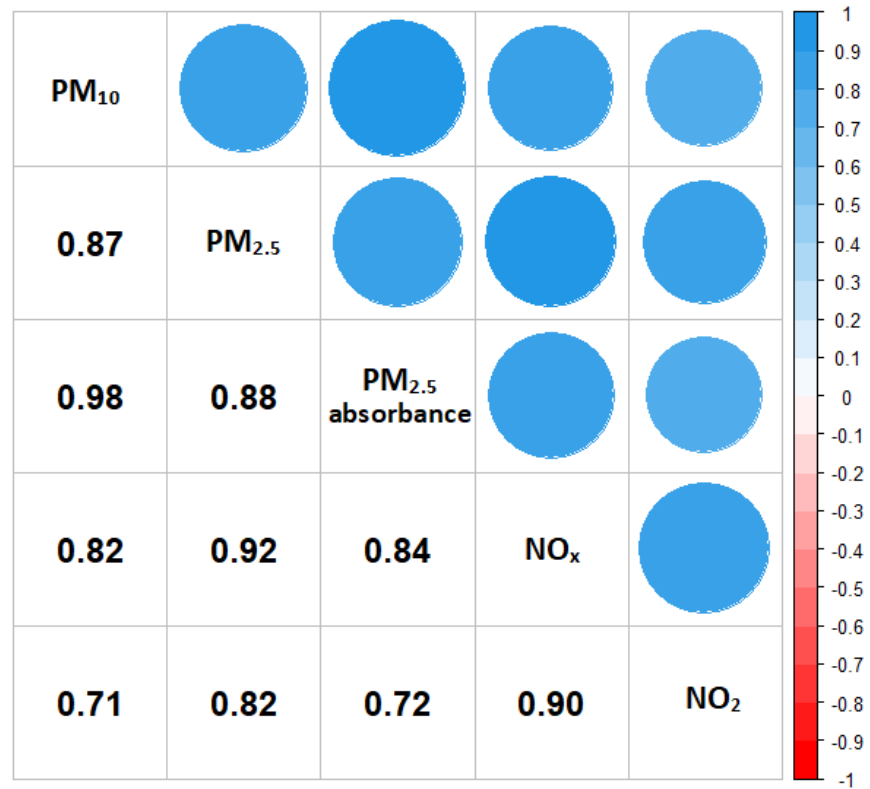


Supplementary Material

Air Pollution and the Risk of Dementia: The Rotterdam Study



Supplementary Figure 1. Spearman's correlation coefficients between the air pollutant concentrations. NO, nitrogen oxide; PM, particulate matter.

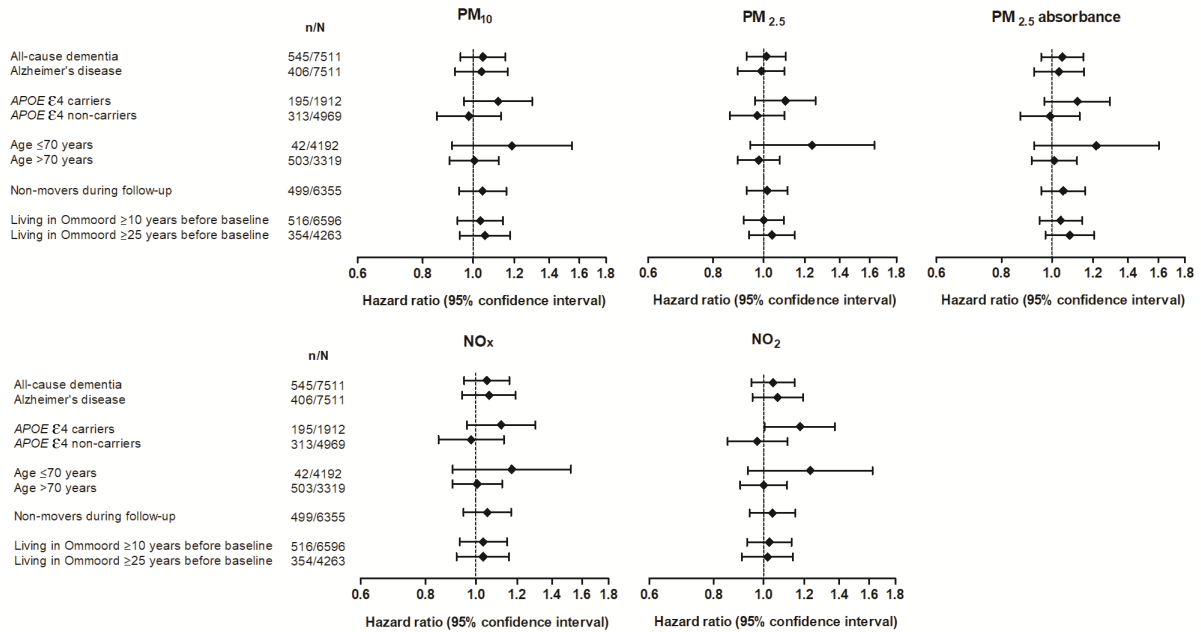
Supplementary Table 1. Land use regression (LUR) models used to determine air pollutant concentrations in the district of Ommoord, the Netherlands.

Pollutant	LUR models
Particulate matter with an aerodynamic diameter of 2.5 μm (PM _{2.5})	9.46 + 0.42*(a regional background concentration estimate ($\mu\text{g}/\text{m}^3$)) + 0.01*(road length (m) of major roads within a buffer of 50 meter) + 2.28*10 ⁻⁹ *(total traffic load (vehicles·day ⁻¹ ·m) or major roads within a buffer of 1000 meters (sum of (traffic intensity*length of all segments)))
Particulate matter with an aerodynamic diameter of 2.5 μm absorbance (PM _{2.5} absorbance)	0.07 + 2.95*10 ⁻⁹ *(total traffic load (vehicles·day ⁻¹ ·m) of all roads within a buffer of 500 meters (sum of (traffic intensity*length of all segments))) + 2.93*10 ⁻³ *(road length of major roads within a buffer of 50 meters) + 0.85*(a regional background concentration estimate (10 ⁻⁵ /m)) + 7.90*10 ⁻⁹ *(surface are (m ²) of all residential land within a buffer of 5000 meters) + 1.72*10 ⁻⁶ *(total heavy-duty traffic load (vehicles·day ⁻¹ ·m) within a buffer of 50 meters (sum of (traffic intensity*length of all roads segments)))
Particulate matter with an aerodynamic diameter of 10 μm (PM ₁₀)	23.71 + 2.16*10 ⁻⁸ *(total traffic load (vehicles·day ⁻¹ ·m) of major roads within a buffer of 500 meters (sum of (traffic intensity* length of all segments))) + 6.68*10 ⁻⁶ *(population (N) within a buffer of 5000 meters) + 0.02*(road length (m) of major roads within a buffer of 50 meters)
Nitrogen dioxide (NO ₂)	-7.80 + 1.18*(a regional background concentration estimates ($\mu\text{g}/\text{m}^3$)) + 2.30*10 ⁻⁵ *(population (N) within a buffer of 5000 meters) + 2.46*10 ⁻⁶ *(total traffic load (vehicles·day ⁻¹ ·m) of all roads within a buffer of 50 meters (sum of (traffic intensity*length of all segments))) + 1.06*10 ⁻⁴ *(road length (m) of all roads within a buffer of 1000 meters) + 9.84*10 ⁻⁵ *(total heavy-duty traffic load (vehicles·day ⁻¹ ·m) of all roads in a buffer of 25 meters (sum of (heavy-duty traffic intensity*length of all segments))) + 12.19*(inverse distance (m ⁻¹) to the nearest road of the central road network) + 4.47*10 ⁻⁷ *(total heavy-duty traffic load (vehicles·day ⁻¹ ·m) of all roads within a buffer between 25 and 500 meters (sum of (heavy-duty traffic intensity*length of all segments)))
Nitrogen oxides (NO _x)	3.25 + 0.74*(a regional background concentration estimate ($\mu\text{g}/\text{m}^3$)) + 4.22*10 ⁻⁶ *(total traffic load of all roads within a buffer of 50 meters (sum of (traffic intensity*length of all segments))) + 6.36*10 ⁻⁴ *(population (N) within a buffer of 1000 meters) + 2.39*10 ⁻⁶ *(total heavy-duty traffic load of all roads within a buffer of 500 meters (sum of (heavy-duty traffic intensity*length of all segments))) + 71.65*(inverse distance (m ⁻¹) to the nearest major road) + 0.21*(road length of major roads in a buffer of 25 meters)

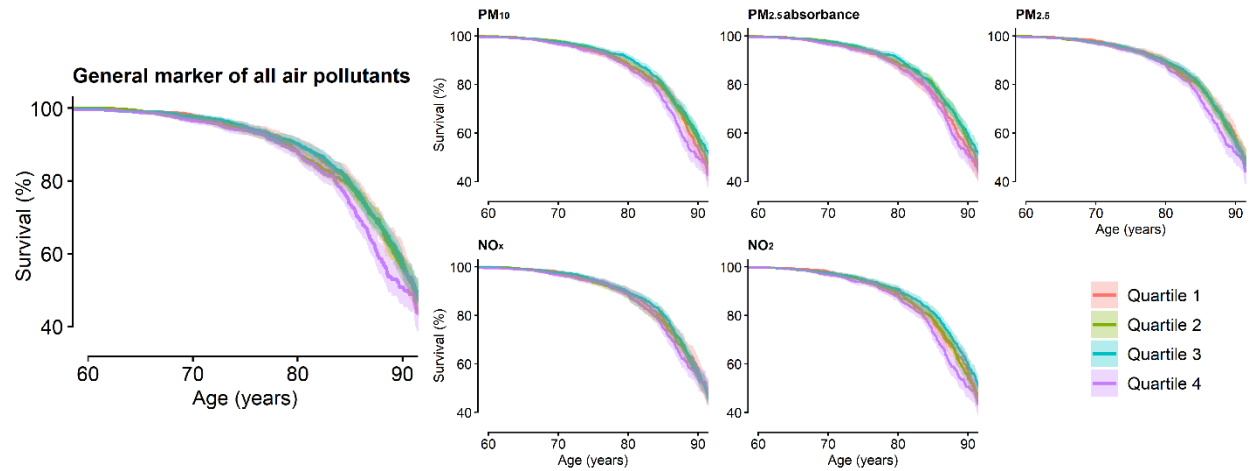
Supplementary Table 2. Factor loadings for each air pollutant to determine a general marker of all air pollutants.

	Loadings per air pollutant
PM₁₀	0.97
PM_{2.5}	0.83
PM_{2.5} Absorbance	0.97
NO_x	0.96
NO₂	0.90

The general marker and factor loadings were obtained from the first unrotated component of a principle component analysis. NO, nitrogen oxide; PM, particulate matter.



Supplementary Figure 2. Subgroup and sensitivity analyses for the association of exposure to PM₁₀, PM_{2.5}, PM_{2.5} absorbance, NO_x and NO₂ with the risk of dementia. Effect estimates are shown per standard deviation increase (1.02 for PM₁₀, 0.4 for PM_{2.5}, 0.145 for PM_{2.5} absorbance, 12.18 for NO_x, and 3.38 for NO₂) and adjusted for age, sex, level of education, smoking status, monthly household income, alcohol intake, physical activity, hours from home, body mass index, and depressive symptoms. n, number of participants with incident dementia; N, total number of participants; APOE, Apolipoprotein E; NO, nitrogen oxide; PM, particulate matter.



Supplementary Figure 3. Kaplan-Meier survival curves per quartile of the general marker of all air pollutants with advancing age. NO, nitrogen oxide; PM, particulate matter.

Supplementary Table 3. Characteristics of total study population and for the subsample with data on cognitive performance.

	Total study sample (n=7,511)	Subsample with data on cognitive performance	
		Total (n=5,969)	With reexamination (n=2,268)
Age, y	68.7 (10.9)	67.8 (10.4)	74.1 (6.0)
Female sex	4,401 (58.6)	3,466 (58.1)	1,343 (59.2)
Level of education			
Primary	745 (10.0)	505 (8.5)	153 (6.9)
Lower	3007 (40.4)	2,336 (39.5)	960 (42.1)
Intermediate	2176 (29.3)	1,790 (30.3)	716 (32.2)
Higher	1510 (20.3)	1,277 (21.6)	396 (17.8)
Smoking status			
Never	2,390 (31.9)	1,895 (31.8)	762 (33.6)
Former	3,639 (48.6)	2,960 (49.6)	1,252 (55.2)
Current	1,459 (19.5)	1,108 (18.6)	254 (11.2)
Household income, euros/month			
≤1050	506 (7.5)	349 (6.5)	138 (6.9)
1050-1500	881 (13.1)	656 (12.2)	241 (12.0)
1500-2100	1,553 (23.1)	1,216 (22.6)	552 (24.7)
2100-2900	1,838 (27.3)	1,528 (28.3)	611 (20.4)
>2900	1,945 (28.9)	1,643 (30.5)	471 (23.4)
Alcohol intake, grams/day	7.8 (9.3)	7.6 (8.5)	6.9 (8.0)
Physical activity, MET h/week)	55.8 (56.5)	56.0 (56.5)	56.6 (57.7)
Hours from home per week	15.3 (25.5)	15.5 (26.1)	8.0 (7.7)
Body mass index, kg/m ²	27.7 (4.4)	27.6 (4.4)	27.7 (4.2)
CES-D, score	6.6 (7.4)	5.7 (7.1)	5.7 (6.9)
<i>APOE</i> ε4 carrier	1,912 (27.8)	1,618 (28.4)	546 (25.6)
General marker of all air pollutants	0.0 (1.0)	0.0 (1.0)	0.1 (1.0)
PM ₁₀	26.1 (1.0)	26.1 (1.0)	26.1 (1.0)
PM _{2.5}	16.7 (0.4)	16.7 (0.4)	16.8 (0.4)
PM _{2.5} absorbance	1.5 (0.1)	1.5 (0.1)	1.5 (0.1)
NO _x	46.1 (12.2)	46.2 (12.5)	47.0 (12.6)
NO ₂	32.6 (3.4)	32.6 (3.5)	32.9 (3.4)
Dementia cases	545 (7.3)	360 (6.0)	134 (5.9)

Data are shown for non-imputed data and are either presented as frequency (%) or mean (standard deviation). *APOE*, Apolipoprotein; CES-D, Center for Epidemiologic Studies Depression Scale; MET h, Metabolic Equivalent of Task hours; PM, particulate matter; NO, nitrogen oxide; n, number of participants.

Supplementary Table 4. Association of exposure to PM₁₀, PM_{2.5}, PM_{2.5} absorbance, NO_x and NO₂ with cognitive test scores, main effect of linear mixed models.

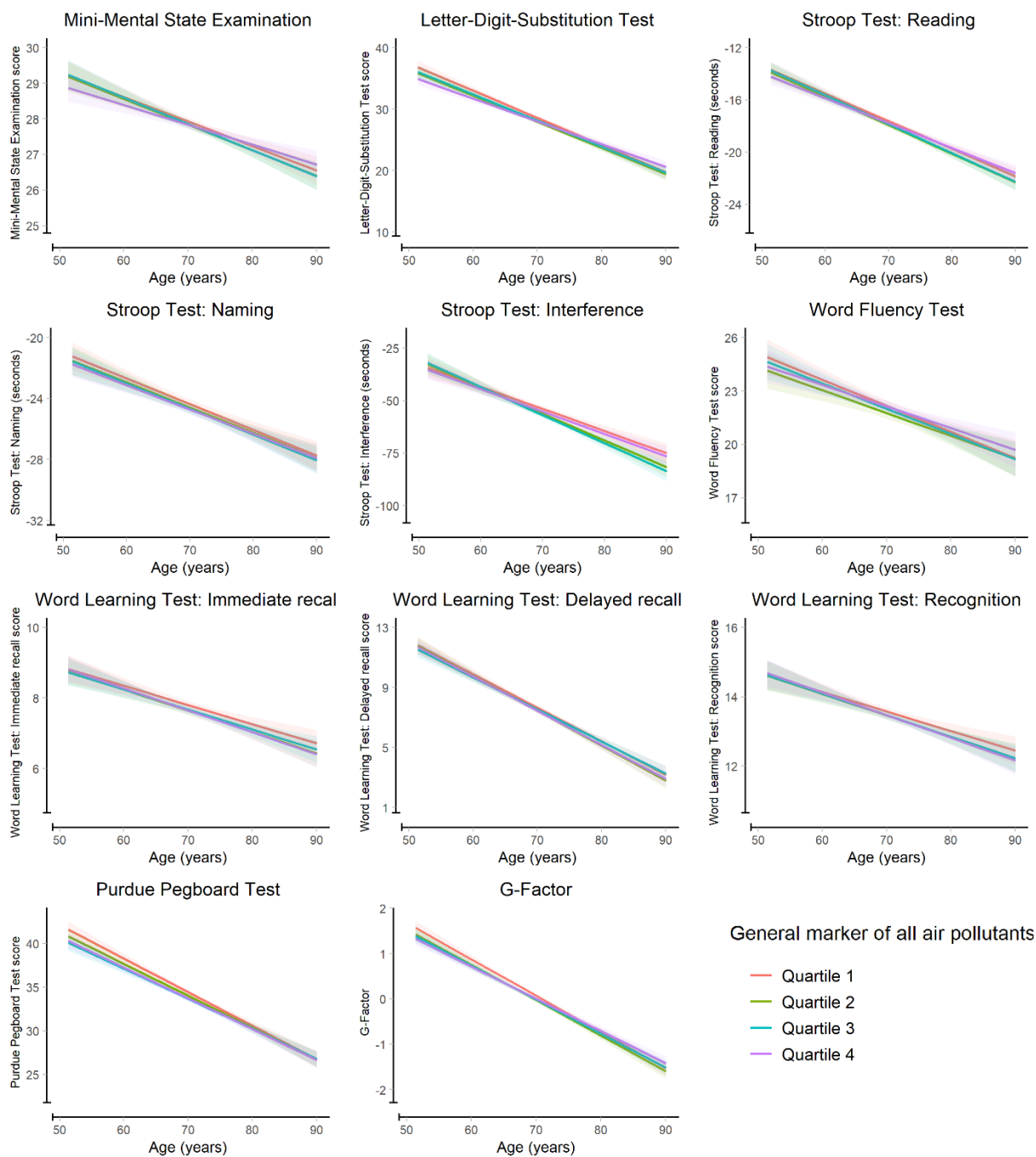
Cognitive test scores	Mean difference (95% confidence interval)					
	General marker of all air pollutants	PM ₁₀	PM _{2.5}	PM _{2.5} absorbance	NO _x	NO ₂
Mini-Mental State Examination	-0.02 (-0.07;0.03)	-0.02 (-0.07;0.03)	-0.02 (-0.07;0.03)	-0.02 (-0.07;0.02)	-0.02 (-0.06;0.03)	-0.02 (-0.07;0.03)
Letter-digit substitution test	-0.14 (-0.29;0.01)	-0.14 (-0.30;0.01)	-0.13 (-0.29;0.03)	-0.18 (-0.33;-0.02)	-0.08 (-0.23;0.07)	-0.13 (-0.28;0.02)
Stroop test: Reading	0.03 (-0.05;0.12)	0.05 (-0.04;0.13)	0.01 (-0.08;0.10)	0.03 (-0.06;0.11)	0.05 (-0.04;0.13)	0.03 (-0.06;0.11)
Stroop test: Naming	-0.03 (-0.16;0.11)	-0.01 (-0.15;0.12)	-0.05 (-0.19;0.09)	-0.05 (-0.18;0.09)	-0.01 (-0.15;0.12)	-0.02 (-0.15;0.11)
Stroop test: interference	0.23 (-0.39;0.84)	0.40 (-0.21;1.02)	-0.07 (-0.71;0.57)	0.21 (-0.41;0.84)	0.27 (-0.34;0.88)	0.19 (-0.42;0.80)
Word Fluency test	0.00 (-0.13;0.14)	0.03 (-0.10;0.17)	-0.07 (-0.22;0.07)	0.00 (-0.14;0.14)	0.03 (-0.11;0.16)	0.01 (-0.13;0.14)
Word learning test: Immediate recall	-0.05 (-0.10;0.00)	-0.05 (-0.10;0.00)	-0.06 (-0.11;0.00)	-0.05 (-0.10;0.00)	-0.04 (-0.09;0.01)	-0.06 (-0.10;-0.01)
Word Learning test: Delayed recall	-0.03 (-0.10;0.04)	-0.02 (-0.10;0.05)	-0.03 (-0.10;0.05)	-0.03 (-0.10;0.04)	-0.02 (-0.09;0.05)	-0.04 (-0.11;0.03)
Word Learning test: Recognition	-0.02 (-0.07;0.03)	-0.02 (-0.07;0.03)	-0.04 (-0.10;0.01)	-0.02 (-0.07;0.03)	-0.01 (-0.06;0.04)	-0.01 (-0.06;0.04)
Purdue Pegboard test	-0.19 (-0.30;-0.07)	-0.16 (-0.27;-0.04)	-0.17 (-0.29;-0.05)	-0.20 (-0.31;-0.08)	-0.17 (-0.28;-0.06)	-0.19 (-0.30;-0.07)
G-factor	-0.01 (-0.03;0.01)	-0.01 (-0.03;0.01)	-0.01 (-0.04;0.01)	-0.01 (-0.04;0.01)	-0.01 (-0.03;0.02)	-0.02 (-0.04;0.00)

Effect estimates are presented per standard deviation increase (1.02 for PM₁₀, 0.4 for PM_{2.5}, 0.145 for PM_{2.5} absorbance, 12.18 for NO_x, and 3.38 for NO₂) and adjusted for age, sex, level of education, smoking status, monthly household income, alcohol intake, physical activity, hours from home, body mass index, and depressive symptoms. Stroop scores are inversely transformed, meaning that higher scores for all cognitive tests indicate better cognitive performance. NO, nitrogen oxide; PM, particulate matter.

Supplementary Table 5. Association of exposure to PM₁₀, PM_{2.5}, PM_{2.5} absorbance, NO_x and NO₂ with cognitive decline, slope of linear mixed models.

Cognitive test scores	Mean difference (95% confidence interval)					
	General marker of all air pollutants	PM ₁₀	PM _{2.5}	PM _{2.5} absorbance	NO _x	NO ₂
Mini-Mental State Examination	0.01 (-0.01;0.03)	0.01 (-0.01;0.03)	0.01 (-0.01;0.03)	0.01 (-0.01;0.03)	0.01 (-0.01;0.03)	0.01 (-0.01;0.03)
Letter-digit substitution test	0.03 (-0.01;0.08)	0.04 (0.00;0.08)	0.01 (-0.04;0.05)	0.04 (0.00;0.08)	0.04 (-0.01;0.08)	0.04 (-0.01;0.08)
Stroop test: Reading	0.02 (-0.01;0.04)	0.01 (-0.01;0.04)	0.01 (-0.01;0.04)	0.02 (-0.01;0.04)	0.01 (-0.01;0.04)	0.02 (-0.01;0.04)
Stroop test: Naming	0.00 (-0.04;0.04)	0.00 (-0.03;0.04)	0.01 (-0.03;0.05)	0.00 (-0.03;0.04)	0.00 (-0.04;0.03)	0.00 (-0.04;0.03)
Stroop test: interference	-0.01 (-0.20;0.19)	0.01 (-0.19;0.20)	-0.04 (-0.25;0.16)	0.01 (-0.18;0.21)	0.00 (-0.20;0.19)	-0.01 (-0.21;0.19)
Word Fluency test	0.01 (-0.03;0.05)	0.01 (-0.03;0.05)	0.01 (-0.03;0.05)	0.01 (-0.03;0.06)	0.01 (-0.03;0.05)	0.00 (-0.04;0.04)
Word learning test: Immediate recall	0.02 (0.00;0.03)	0.02 (0.00;0.03)	0.01 (-0.01;0.03)	0.01 (0.00;0.03)	0.02 (0.00;0.04)	0.02 (0.01;0.04)
Word Learning test: Delayed recall	0.02 (0.00;0.04)	0.02 (0.00;0.04)	0.02 (0.00;0.04)	0.02 (0.00;0.04)	0.02 (0.00;0.04)	0.02 (0.00;0.04)
Word Learning test: Recognition	0.00 (-0.02;0.02)	0.00 (-0.02;0.02)	0.01 (-0.01;0.03)	0.00 (-0.02;0.02)	0.00 (-0.02;0.02)	0.00 (-0.02;0.02)
Purdue Pegboard test	0.01 (-0.03;0.05)	0.01 (-0.03;0.05)	0.01 (-0.03;0.05)	0.01 (-0.02;0.05)	0.01 (-0.03;0.05)	-0.01 (-0.05;0.03)
G-factor	0.01 (0.01;0.02)	0.01 (0.00;0.02)	0.01 (0.00;0.02)	0.01 (0.01;0.02)	0.01 (0.00;0.02)	0.01 (0.01;0.02)

Effect estimates are presented per standard deviation increase (1.02 for PM₁₀, 0.4 for PM_{2.5}, 0.145 for PM_{2.5} absorbance, 12.18 for NO_x, and 3.38 for NO₂) and adjusted for age, sex, level of education, smoking status, monthly household income, alcohol intake, physical activity, hours from home, body mass index, and depressive symptoms. Stroop scores are inversely transformed, meaning that higher scores for all cognitive tests indicate better cognitive performance. NO, nitrogen oxide; PM, particulate matter.



Supplementary Figure 4. Cognitive performance per quartile of the general marker of all air pollutants with advancing age. Models are adjusted for date of birth, sex, level of education, smoking status, monthly household income, alcohol intake, physical activity, hours from home, body mass index, and depressive symptoms. Stroop scores are inversely transformed, meaning that higher scores for all cognitive tests indicate better cognitive performance.