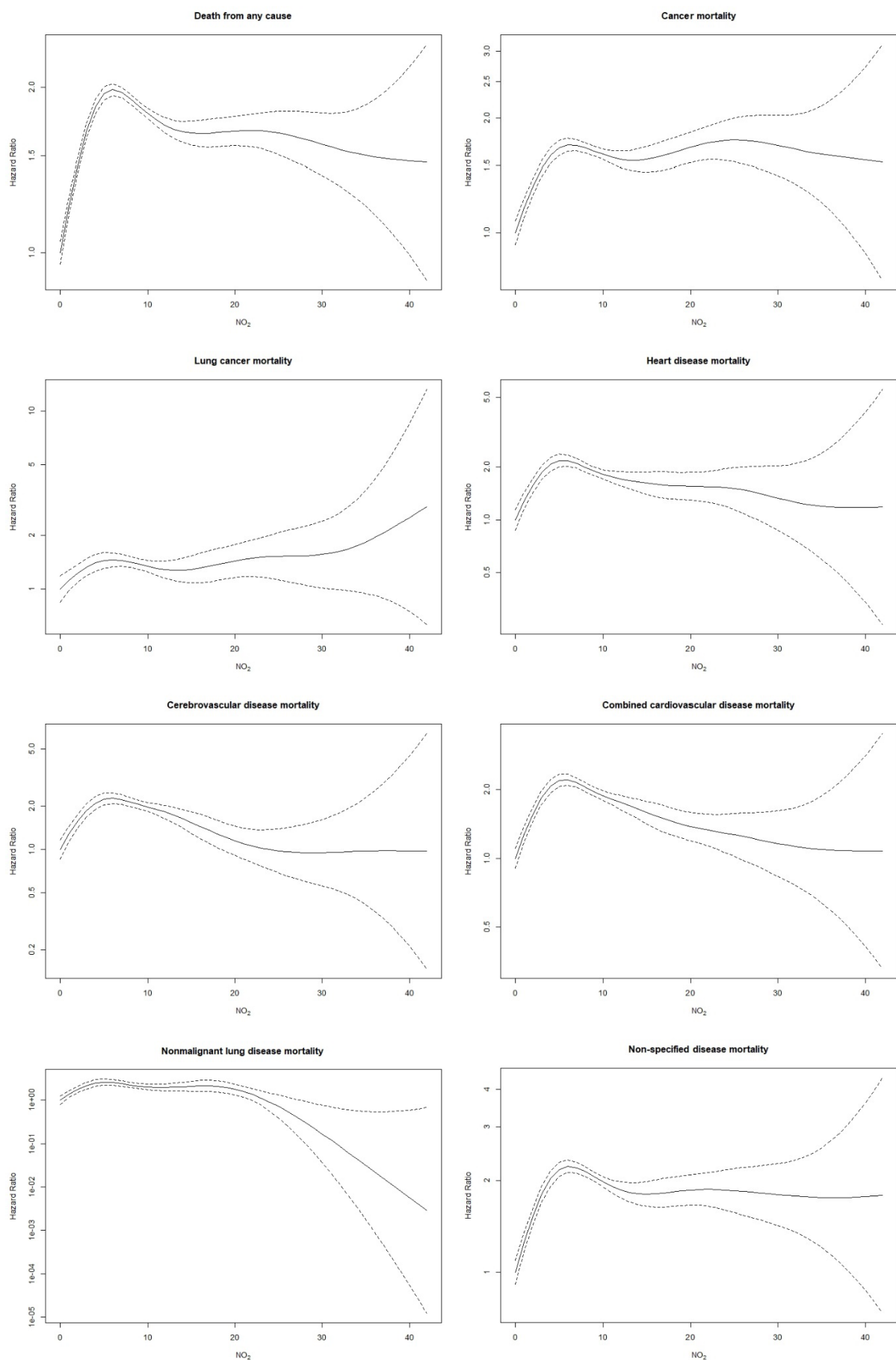


Figure A7: Penalized spline analysis (with 4 degrees of freedom) examining relationship between NO_2 exposure and all-cause and cause-specific mortality within the Japan Public Health Center-based Prospective Study (JPHC) (Model 3).

Table A50. Hazard ratios (and 95% confidence intervals) for specific causes of death among the Japan Public Health Center-based Prospective Study (JPHC) by quartile of PM_{2.5} (Model 3)

	n. events (total = 78,142)	Q1 (<7.7 µg/m ³)	Q2 (7.7–10.6 µg/m ³)	Q3 (10.6–12.3 µg/m ³)	Q4 (12.3–17.1 µg/m ³)
All-cause	15,700	1.00 (ref)	1.07 (1.02, 1.12)	1.11 (1.05, 1.18)	1.14 (1.07, 1.20)
All cancer	6,417	1.00 (ref)	1.06 (0.99, 1.14)	1.08 (0.98, 1.18)	1.25 (1.14, 1.36)
Lung cancer	1,246	1.00 (ref)	0.88 (0.75, 1.03)	0.79 (0.64, 0.97)	1.06 (0.87, 1.29)
Cardiac disease	2,045	1.00 (ref)	1.17 (1.03, 1.33)	1.13 (0.97, 1.32)	1.05 (0.9, 1.22)
Cerebrovascular disease	1,599	1.00 (ref)	1.38 (1.19, 1.59)	1.66 (1.39, 1.99)	1.26 (1.04, 1.52)
Combined cardiovascular	3,644	1.00 (ref)	1.26 (1.14, 1.38)	1.33 (1.19, 1.49)	1.13 (1.00, 1.27)
Nonmalignant lung disease	1,030	1.00 (ref)	0.81 (0.67, 0.98)	0.93 (0.76, 1.13)	0.71 (0.58, 0.88)
“Other” deaths	4,609	1.00 (ref)	1.02 (0.94, 1.11)	1.06 (0.96, 1.18)	1.11 (1.00, 1.23)

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, occupation, diet, and alcohol intake.

Table A51. Hazard ratios (and 95% confidence intervals) for specific causes of death among the Japan Public Health Center-based Prospective Study (JPHC) by quartile of NO₂ (Model 3)

	n. events (total = 76,075)	Q1 (<5 ppb)	Q2 (5–8 ppb)	Q3 (8–11 ppb)	Q4 (11–42 ppb)
All-cause	13,597	1.00 (ref)	1.16 (1.10, 1.22)	1.16 (1.10, 1.21)	1.14 (1.08, 1.21)
All cancer	5,664	1.00 (ref)	1.09 (1.01, 1.18)	1.14 (1.06, 1.23)	1.18 (1.08, 1.28)
Lung cancer	1,059	1.00 (ref)	1.11 (0.92, 1.32)	0.99 (0.83, 1.19)	1.12 (0.92, 1.38)
Cardiac disease	1,727	1.00 (ref)	1.06 (0.92, 1.21)	1.09 (0.95, 1.25)	1.02 (0.87, 1.2)
Cerebrovascular disease	1,411	1.00 (ref)	1.09 (0.93, 1.27)	1.17 (1.01, 1.37)	0.92 (0.76, 1.11)
Combined cardiovascular	3,138	1.00 (ref)	1.07 (0.96, 1.19)	1.13 (1.02, 1.25)	0.98 (0.86, 1.1)
Nonmalignant lung disease	822	1.00 (ref)	1.32 (1.08, 1.62)	1.10 (0.89, 1.35)	1.17 (0.93, 1.48)
“Other” deaths	3,973	1.00 (ref)	1.29 (1.17, 1.42)	1.20 (1.10, 1.33)	1.21 (1.09, 1.35)

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, occupation, diet, and alcohol intake.

Table A52. Hazard ratios (and 95% confidence intervals) for a 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ and specific causes of death within the Japan Public Health Center-based Prospective Study (JPHC) after adapting variables which potentially violated the proportional hazards assumption

	n. events (total = 78,142)	HR (95% CI)
All-cause	15,700	1.07 (1.04, 1.10)
All cancer	6,417	1.12 (1.07, 1.18)
Lung cancer	1,246	1.04 (0.94, 1.16)
Cardiac disease	2,045	1.02 (0.95, 1.11)
Cerebrovascular disease	1,599	1.13 (1.03, 1.24)
Combined cardiovascular disease	3,644	1.07 (1.00, 1.13)
Nonmalignant lung disease	1,030	0.86 (0.77, 0.96)
“Other” deaths	4,609	1.06 (1.01, 1.12)

Potential assumption violators were vegetable/fruit intake (removed from analysis) and sex, recruitment year, BMI, and occupation (stratified).

Table A53. Beta coefficient and time interaction for NO_2 exposure and specific causes of death within the Japan Public Health Center-based Prospective Study (JPHC)

	n. events (total = 76,075)	Effect for NO_2 Beta Coefficient	Time interaction
All-cause	13,597	0.37	-0.026
All cancer	5,664	0.37	-0.027
Lung cancer	1,059	0.35	-0.026
Cardiac disease	1,727	0.37	-0.026
Cerebrovascular disease	1,411	0.38	-0.028
Combined cardiovascular	3,138	0.37	-0.027
Nonmalignant lung disease	822	0.37	-0.024
“Other” deaths	3,973	0.36	-0.025

Time interaction based upon follow-up time.

Supplementary Tables and Figures: Korean Multi-center Cancer Cohort Study (KMCC)

Table A54. Demographic features of the Korean Multi-center Cancer Cohort Study (KMCC)

		Mean (sd) or n (%)	n. missing values
Number of participants		18,529	
Age at recruitment		55 (14)	
Sex			
	Male	7,459 (40%)	
	Female	11,070 (60%)	
Recruitment year			
	1993	1,333 (7%)	
	1994	1 (<1%)	
	1995	938 (5%)	
	1996	1,653 (9%)	
	1997	2,485 (13%)	
	1998	1,677 (9%)	
	1999	1,318 (7%)	
	2000	1,338 (7%)	
	2001	1,569 (8%)	
	2002	1,017 (5%)	
	2003	2,018 (11%)	
	2004	2,011 (11%)	
	2005	1,171 (6%)	
Follow-up time (years)		13 (4.5)	
Smoking status			209
	Never	11,456 (63%)	
	Former	1,971 (11%)	
	Current	4,893 (27%)	
Pack-years (current or former smokers)		27 (23)	1,496
BMI		23.6 (3.3)	1,342
	<20	2,197 (13%)	
	20-25	9,557 (56%)	
	25-30	4,830 (28%)	
	>30	603 (4%)	
Education			157
	None	3,852 (21%)	
	Primary	9,359(51%)	
	Secondary	4,541(25%)	
	Trade/Technical	0 (0)	
	University	577 (3%)	
	Post-university	43 (<1%)	
Occupation			2,560
	Unemployed	1,152 (7%)	
	Employed	12,071 (76%)	
	Student	412 (3%)	
	Housewife	1,920 (12%)	
	Other	414 (3%)	
Alcohol (g/week)		3.5 (21)	
Mortality			
	All-cause	3,411	
	Nonaccidental	2,983	

All cancer	1,072
Lung cancer	282
Cardiovascular disease	666
Nonmalignant lung disease	285

Table A55. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ in the Korean Multi-center Cancer Cohort Study (KMCC)

	Model 1		Model 2		Model 3	
	n. events (total = 18,529)	HR (95% CI)	n. events (total = 18,529)	HR (95% CI)	n. events (total = 12,988)	HR (95% CI)
All-cause	3,411	0.77 (0.72, 0.82)	3,411	0.80 (0.72, 0.90)	1,857	0.80 (0.69, 0.93)
Nonaccidental	2,983	0.76 (0.71, 0.81)	2,983	0.81 (0.72, 0.92)	1,596	0.82 (0.69, 0.96)
All cancer	1,072	0.77 (0.69, 0.87)	1,072	0.73 (0.60, 0.90)	608	0.80 (0.61, 1.04)
Lung cancer	282	0.70 (0.55, 0.89)	282	0.56 (0.37, 0.85)	149	0.66 (0.39, 1.15)
Cardiovascular disease	666	0.71 (0.61, 0.83)	666	0.84 (0.65, 1.09)	367	0.93 (0.67, 1.31)
Nonmalignant lung disease	285	0.78 (0.62, 0.99)	285	0.94 (0.64, 1.39)	138	0.83 (0.49, 1.41)

Model 1: Unadjusted.

Model 2: Adjusted for recruitment year and sex.

Model 3: Adjusted for recruitment year, sex, smoking status and intensity, BMI, education, occupation, and alcohol intake.

Table A56. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 10-ppb increase in NO_2 in the Korean Multi-center Cancer Cohort Study (KMCC)

	Model 1		Model 2		Model 3	
	n. events (total = 18,517)	HR (95% CI)	n. events (total = 18,517)	HR (95% CI)	n. events (total = 12,981)	HR (95% CI)
All-cause	3,411	0.79 (0.68, 0.90)	3,411	0.79 (0.68, 0.92)	1,857	0.84 (0.68, 1.03)
Nonaccidental	2,983	0.77 (0.66, 0.89)	2,983	0.79 (0.67, 0.93)	1,596	0.85 (0.68, 1.07)
All cancer	1,072	0.88 (0.69, 1.12)	1,072	0.85 (0.65, 1.11)	608	0.88 (0.61, 1.26)
Lung cancer	282	0.86 (0.53, 1.39)	282	0.68 (0.40, 1.15)	149	0.67 (0.32, 1.38)
Cardiovascular disease	666	0.73 (0.53, 1.00)	666	0.84 (0.59, 1.19)	367	1.17 (0.74, 1.87)
Nonmalignant lung disease	285	1.05 (0.66, 1.68)	285	1.05 (0.62, 1.78)	138	0.96 (0.45, 2.06)

Model 1: Unadjusted.

Model 2: Adjusted for recruitment year and sex.

Model 3: Adjusted for recruitment year, sex, smoking status and intensity, BMI, education, occupation, and alcohol intake.

Table A57: Hazard ratios (and 95% confidence intervals) for specific causes of death for a two-pollutant model in the Korean Multi-center Cancer Cohort Study (KMCC) (Model 3)

	n. events (total = 12,981)	PM _{2.5} HR (95% CI)	NO ₂ HR (95% CI)
All-cause	1,857	0.80 (0.67, 0.95)	1.00 (0.78, 1.29)
Nonaccidental	1,596	0.82 (0.67, 0.99)	1.00 (0.77, 1.31)
All cancer	608	0.78 (0.57, 1.08)	1.05 (0.68, 1.62)
Lung cancer	149	0.71 (0.38, 1.33)	0.85 (0.37, 1.98)
Cardiovascular disease	367	0.82 (0.55, 1.23)	1.37 (0.78, 2.39)
Nonmalignant lung disease	138	0.78 (0.41, 1.47)	1.18 (0.48, 2.94)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂.

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, education, occupation, and alcohol intake.

Table A58. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ in the Korean Multi-center Cancer Cohort Study (KMCC), stratified by smoking status (Model 3)

	Never smokers		Former smokers		Current smokers	
	n. events (total = 8,865)	HR (95% CI)	n. events (total = 1,126)	HR (95% CI)	n. events (total = 2,997)	HR (95% CI)
All-cause	948	0.78 (0.63, 0.96)	234	0.86 (0.61, 1.23)	675	0.72 (0.54, 0.96)
Nonaccidental	817	0.79 (0.63, 0.99)	203	0.87 (0.60, 1.27)	576	0.74 (0.54, 1.01)
All cancer	266	0.70 (0.48, 1.04)	78	1.24 (0.67, 2.31)	264	0.69 (0.43, 1.11)
Lung cancer	37	0.56 (0.19, 1.63)	16	1.01 (0.20, 5.02)	96	0.61 (0.30, 1.25)
Cardiovascular disease	222	0.93 (0.60, 1.43)	40	0.73 (0.31, 1.77)	105	0.78 (0.38, 1.61)
Nonmalignant lung disease	57	0.74 (0.31, 1.69)	31	0.61 (0.25, 1.51)	50	1.24 (0.41, 3.70)

Models adjusted for recruitment year, sex, smoking intensity (current/former smokers only), BMI, education, occupation, and alcohol intake.

Table A59. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 10-ppb increase in NO_2 in the Korean Multi-center Cancer Cohort Study (KMCC), stratified by smoking status (Model 3)

	Never smokers		Former smokers		Current smokers	
	n. events (total = 8,859)	HR (95% CI)	n. events (total = 1,126)	HR (95% CI)	n. events (total = 2,996)	HR (95% CI)
All-cause	948	0.99 (0.74, 1.33)	234	0.59 (0.33, 1.06)	675	0.66 (0.46, 0.95)
Nonaccidental	817	1.04 (0.76, 1.43)	203	0.53 (0.28, 1.00)	576	0.67 (0.46, 0.99)
All cancer	266	1.09 (0.63, 1.89)	78	0.77 (0.27, 2.19)	264	0.67 (0.38, 1.19)
Lung cancer	37	0.89 (0.21, 3.81)	16	0.83 (0.06, 10.7)	96	0.52 (0.20, 1.31)
Cardiovascular disease	222	1.31 (0.72, 2.39)	40	0.56 (0.13, 2.33)	105	0.80 (0.32, 2.02)
Nonmalignant lung disease	57	0.47 (0.14, 1.62)	31	0.61 (0.11, 3.31)	50	2.33 (0.68, 8.01)

Models adjusted for recruitment year, sex, smoking intensity (current/former smokers only), BMI, education, occupation, and alcohol intake.

Table A60. Hazard ratios (and 95% confidence intervals) for specific causes of death among nonsmoking women within the Korean Multi-center Cancer Cohort Study (KMCC)

	PM _{2.5}		NO ₂	
	n. events (total = 7,774)	HR (95% CI)	n. events (total = 7,769)	HR (95% CI)
All-cause	771	0.79 (0.63, 1.00)	771	1.08 (0.78, 1.49)
Nonaccidental	676	0.80 (0.63, 1.03)	676	1.08 (0.76, 1.53)
All cancer	209	0.65 (0.41, 1.02)	209	1.00 (0.54, 1.87)
Lung cancer	30	0.63 (0.20, 2.00)	30	1.02 (0.21, 4.96)
Cardiovascular disease	191	0.99 (0.62, 1.57)	191	1.27 (0.66, 2.43)
Nonmalignant lung disease	47	0.66 (0.27, 1.62)	47	0.44 (0.11, 1.71)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Models adjusted for recruitment year, BMI, education, occupation, and alcohol intake.

Table A61. Hazard ratios (and 95% confidence intervals) for specific causes of death among members of the Korean Multi-center Cancer Cohort Study (KMCC) who had no prevalent disease at recruitment (Model 3)

	PM _{2.5}		NO ₂	
	n. events (total = 9,676)	HR (95% CI)	n. events (total = 9,672)	HR (95% CI)
All-cause	1,219	0.81 (0.66, 0.99)	1,219	0.93 (0.72, 1.20)
Nonaccidental	1,032	0.83 (0.66, 1.04)	1,032	0.95 (0.72, 1.26)
All cancer	437	0.68 (0.48, 0.97)	437	0.89 (0.58, 1.37)
Lung cancer	108	0.51 (0.24, 1.12)	108	0.63 (0.26, 1.53)
Cardiovascular disease	210	1.15 (0.70, 1.89)	210	1.53 (0.82, 2.85)
Nonmalignant lung disease	98	0.89 (0.45, 1.76)	98	1.24 (0.51, 3.04)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, education, occupation, and alcohol intake.

Table A62. Hazard ratios (and 95% confidence intervals) for specific causes of death among members of the Korean Multi-center Cancer Cohort Study (KMCC) who were alive in 1998 (Model 3)

	PM _{2.5}		NO ₂	
	n. events (total = 12,949)	HR (95% CI)	n. events (total = 12,942)	HR (95% CI)
All-cause	1,820	0.80 (0.69, 0.93)	1,820	0.84 (0.68, 1.04)
Nonaccidental	1,564	0.82 (0.70, 0.96)	1,564	0.86 (0.68, 1.08)
All cancer	597	0.80 (0.61, 1.04)	597	0.88 (0.61, 1.27)
Lung cancer	147	0.66 (0.38, 1.14)	147	0.64 (0.31, 1.33)
Cardiovascular disease	358	0.93 (0.67, 1.31)	358	1.18 (0.74, 1.89)
Nonmalignant lung disease	138	0.83 (0.49, 1.41)	138	0.96 (0.45, 2.05)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, education, occupation, and alcohol intake.

Table A63. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ after additional adjustment for specific urban scenarios within the Korean Multi-center Cancer Cohort Study (KMCC)

	Within Urban Center Y/N*		Degree of Urbanicity† in 2000		Degree of Urbanicity in 2010	
	n. events (total = 12,988)	HR (95% CI)	n. events (total = 12,988)	HR (95% CI)	n. events (total = 12,988)	HR (95% CI)
All-cause	1,857	0.83 (0.65, 1.05)	1,857	0.81 (0.65, 1.01)	1,857	0.81 (0.65, 1.00)
Nonaccidental	1,596	0.90 (0.69, 1.16)	1,596	0.82 (0.64, 1.04)	1,596	0.82 (0.64, 1.03)
All cancer	608	0.94 (0.62, 1.42)	608	0.83 (0.56, 1.23)	608	0.83 (0.56, 1.22)
Lung cancer	149	0.79 (0.34, 1.84)	149	0.72 (0.33, 1.60)	149	0.72 (0.33, 1.58)
Cardiovascular disease	367	1.00 (0.59, 1.70)	367	0.90 (0.55, 1.48)	367	0.90 (0.55, 1.47)
Nonmalignant lung disease	138	0.82 (0.33, 2.04)	138	0.63 (0.27, 1.47)	138	0.64 (0.28, 1.46)

*: Refers to a participant being within an urban center as defined by the Global Human Settlement Layer.

†: Refers to gradient values for urbanicity as described by Gao & O'Neill (2020).

Models additionally adjusted for recruitment year, sex, smoking status and intensity, BMI, education, occupation, and alcohol intake.

Table A64. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 10-ppb increase in NO_2 after additional adjustment for specific urban scenarios within the Korean Multi-center Cancer Cohort Study (KMCC)

	Within Urban Center Y/N*		Degree of Urbanicity† in 2000		Degree of Urbanicity in 2010	
	n. events (total = 12,981)	HR (95% CI)	n. events (total = 12,981)	HR (95% CI)	n. events (total = 12,981)	HR (95% CI)
All-cause	1,857	0.97 (0.86, 1.09)	1,857	0.97 (0.86, 1.10)	1,857	0.97 (0.86, 1.09)
Nonaccidental	1,596	0.99 (0.87, 1.12)	1,596	0.97 (0.85, 1.10)	1,596	0.97 (0.85, 1.10)
All cancer	608	1.02 (0.83, 1.25)	608	1.00 (0.81, 1.24)	608	1.00 (0.81, 1.23)
Lung cancer	149	0.91 (0.61, 1.36)	149	0.90 (0.59, 1.37)	149	0.90 (0.59, 1.36)
Cardiovascular disease	367	1.15 (0.89, 1.49)	367	1.13 (0.86, 1.48)	367	1.13 (0.86, 1.48)
Nonmalignant lung disease	138	1.05 (0.68, 1.62)	138	0.98 (0.62, 1.53)	138	0.97 (0.62, 1.53)

*: Refers to a participant being within an urban center as defined by the Global Human Settlement Layer.

†: Refers to gradient values for urbanicity as described by Gao & O'Neill (2020).

Models additionally adjusted for recruitment year, sex, smoking status and intensity, BMI, education, occupation, and alcohol intake.

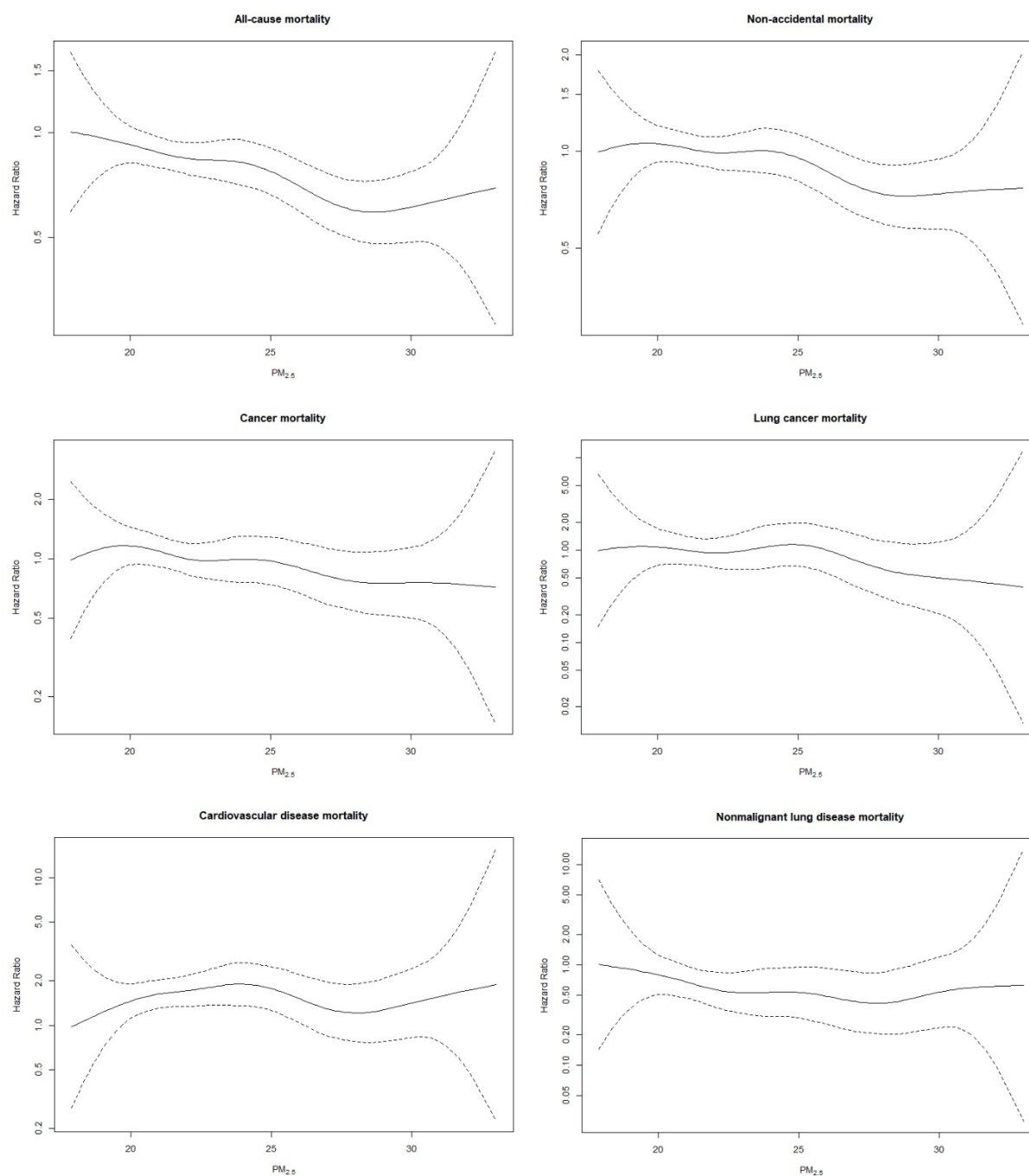


Figure A8: Penalized spline analysis (with 4 degrees of freedom) examining relationship between $PM_{2.5}$ exposure and all-cause and cause-specific mortality within the Korean Multi-center Cancer Cohort Study (KMCC) (Model 3).

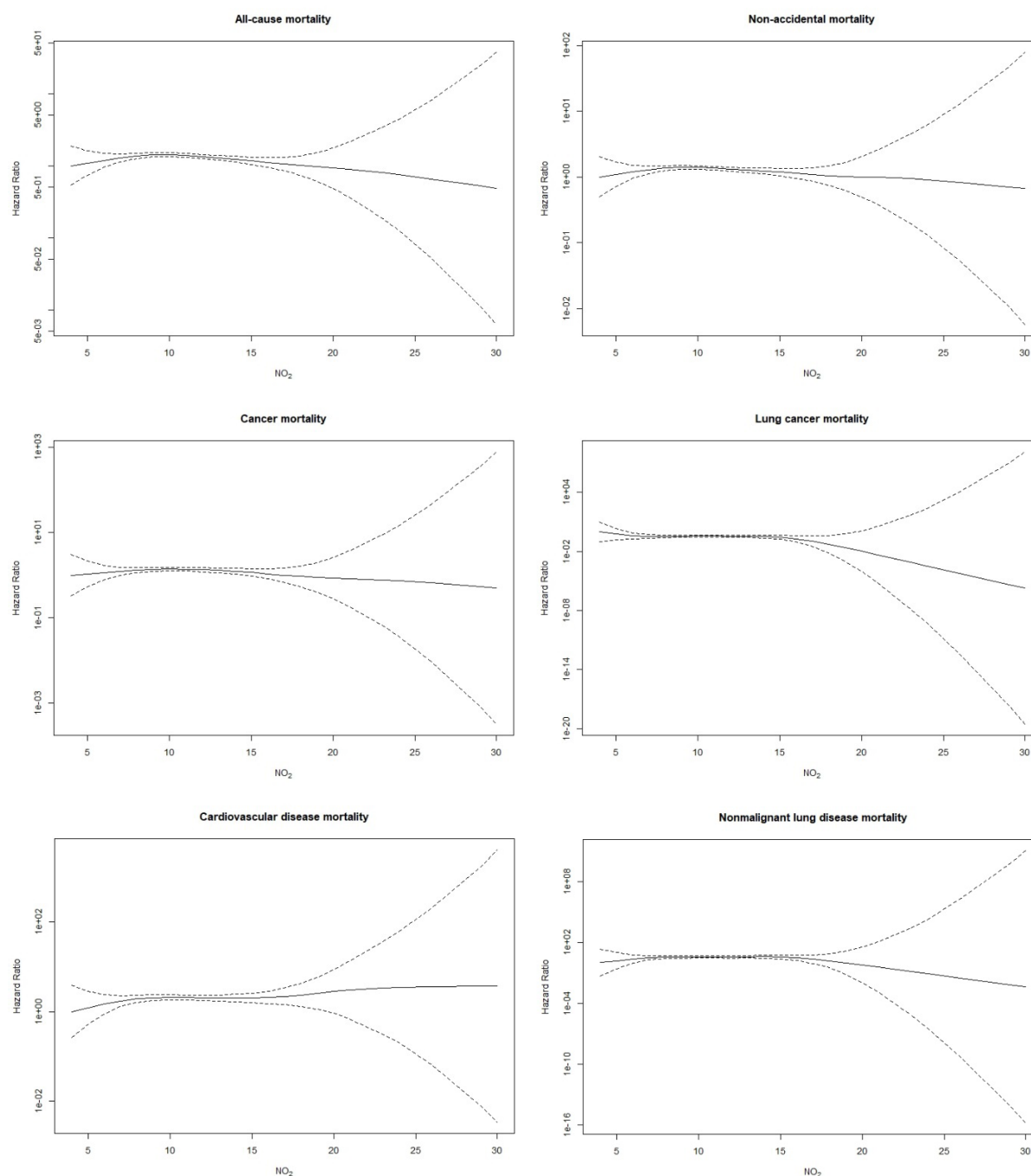


Figure A9: Penalized spline analysis (with 4 degrees of freedom) examining relationship between NO₂ exposure and all-cause and cause-specific mortality within the Korean Multi-center Cancer Cohort Study (KMCC) (Model 3).

Table A65. Hazard ratios (and 95% confidence intervals) for specific causes of death among the Korean Multi-center Cancer Cohort Study (KMCC) by quartile of PM_{2.5} (Model 3)

	n. events (total = 12,988)	Q1 (<20.2 µg/m ³)	Q2 (20.2–21.6 µg/m ³)	Q3 (21.6–24.8 µg/m ³)	Q4 (>24.8 µg/m ³)
All-cause	1,857	1.00	1.02 (0.90, 1.16)	0.90 (0.72, 1.11)	0.77 (0.60, 0.99)
Nonaccidental	1,596	1.00	1.04 (0.91, 1.19)	0.96 (0.76, 1.21)	0.83 (0.63, 1.09)
All cancer	608	1.00	1.09 (0.87, 1.36)	0.88 (0.59, 1.31)	0.85 (0.53, 1.34)
Lung cancer	149	1.00	1.32 (0.83, 2.09)	0.70 (0.27, 1.81)	0.87 (0.31, 2.43)
Cardiovascular disease	367	1.00	1.13 (0.84, 1.51)	1.08 (0.68, 1.72)	0.92 (0.52, 1.61)
Nonmalignant lung disease	138	1.00	0.91 (0.57, 1.46)	0.54 (0.22, 1.31)	0.45 (0.17, 1.23)

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, education, occupation, and alcohol intake.

Table A66. Hazard ratios (and 95% confidence intervals) for specific causes of death among the Korean Multi-center Cancer Cohort Study (KMCC) by quartile of NO₂ (Model 3)

	n. events (total = 12,981)	Q1 (<9ppb)	Q2 (9–11ppb)	Q3 (11–13ppb)	Q4 (>13ppb)
All-cause	1,857	1.00	1.09 (0.97, 1.23)	0.91 (0.79, 1.06)	0.90 (0.76, 1.06)
Nonaccidental	1,596	1.00	1.07 (0.95, 1.22)	0.91 (0.77, 1.06)	0.92 (0.77, 1.10)
All cancer	608	1.00	1.15 (0.94, 1.41)	0.98 (0.76, 1.26)	0.90 (0.67, 1.20)
Lung cancer	149	1.00	1.33 (0.89, 2.00)	0.94 (0.57, 1.56)	0.82 (0.45, 1.50)
Cardiovascular disease	367	1.00	1.06 (0.81, 1.38)	0.97 (0.69, 1.35)	1.11 (0.78, 1.60)
Nonmalignant lung disease	138	1.00	0.92 (0.59, 1.43)	0.93 (0.55, 1.59)	0.87 (0.48, 1.58)

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, education, occupation, and alcohol intake.

Table A67. Hazard ratios (and 95% confidence intervals) for specific causes of death within the Korean Multi-center Cancer Cohort Study (KMCC) after adapting variables which potentially violated the proportional hazards assumption

	PM _{2.5}		NO ₂	
	n. events (total = 12,988)	HR (95% CI)	n. events (total = 12,981)	HR (95% CI)
All-cause	1,857	0.76 (0.66, 0.88)	1,857	0.75 (0.62, 0.92)
Nonaccidental	1,596	0.77 (0.66, 0.90)	1,596	0.75 (0.60, 0.93)
All cancer	608	0.75 (0.58, 0.97)	608	0.80 (0.57, 1.13)
Lung cancer	149	0.61 (0.36, 1.04)	149	0.70 (0.36, 1.36)
Cardiovascular disease	367	0.86 (0.62, 1.20)	367	1.02 (0.65, 1.60)
Nonmalignant lung disease	138	0.92 (0.55, 1.52)	138	0.87 (0.44, 1.73)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Potential assumption violators were pack-years (removed from analysis), smoking status, occupation, and sex (stratified).

Supplementary Tables and Figures: Mumbai Cohort Study (MCS)

Table A68. Demographic features of the Mumbai Cohort Study (MCS)

		Mean (sd) or n (%)
Number of participants		141,238
Age at recruitment		51 (11)
Sex		
	Male	82,054 (58%)
	Female	59,184 (42%)
Recruitment year		
	1991	18,892 (13%)
	1992	35,851 (25%)
	1993	36,593 (26%)
	1994	15,583 (11%)
	1995	12,082 (9%)
	1996	13,042 (9%)
	1997	9,195 (7%)
Follow-up time (years)		5 (1.5)
Smoking status		
	Never	115,340 (82%)
	Former	5,126 (4%)
	Current	20,772 (15%)
Pack-years (current or former smokers)		7 (16)
BMI		22 (4.2)
	<20	43,020 (30%)
	20-25	63,746 (45%)
	25-30	28,14 (20%)
	>30	6,328 (4%)
Education		
	Primary	40,116 (28%)
	Secondary	52,147 (37%)
	Trade/Technical	32,473 (23%)
	University	10,090 (7%)
	Post-University	6,412 (5%)
Mortality		
	All-cause	12,934
	Nonaccidental	8,689
	All cancer	793
	Lung cancer	78
	Cardiovascular disease	3,306
	Nonmalignant lung disease	1,255
	Cause not coded	4,245

There was no missing information on covariates.

Table A69. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ in the Mumbai Cohort Study (MCS)

	Model 1		Model 2		Model 3	
	n. events (total = 126,377)	HR (95% CI)	n. events (total = 126,377)	HR (95% CI)	n. events (total = 126,377)	HR (95% CI)
All-cause	11,777	1.30 (1.22, 1.39)	11,777	1.18 (1.10, 1.27)	11,777	1.15 (1.07, 1.24)
Nonaccidental	7,881	1.31 (1.20, 1.42)	7,881	1.16 (1.07, 1.27)	7,881	1.15 (1.05, 1.25)
All cancer	721	1.06 (0.80, 1.40)	721	0.95 (0.70, 1.28)	721	0.95 (0.70, 1.28)
Lung cancer	75	1.50 (0.68, 3.29)	75	1.79 (0.74, 4.30)	75	1.74 (0.72, 4.21)
Cardiovascular disease	2,976	1.19 (1.04, 1.37)	2,976	1.26 (1.08, 1.46)	2,976	1.25 (1.08, 1.46)
Nonmalignant lung disease	1,168	1.61 (1.32, 1.97)	1,168	1.17 (0.94, 1.46)	1,168	1.11 (0.89, 1.38)

Model 1: Unadjusted.

Model 2: Adjusted for recruitment year and sex.

Model 3: Adjusted for recruitment year, sex, smoking status and intensity, BMI, and education.

Table A70. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 10-ppb increase in NO_2 in the Mumbai Cohort Study (MCS)

	Model 1		Model 2		Model 3	
	n. events (total = 126,401)	HR (95% CI)	n. events (total = 126,401)	HR (95% CI)	n. events (total = 126,401)	HR (95% CI)
All-cause	11,779	1.17 (1.07, 1.27)	11,779	1.11 (1.02, 1.20)	11,779	1.27 (1.17, 1.38)
Nonaccidental	7,883	1.23 (1.11, 1.37)	7,883	1.23 (1.11, 1.36)	7,883	1.36 (1.23, 1.51)
All cancer	721	1.37 (0.98, 1.93)	721	1.37 (0.97, 1.92)	721	1.51 (1.07, 2.14)
Lung cancer	75	0.98 (0.35, 2.75)	75	1.06 (0.36, 3.13)	75	1.39 (0.47, 4.14)
Cardiovascular disease	2,977	1.29 (1.09, 1.53)	2,977	1.38 (1.16, 1.65)	2,977	1.38 (1.16, 1.65)
Nonmalignant lung disease	1,168	1.09 (0.83, 1.42)	1,168	0.99 (0.77, 1.27)	1,168	1.22 (0.95, 1.58)

Model 1: Unadjusted.

Model 2: Adjusted for recruitment year and sex.

Model 3: Adjusted for recruitment year, sex, smoking status and intensity, BMI, and education.

Table A71. Hazard ratios (and 95% confidence intervals) for specific causes of death for a two-pollutant model in the Mumbai Cohort Study (MCS) (Model 3)

	n. events (total = 126,377)	PM _{2.5} HR (95% CI)	NO ₂ HR (95% CI)
All-cause	11,777	1.19 (1.11, 1.28)	1.30 (1.20, 1.41)
Nonaccidental	7,881	1.20 (1.09, 1.31)	1.39 (1.25, 1.54)
All cancer	721	0.99 (0.72, 1.35)	1.51 (1.07, 2.13)
Lung cancer	75	1.79 (0.73, 4.39)	1.45 (0.50, 4.17)
Cardiovascular disease	2,976	1.29 (1.10, 1.50)	1.41 (1.18, 1.67)
Nonmalignant lung disease	1,168	1.16 (0.93, 1.45)	1.26 (0.98, 1.63)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂.

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, and education.

Table A72. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 5- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ in the Mumbai Cohort Study (MCS), stratified by smoking status (Model 3)

	Never smokers		Former smokers		Current smokers	
	n. events (total = 102,264)	HR (95% CI)	n. events (total = 4,917)	HR (95% CI)	n. events (total = 19,196)	HR (95% CI)
All-cause	8,302	1.08 (0.99, 1.18)	1,118	1.39 (0.99, 1.94)	2,357	1.34 (1.16, 1.55)
Nonaccidental	5,582	1.08 (0.97, 1.19)	816	1.43 (0.97, 2.10)	1,483	1.387 (1.14, 1.66)
All cancer	455	1.00 (0.70, 1.43)	89	1.07 (0.29, 3.96)	177	0.82 (0.42, 1.60)
Lung cancer	33	1.78 (0.53, 6.01)	12	13.28 (1.02, 172)	30	0.96 (0.19, 4.88)
Cardiovascular disease	2,136	1.18 (0.99, 1.41)	316	1.36 (0.70, 2.64)	524	1.45 (1.05, 2.01)
Nonmalignant lung disease	802	1.01 (0.77, 1.30)	147	1.36 (0.55, 3.41)	219	1.65 (1.03, 2.63)

Models adjusted for recruitment year, sex, smoking intensity (current/former smokers only), BMI, and education.

Table A73. Hazard ratios (and 95% confidence intervals) for specific causes of death in relation to 10-ppb increase in NO_2 in the Mumbai Cohort Study (MCS), stratified by smoking status (Model 3)

	Never smokers		Former smokers		Current smokers	
	n. events (total = 102,284)	HR (95% CI)	n. events (total = 4,918)	HR (95% CI)	n. events (total = 19,199)	HR (95% CI)
All-cause	8,304	1.22 (1.10, 1.34)	1,118	1.51 (1.09, 2.09)	2,357	1.32 (1.11, 1.56)
Nonaccidental	5,584	1.34 (1.18, 1.51)	816	1.30 (0.89, 1.90)	1,483	1.36 (1.09, 1.69)
All cancer	455	1.25 (0.82, 1.91)	89	0.50 (0.16, 1.55)	177	3.22 (1.56, 6.68)
Lung cancer	33	0.97 (0.21, 4.60)	12	1.51 (0.06, 37.9)	30	2.09 (0.35, 12.48)
Cardiovascular disease	2,137	1.28 (1.04, 1.58)	316	2.23 (1.18, 4.22)	524	1.46 (1.00, 2.13)
Nonmalignant lung disease	802	1.20 (0.88, 1.63)	147	2.78 (1.10, 7.00)	219	0.81 (0.47, 1.39)

Models adjusted for recruitment year, sex, smoking intensity (current/former smokers only), BMI, and education.

Table A74. Hazard ratios (and 95% confidence intervals) for specific causes of death among nonsmoking women within the Mumbai Cohort Study (MCS)

	PM _{2.5}		NO ₂	
	n. events (total = 50,777)	HR (95% CI)	n. events (total = 50,779)	HR (95% CI)
All-cause	2,970	1.10 (0.97, 1.24)	2,972	1.17 (1.00, 1.36)
Nonaccidental	2,052	1.03 (0.89, 1.20)	2,054	1.31 (1.09, 1.58)
All cancer	212	1.05 (0.66, 1.68)	212	1.26 (0.71, 2.26)
Lung cancer	16	1.89 (0.41, 8.72)	16	1.23 (0.16, 9.66)
Cardiovascular disease	648	1.39 (1.08, 1.81)	649	1.06 (0.76, 1.48)
Nonmalignant lung disease	364	0.74 (0.51, 1.07)	364	1.39 (0.90, 2.13)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Models adjusted for recruitment year, BMI, and education.

Table A75. Hazard ratios (and 95% confidence intervals) for specific causes of death among members of the Mumbai Cohort Study (MCS) who were alive in 1998 (Model 3)

	PM _{2.5}		NO ₂	
	n. events (total = 96,490)	HR (95% CI)	n. events (total = 96,509)	HR (95% CI)
All-cause	4,737	1.34 (1.10, 1.63)	4,737	1.32 (1.14, 1.53)
Nonaccidental	2,917	1.53 (1.18, 1.98)	2,917	1.50 (1.24, 1.82)
All cancer	253	1.85 (0.80, 4.27)	253	2.37 (1.23, 4.56)
Lung cancer	31	0.91, 61)	31	0.64 (0.09, 4.84)
Cardiovascular disease	1,239	1.64 (1.07, 2.50)	1,239	2.19 (1.61, 2.98)
Nonmalignant lung disease	401	1.63 (0.83, 3.18)	401	0.92 (0.55, 1.55)

Hazard ratios provided for a 5- $\mu\text{g}/\text{m}^3$ increase in PM_{2.5} and a 10-ppb increase in NO₂ (each are single pollutant models).

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, and education.

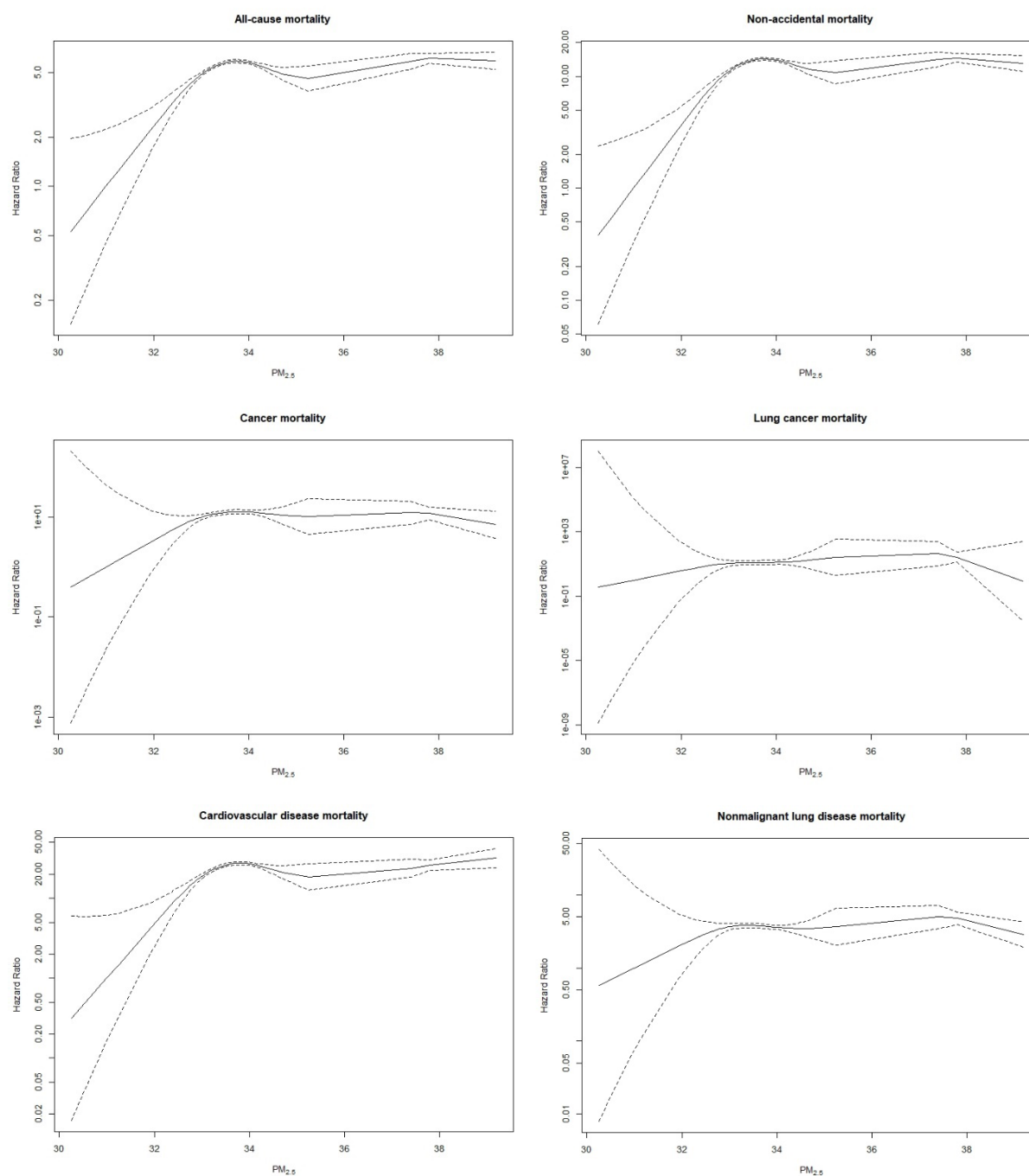


Figure A10: Penalized spline analysis (with 4 degrees of freedom) examining relationship between PM_{2.5} exposure and all-cause and cause-specific mortality within the Mumbai Cohort Study (MCS) (Model 3).

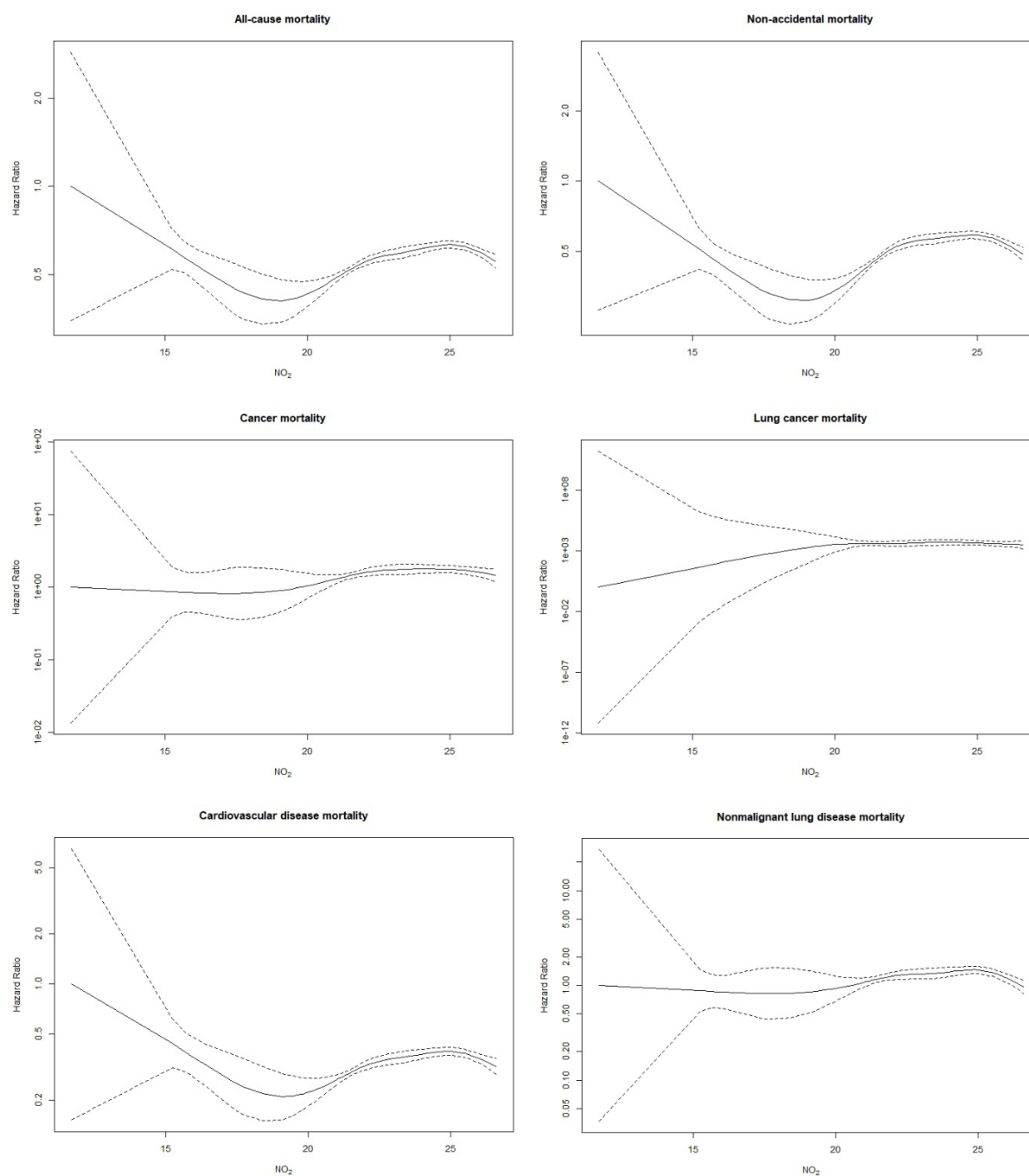


Figure A11: Penalized spline analysis (with 4 degrees of freedom) examining relationship between NO_2 exposure and all-cause and cause-specific mortality within the Mumbai Cohort Study (MCS) (Model 3).

Table A76. Hazard ratios (and 95% confidence intervals) for specific causes of death among the Mumbai Cohort Study (MCS) by quartile of PM_{2.5} (Model 3)

	n. events (total = 126,377)	Q1 (<33.25 µg/m ³)	Q2 (33.26–33.67 µg/m ³)	Q3 (33.67–34.03 µg/m ³)	Q4 (>34.03 µg/m ³)
All-cause	11,777	1.00	1.18 (1.12, 1.25)	1.14 (1.12, 1.21)	1.11 (1.05, 1.18)
Nonaccidental	7,881	1.00	1.32 (1.23, 1.41)	1.20 (1.23, 1.29)	1.21 (1.12, 1.30)
All cancer	721	1.00	1.26 (1.01, 1.58)	1.14 (1.01, 1.45)	1.17 (0.92, 1.48)
Lung cancer	75	1.00	1.12 (0.56, 2.25)	0.96 (0.56, 2.07)	1.52 (0.77, 3.03)
Cardiovascular disease	2,976	1.00	1.46 (1.30, 1.654)	1.44 (1.30, 1.62)	1.35 (1.19, 1.53)
Nonmalignant lung disease	1,168	1.00	1.02 (0.85, 1.21)	0.88 (0.85, 1.06)	0.96 (0.80, 1.15)

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, and education.

Table A77. Hazard ratios (and 95% confidence intervals) for specific causes of death among the Mumbai Cohort Study (MCS) by quartile of NO₂ (Model 3)

	n. events (total = 126,401)	Q1 (<21.4 ppb)	Q2 (21.4–22.9 ppb)	Q3 (22.9–24.8 ppb)	Q4 (>24.8 ppb)
All-cause	11,779	1.00	1.13 (1.07, 1.20)	1.27 (1.07, 1.34)	1.18 (1.12, 1.25)
Nonaccidental	7,883	1.00	1.26 (1.18, 1.35)	1.35 (1.18, 1.44)	1.26 (1.18, 1.35)
All cancer	721	1.00	1.28 (1.02, 1.61)	1.35 (1.02, 1.67)	1.33 (1.07, 1.65)
Lung cancer	75	1.00	0.66 (0.31, 1.41)	1.33 (0.31, 2.41)	0.84 (0.43, 1.66)
Cardiovascular disease	2,977	1.00	1.21 (1.08, 1.36)	1.34 (1.08, 1.48)	1.31 (1.18, 1.46)
Nonmalignant lung disease	1,168	1.00	1.41 (1.17, 1.68)	1.42 (1.17, 1.68)	1.17 (0.99, 1.40)

Models adjusted for recruitment year, sex, smoking status and intensity, BMI, and education.

Table A78. Beta coefficient and time interaction for PM_{2.5} exposure and specific causes of death within the Mumbai Cohort Study (MCS)

	n. events (total = 126,377)	Effect for PM _{2.5} Beta Coefficient	Time interaction
All-cause	11,777	0.15	-0.026
Nonaccidental	7,881	0.15	-0.027
All cancer	721	0.11	-0.028
Lung cancer	75	0.22	-0.027
Cardiovascular disease	2,976	0.16	-0.027
Nonmalignant lung disease	1,168	0.15	-0.026

Time interaction based upon follow-up time.

Table A79. Hazard ratios (and 95% confidence intervals) for NO₂ and specific causes of death within the Mumbai Cohort Study (MCS) after adapting variables which potentially violated the proportional hazards assumption

	n. events (total = 126,401)	HR (95% CI)
All-cause	11,779	1.26 (1.16, 1.37)
Nonaccidental	7,883	1.35 (1.22, 1.50)
All cancer	721	1.50 (1.06, 2.12)
Lung cancer	75	1.43 (0.48, 4.29)
Cardiovascular disease	2,977	1.38 (1.15, 1.64)
Nonmalignant lung disease	1,168	1.20 (0.93, 1.55)

Hazard ratios provided a 10-ppb increase in NO₂.

Potential assumption violators were sex and smoking status (stratified).