

Supplemental material

Long-term exposure to air pollution and incidence of Parkinson's disease in a large metropolitan cohort

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eTable 1. Drugs and ATC codes for Parkinson cases' selection.

Name	ATC code
Levodopa	N04BA01
Levodopa and decarboxylase inhibitor	N04BA02
Levodopa, decarboxylase inhibitor and COMT inhibitor	N04BA03
Pergolide	N04BC02
Ropinirole	N04BC04
Pramipexole	N04BC05
Entacapone	N04BX02

eTable 2. Pearson correlation coefficients of individual exposures to air pollutants.

	PM ₁₀	Coarse PM	PM ₂₅	PM ₂₅ absorbance	NO ₂	NO _x	O ₃
PM ₁₀	1.00						
Coarse PM	0.93	1.00					
PM ₂₅	0.93	0.91	1.00				
PM ₂₅ absorbance	0.60	0.65	0.65	1.00			
NO ₂	0.59	0.71	0.65	0.61	1.00		
NO _x	0.55	0.62	0.61	0.52	0.71	1.00	
O ₃	-0.03	-0.02	-0.02	-0.07	-0.12	-0.13	1.00

eTable 3. Association between long-term air pollution exposure and incidence of Parkinson's disease in subjects with previous acute myocardial infarction (AMI) or stroke.

Exposure	Case definition: PD	Case definition: PD
	with AMI or stroke	without AMI and stroke
	(N=1,513)	(N=11,590)
	HR ^a	HR ^a
	(95%CI)	(95%CI)
PM ₁₀ (10µg/m ³)	0.99 (0.89, 1.08)	0.98 (0.95, 1.02)
Coarse PM (5µg/m ³)	0.98 (0.91, 1.08)	0.98 (0.95, 1.00)
PM ₂₅ (5µg/m ³)	0.99 (0.86, 1.12)	0.96 (0.91, 1.01)
PM ₂₅ absorbance (10 ⁻⁵ /m)	1.00 (0.89, 1.10)	0.94 (0.90, 0.98)
NO ₂ (10µg/m ³)	0.97 (0.92, 1.02)	0.98 (0.96, 0.99)
NOx (20µg/m ³)	0.99 (0.94, 1.03)	0.97 (0.95, 0.98)
O ₃ (10µg/m ³)	1.06 (0.97, 1.14)	1.02 (0.99, 1.05)

a Models adjusted for place of birth, education, socioeconomic status and marital status, stratified by sex

eTable 4. Association between long-term air pollution exposure and incidence of Parkinson's disease in subjects who had at least three prescriptions for cardiovascular drugs during the year before identification of PD.

Exposure	Antihypertensives		Diuretics		Beta Blocking agents, Calcium channel blockers and agents acting on the renin-angiotensin system	
	Yes	No	Yes	No	Yes	No
	(N=543)	(N=12,561)	(N=2,173)	(N=10,931)	(N=8,410)	(N=4,694)
	HR ^a	HR ^a	HR ^a	HR ^a	HR ^a	HR ^a
	(95%CI)	(95%CI)	(95%CI)	(95%CI)	(95%CI)	(95%CI)
PM ₁₀ (10µg/m ³)	0.92 (0.75, 1.08)	0.99 (0.95, 1.02)	0.92 (0.84, 1.00)	0.99 (0.96, 1.03)	0.99 (0.95, 1.03)	0.97 (0.92, 1.03)
Coarse PM (5µg/m ³)	0.94 (0.81, 1.07)	0.98 (0.95, 1.01)	0.93 (0.86, 0.99)	0.99 (0.96, 1.02)	0.97 (0.94, 1.01)	0.99 (0.94, 1.03)
PM ₂₅ (5µg/m ³)	0.86 (0.64, 1.09)	0.97 (0.92, 1.02)	0.90 (0.79, 1.01)	0.98 (0.93, 1.03)	0.97 (0.92, 1.03)	0.95 (0.88, 1.03)
PM ₂₅ absorbance (10 ⁻⁵ /m)	0.92 (0.74, 1.11)	0.95 (0.91, 0.99)	0.88 (0.79, 0.97)	0.96 (0.92, 1.00)	0.95 (0.91, 1.00)	0.94 (0.88, 1.01)
NO ₂ (10µg/m ³)	0.96 (0.87, 1.04)	0.98 (0.96, 0.99)	0.94 (0.90, 0.98)	0.98 (0.97, 1.00)	0.98 (0.95, 1.00)	0.98 (0.95, 1.00)
NO _x (20µg/m ³)	0.96 (0.89, 1.03)	0.97 (0.96, 0.99)	0.95 (0.92, 0.99)	0.97 (0.96, 0.99)	0.97 (0.96, 0.99)	0.97 (0.94, 0.99)
O ₃ (10µg/m ³)	0.95 (0.81, 1.08)	1.03 (1.00, 1.06)	1.02 (0.95, 1.09)	1.03 (0.99, 1.06)	1.01 (0.98, 1.05)	1.05 (1.00, 1.10)

a Models adjusted for place of birth, education, socioeconomic status and marital status, stratified by sex

eTable 5. Association between long-term air pollution exposure and incidence of Parkinson's disease from different data sources.

Exposure	HR ^a (95%CI)	HR ^a (95%CI)	HR ^a (95%CI)
Data sources	HDR ^b	RDR ^c	ECR ^d
N subjects	3,872	12,706	1,513
PM ₁₀ (10µg/m ³)	0.96 (0.90, 1.02)	0.99 (0.96, 1.02)	1.00 (0.90, 1.09)
Coarse PM (5µg/m ³)	0.94 (0.90, 0.99)	0.99 (0.96, 1.01)	1.01 (0.94, 1.09)
PM ₂₅ (5µg/m ³)	0.93 (0.85, 1.01)	0.98 (0.93, 1.02)	0.98 (0.84, 1.11)
PM ₂₅ absorbance (10 ⁻⁵ /m)	0.89 (0.82, 0.96)	0.96 (0.92, 0.99)	1.00 (0.90, 1.11)
NO ₂ (10µg/m ³)	0.93 (0.90, 0.97)	0.98 (0.96, 1.00)	1.01 (0.96, 1.06)
NO _x (20µg/m ³)	0.94 (0.91, 0.97)	0.98 (0.96, 0.99)	1.00 (0.96, 1.04)
O ₃ (10µg/m ³)	1.01 (0.96, 1.06)	1.03 (1.00, 1.06)	1.06 (0.97, 1.14)

a Models adjusted for place of birth, education, socioeconomic status and marital status, stratified by sex

b Hospital Discharge Registry

c Regional Drug Registry

d Exempt from Copays Registry

eTable 6. Association between long-term air pollution exposure and incidence of Parkinson's disease using Inverse Probability Weighting (IPW).

Exposure	HR^a (95%CI)
PM ₁₀ (10µg/m ³)	0.98 (0.95, 1.01)
Coarse PM (5µg/m ³)	0.97 (0.95, 1.00)
PM ₂₅ (5µg/m ³)	0.96 (0.92, 1.01)
PM ₂₅ absorbance (10 ⁻⁵ /m)	0.94 (0.91, 0.98)
NO ₂ (10µg/m ³)	0.97 (0.96, 0.99)
NO _x (20µg/m ³)	0.97 (0.96, 0.98)
O ₃ (10µg/m ³)	1.02 (0.99, 1.05)

a Models adjusted for gender, place of birth, education, socioeconomic status and marital status

eTable 7. Association between long-term air pollution exposure and incidence of Parkinson's disease allowing for competing risk of death.

Exposure	HR^a (95%CI)
PM ₁₀ (10µg/m ³)	0.98 (0.95, 1.01)
Coarse PM (5µg/m ³)	0.98 (0.96, 1.01)
PM ₂₅ (5µg/m ³)	0.97 (0.92, 1.01)
PM ₂₅ absorbance (10 ⁻⁵ /m)	0.95 (0.91, 0.99)
NO ₂ (10µg/m ³)	0.98 (0.96, 0.99)
NO _x (20µg/m ³)	0.97 (0.96, 0.99)
O ₃ (10µg/m ³)	1.02 (0.99, 1.05)

a Models adjusted for gender, place of birth, education, socioeconomic status and marital status

eTable 8. Association between long-term air pollution exposure and incidence of Parkinson's disease. Subject aged 50+ at the time of inclusion.

Exposure	HR^a (95%CI)
PM ₁₀ (10µg/m ³)	0.98 (0.95, 1.01)
Coarse PM (5µg/m ³)	0.97 (0.95, 1.00)
PM ₂₅ (5µg/m ³)	0.96 (0.92, 1.01)
PM ₂₅ absorbance (10 ⁻⁵ /m)	0.94 (0.91, 0.98)
NO ₂ (10µg/m ³)	0.97 (0.96, 0.99)
NO _x (20µg/m ³)	0.97 (0.96, 0.98)
O ₃ (10µg/m ³)	1.02 (0.99, 1.05)

a Models adjusted for place of birth, education, socioeconomic status and marital status, stratified by sex

eTable 9 Association between long-term air pollution exposure and incidence of Parkinson's disease in long-term residents (subgroup of subjects who did not change their residence address since 1986).

Exposure	HR^a (95%CI) (N=467,132)
PM ₁₀ *(10µg/m ³)	0.98 (0.94, 1.02)
Coarse *(5µg/m ³)	0.97 (0.94, 1.01)
PM ₂₅ *(5µg/m ³)	0.96 (0.91, 1.02)
PM ₂₅ abs *(10 ⁻⁵ /m)	0.94 (0.89, 0.99)
NO ₂ *(10µg/m ³)	0.97 (0.95, 0.99)
NO _x *(20µg/m ³)	0.97 (0.95, 0.98)
O ₃ *(10µg/m ³)	1.01 (0.98, 1.05)

a Models adjusted for place of birth, education, socioeconomic status and marital status, stratified by sex

eTable 10. Association between long-term air pollution exposure and incidence of Parkinson's disease using the exposure assessment on 2001 addresses.

Exposure	HR^a (95%CI) (N=467,132)
PM ₁₀ *(10µg/m ³)	0.98 (0.95, 1.02)
Coarse *(5µg/m ³)	0.98 (0.95, 1.00)
PM ₂₅ *(5µg/m ³)	0.97 (0.92, 1.01)
PM ₂₅ abs *(10 ⁻⁵ /m)	0.95 (0.91, 0.98)
NO ₂ *(10µg/m ³)	0.98 (0.96, 0.99)
NO _x *(20µg/m ³)	0.97 (0.96, 0.99)
O ₃ *(10µg/m ³)	1.02 (0.99, 1.05)

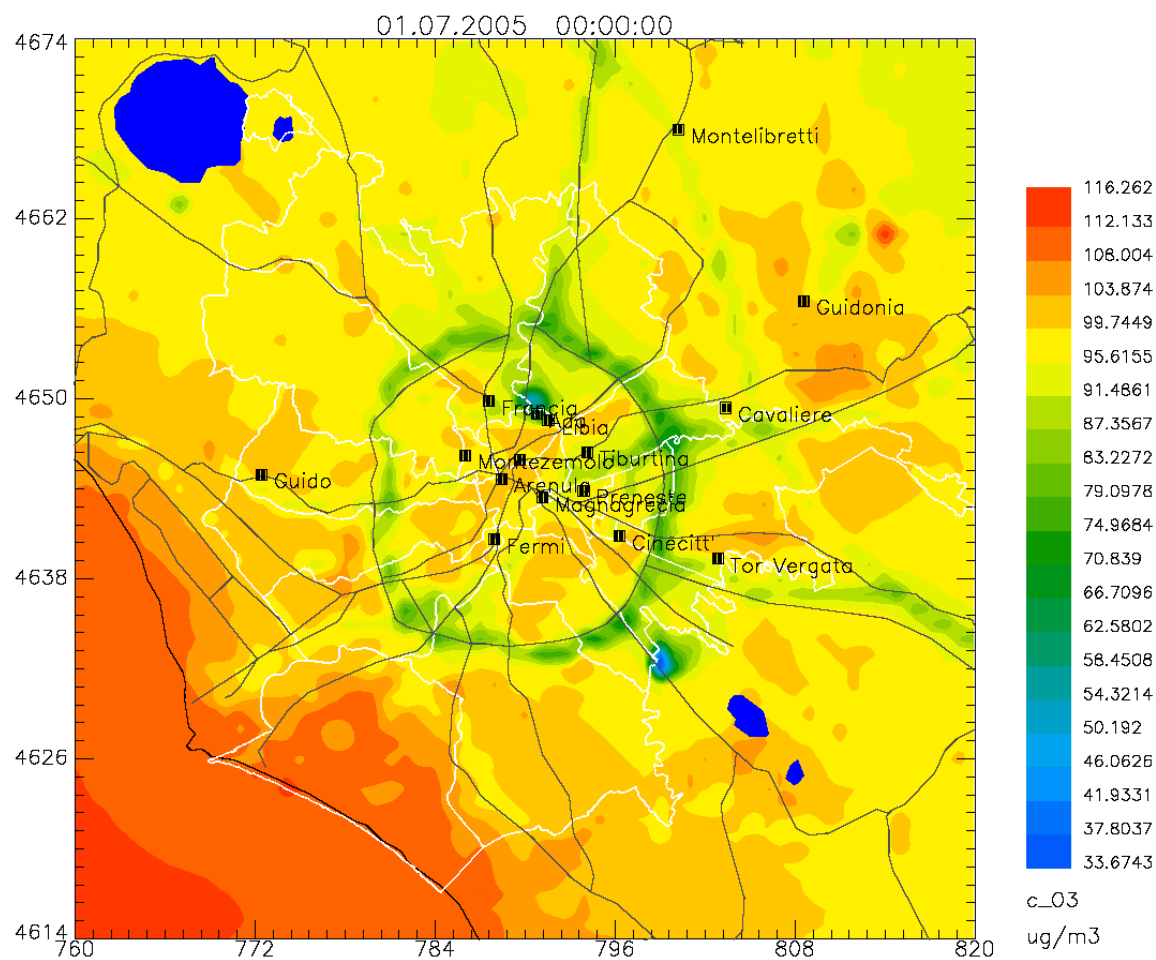
a Models adjusted for place of birth, education, socioeconomic status and marital status, stratified by sex

eTable 11. Association between long-term air pollution exposure and smoking habit (never vs. ever) in a subset of the cohort.

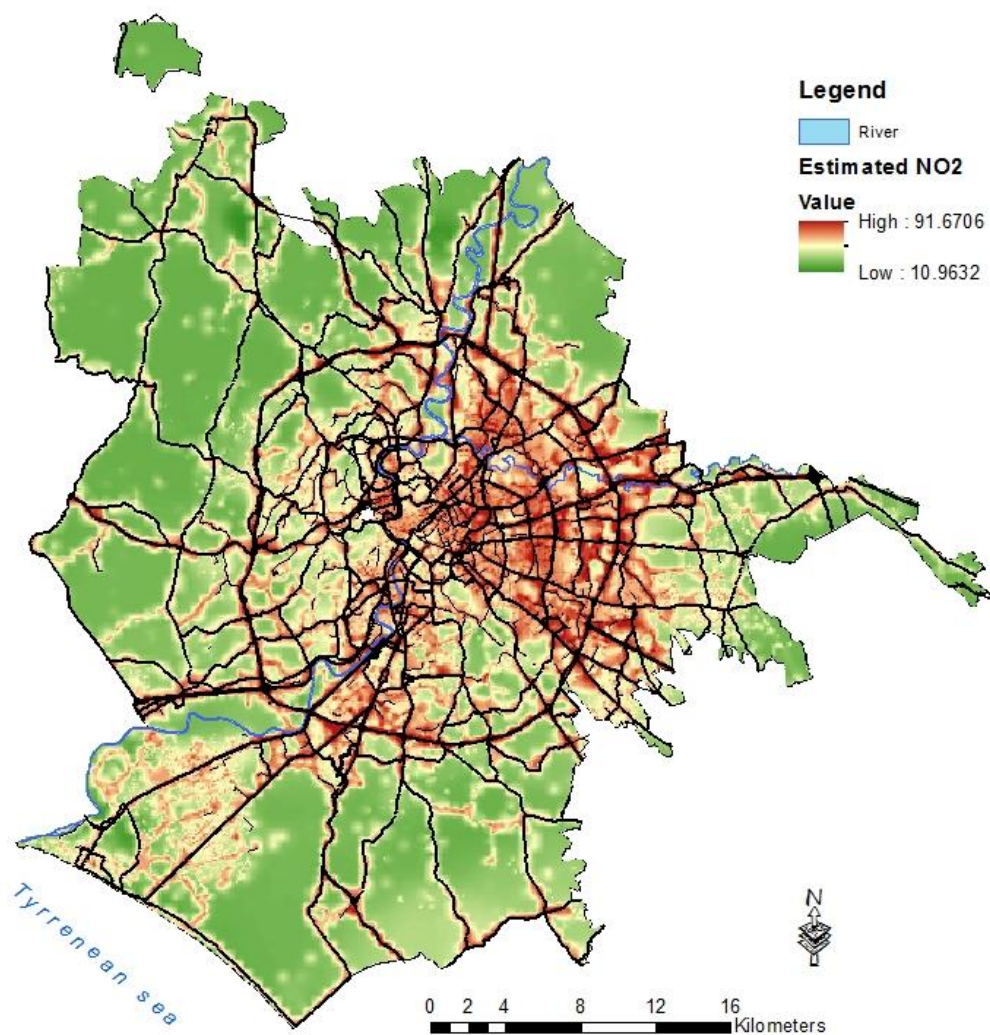
Exposure	Crude OR (95%CI)	Adjusted OR^a (95%CI)
PM ₁₀ (10µg/m ³)	0.99 (0.98, 1.00)	0.99 (0.98, 1.00)
Coarse PM (5µg/m ³)	0.98 (0.96, 0.99)	0.98 (0.97, 1.00)
PM ₂₅ (5µg/m ³)	0.97 (0.94, 1.00)	0.98 (0.95, 1.01)
PM ₂₅ absorbance (10 ⁻⁵ /m)	0.94 (0.85, 1.04)	0.97 (0.87, 1.08)
NO ₂ (10µg/m ³)	1.00 (0.99, 1.00)	1.00 (0.99, 1.00)
NO _x (20µg/m ³)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
O ₃ (10µg/m ³)	1.00 (0.99, 1.01)	1.00 (0.99, 1.01)

a from logistic regression adjusted for gender, place of birth, education, socioeconomic status and marital status

eFigure 1. Map of Rome with predicted summer O3 levels in 2005.



eFigure 2. Map of Rome with predicted NO₂ levels in 2010.



eFigure 3. Estimated concentration–response curves (solid lines) and 95% CIs (dashed lines) for O₃ (A), NO₂ (B) and PM_{2.5} absorbance(C). Cox models adjusted for place of birth, education, socioeconomic status and marital status, stratified by sex.

