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Supplementary appendix

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Supplementary Material

Canning et al. Associations between life course exposure to ambient air pollution with cognition and later-life brain structure: a population-based study of the 1946 British Birth Cohort

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Supplementary Methods: Full covariate description and additional methodology

Sample

In one week of March 1946, 13,687 babies across England, Wales and Scotland were interviewed. This was approximately 91% of all births that week and thus close to a population level sample of births at that time. Two years later, 5,362 mothers and babies from the original sample were followed up. It was not possible to follow the full sample due to funding constraints at that time. This subsample was selected to contain roughly the same number of children from each social class. This was achieved by including all those babies whose fathers worked in a non-manual or an agricultural occupation, and a random selection of one-in-four children whose fathers were employed in manual occupations. They excluded the 672 children born to unmarried mothers, as it was assumed that they would be adopted at birth and would be too difficult to trace. They also excluded 180 multiple births, as they were thought to be too small of a sample size for separate analyses. Full details are provided here: https://archives.ucl.ac.uk/CalmView/record/catalog/NSHD.

Participation has varied over the waves. At age 69, the last major follow up, 2816 were targeted as an analytical sample. Of the remaining 2546 (47%) study members: 957 (18%) had already died, 620 (12%) had previously withdrawn permanently, 574 (11%) lived abroad, and 395 (7%) had remained untraceable for more than 5 years. In total, 2148 participants completed a home visit.[1] Both lifetime and recent contact with the study (at age 69) was associated with being in a non-manual occupational class, and having higher educational qualifications and childhood cognitive ability. At age 53, the sample generally remained representative of census level data. Further detail on participation is available at across a range of cohort profiles.[1–6]

Exposure Modelling

The estimates included in the study reflect exposure levels of the key sources at the time of measurement (e.g. black smoke and SO_2 when coal combustion was a major source, since superseded by monitoring of particulates and NO_2 that capture traffic pollution). Due to data availability of pollutant exposure, annualised mean exposures were assigned to the participants' residential address at the closest wave of data collection and included at that wave, as exposure between years is highly related (e.g. for residential address at the wave of data collection at age 43 we assigned pollutants that were modelled at age 45).

NO_2 was modelled at ages 45, 55 and 64 through three land-use regression models (a Britain-specific contemporary model,[7] Ruimte voor Geoinformatie [RGI],[8] and European Study of Cohorts for Air Pollution

Effects [ESCAPE] models[9]). PM_{10} was modelled at ages 55 and 64 through RGI and ESCAPE models.[8,10] Further ESCAPE pollutants included NO_x, $PM_{2 \cdot 5}$, PM_{coarse} and $PM_{2 \cdot 5}$abs, which were modelled at age 64.[9]

Due to the unavailability of measures for contemporary pollutants for the whole life course, we included three further measures as markers of exposure prior to age 43 and adjusted for these in the analyses.

Prior air pollution exposure

The Douglas-Waller index classified coal consumption in participants' county borough (regions defined by a population limit of 75,000), and was reported as "Low", "Medium" or "High".[11]

The Chronic Health Effects of Smoke and SO_2 (CHESS) land-use regression models were used to estimate mean black smoke (BS – a measure of particulates in the air) and sulphur dioxide (SO_2) exposure at ages 16, 25, 36 and 45, which was included as a mean of all four time-points.[12] Land use regression models were developed using land cover, road network, population and combined with altitude, coordinates and buffers around air pollution measurement sites. Model verification took place with an independent set of monitoring sites, with a slight underprediction (fractional bias: 0∼-0.1) for all years. Data was from the national air quality archive from 1962, 1971, 1981, 1991 which aligned with census years in the UK. Measurement of BS and SO_2 was completed the same across all measurement years. Model performance varied by year (R^2 range 0.31-0.56 for BS, SO_2 0.26 – 0.71), and was maintained in a leave-one-out validation analysis.

NO_2 in 1991

NO_2 exposure in 1991[7] was firstly back extrapolated from two land use regression models from 2001 and 2009 that was then evaluated against a national NO_2 diffusion tube network sample from 1991. Land use regression models for 2001 and 2009 were constructed using land cover, road network, site coordinates and altitude. Back-extrapolation of the 2009 models to 1991 yielded R^2, MSE-R^2, and beta between 0.53−0.55, 0.52− 0.55, and 0.90−0.98, respectively, depending on the model formulation.

RGI (NO_2 and PM_{10} in 2001)

Models for NO_2 and PM_{10} were constructed using 2001 annual mean concentrations from air quality networks, using land use regression models constructed with traffic, population, land use and topography data.[8] Measurements from 156 monitoring stations (NO_2) and 93 for PM_{10} were used to generate great Britain specific models. R2 validation was good for NO_2 (0.62), but poorer for PM_{10} (0.37).

ESCAPE (NO_2, NO_x, PM_{10}, $PM_{2.5}$, PM_{coarse} and $PM_{2.5}$abs)

ESCAPE variables were modelled from monitoring campaigns between 2010-2011 in London, with models developed using a standardised approach across Europe. Land use regression models for London were created using traffic, road and density information for NO_2 and traffic and road distance for particulate matter.[9,10] Due to the poorer performance of particulate matter models 400km from the monitoring area (London and Thames corridor west of London) when evaluated against national network monitoring sites), some addresses were not assigned a PM exposure for age 60-64. R^2 validation was good (R2 = 0.56-0.92 for particulate matter and NO_2/NO_x).

Addenbrooke's cognitive examination III (ACE-III)

Cognitive state at age 69 was assessed using the Addenbrooke's cognitive examination III (ACE-III).[13] The ACE-III is validated for assessing cognitive functioning and screening for cognitive impairment and dementia and has a quasi-normal distribution.[13] Of the 2,148 participants who had a home visit at age 69, over 300 records of ACE-III were incomplete or lost due to an equipment failure, detailed elsewhere.[14]

Covariates

Educational Attainment

Educational achievement was assessed up to age 26 via the Burnham classification codes, and reclassified as "No qualification", "up to 'O' Level" or "A level and above".

Social Class

Father's social class at age 4 and participant's social class at age 43 and/or 53 were defined by a condensed version of the UK Registrar General's social class scheme, which bases social class on specific job standings ("Professional" and "Intermediate", "Skilled (non-manual)", "Skilled (manual)", and "Partly skilled" or "Unskilled").[15]

Childhood externalising and internalising mental health

This was assessed by a teacher-rated survey in childhood at ages 13-15 through a precursor to the Rutter B2 teacher questionnaire[16] with total scores split into "Absent", "Mild", and "Severe" for internalising and externalising components, as previously described.[17]

Childhood cognition at age 15

The Heim Group Ability Test AH4, a 130-item test requiring shape matching and selection, and verbal and number problems, yielding scores for verbal intelligence and non-verbal Intelligence[18] and the Watts-Vernon Reading Test, a 35-item test of reading comprehension requiring the participant to select an appropriate word to complete a sentence,[19] were completed by participants at age 15. A 47-item mathematics test completed at age 15, requiring the use of arithmetic, geometry, trigonometry and algebra was also included. The sum of these three scores was summarised into a z score for the whole NSHD sample, with higher scores indicating better cognition compared to the mean.[20,21]

Neighbourhood deprivation

Neighbourhood deprivation was measured as the proportion of population in participants' local authority who were employed in semi-skilled or unskilled occupations, as previously defined.[22] Neighbourhood deprivation was assessed at age 53 or 60 as a confounder of both pollution exposure and cognitive state.[23]

Multiple Imputation by chained equations

We imputed missing covariate data for three different groups of participants in the cohort due to differing missingness and different participant pool under the missing at random assumption.[24] First, for participants with complete data for verbal memory and processing speed at age 43, 53, 60-64 and 69. Second, for participants with an ACE-III total or fluency score at age 69. Third, for participants with a full data for neuroimaging outcomes. We did not impute air pollution exposure data, aside from our air pollutants which were included as covariates instead of exposures of interest. We performed multiple imputation with chained equations *"mi impute chained"* in Stata 18.0 MP. Imputed variables included father's social class, adult social class, air pollution (coal index, SO_2 and BS), internalising and externalising symptoms at age 13-15, cognition at age 15, neighbourhood deprivation, educational attainment, and lifetime smoking pack years. Complete variables were included in the imputation (assigned sex at birth and cognition outcomes). Missingness is described in Supplementary eTable 1. We imputed 25 datasets. For verbal memory and processing speed, imputation resulted in a sample size of 1298-1534, depending on pollutant. Complete case analysis was N=769-941 Imputation resulted in a sample size of N=1483-1749 for ACE-III analyses, compared to 788-990 complete case analysis for fully adjusted models, with covariates missing between 10 and 359 records. For neuroimaging, fully adjusted models had an imputed N of 391-453. Complete case size was 248-288, with missing covariates ranging from 2 to 102.

	Verbal Memory and Processing speed sample (N=1534) N (%)	ACE-III sample (N=1761) N (%)	Insight 46 sub-cohort (N=453) N (%)
Father's social class at age 4	107 (7.0)	138 (7.8)	16 (3.5)
Social Class at age 43	67 (4.4)	170 (9.7)	26 (5.7)
Social Class at age 53	56 (3.7)	164 (9.3)	14 (3.1)
Highest education attained by age 26	71 (4.6)	86 (4.9)	13 (2.9)
Exposure to air pollution at birth	167 (10.9)	200 (11.4)	38 (8.4)
Smoking – pack/years up to age 63	283 (18.5)	359 (20.4)	102 (22.5)
Neighbourhood deprivation – age 53	8 (0.5)	35 (2.00)	6 (1.3)
Neighbourhood deprivation – age 60	10 (0.7)	127 (7.2)	3 (0.7)
Cognition score at age 15	207 (13.5)	244 (13.9)	34 (7.5)
Internalising symptoms at ages 13-15	142 (9.3)	178 (10.1)	20 (4.4)
Externalising symptoms at ages 13-15	142 (9.3)	178 (10.1)	20 (4.4)
Mean SO_2 (age 16 - 45)	0 (0)	10 (0.6)	2 (0.4)
Mean BS (age 16 - 45)	0 (0)	10 (0.6)	2 (0.4)

Supplementary Methods Table 1: Missingness for each covariate in each analytic sample. Missingness for largest exposure sample only (NO_2 exposure), missingness will vary by exposure as inclusion varied by available exposure data.

Statistical Analysis

Participants with dementia at Insight 46 assessment were excluded (N=2).

Sample equations for analysis

Verbal Memory and Processing Speed

For longitudinal multilevel models between NO_2 and PM_{10} and verbal memory and processing speed, the full model can be seen in equation (1) where y_{ij} represents the outcome variable individual i at time j with random intercept μ_i and residual error ε_{ij}. Time-varying covariates are included at time (t_j) for individual (i), while time-invariant are specified for individual i. β_2- β_{13} represent fixed effects. The parameter of interest is $\beta_1$which is rescaled by the IQR in the model and so changes in outcome y_{ij} was reported as a β and 95% confidence intervals, representing a mean change per IQR increase in exposure. We treated each annual measure of exposure as a time-point with no lag with its corresponding verbal memory or processing speed score, with an additional time-point at age 69 for the cognitive outcomes.

$$(1)\quad y_{ij} = \beta_0 + \beta_1 pollutant_{it_j} + \beta_2 sex_i + \beta_3 father's\ social\ class_i + \beta_4 coal\ index\ at\ birth_i + \beta_5 black\ smoke_i + \beta_6 Sulphur\ Dioxide_i + \beta_7 childhood\ internalising\ problems_i + \beta_8 childhood\ externalising\ problems_i + \beta_9 childhood\ cognition_i + \beta_{10} education_i + \beta_{11} pack-years\ smoking_i + \beta_{12} adult\ social\ class_{it_j} + \beta_{13} neighbourhood\ deprivation_{it_j} + \varepsilon_{ij} + u_j$$

For associations between NO_x, $PM_{2.5}$, PM_{coarse} and $PM_{2.5}abs$ and verbal memory and processing speed, linear regression models used the following equation (2). The parameter of interest is β_1, which is rescaled by the IQR in the model and so changes in outcome y_i was reported as a β and 95% confidence intervals, representing a mean change per IQR increase in exposure:

(2) $y_i = \beta_0 + \beta_1 pollutant_i + \beta_2 sex_i + \beta_3 father's\ social\ class_i + \beta_4 coal\ index\ at\ birth_i + \beta_5 black\ smoke_i + \beta_6 Sulphur\ Dioxide_i + \beta_7 childhood\ internalising\ problems_i + \beta_8 childhood\ externalising\ problems_i + \beta_9 childhood\ cognition_i + \beta_{10} education_i + \beta_{11} pack - years\ smoking_i + \beta_{12} adult\ social\ class_i + \beta_{13} neighbourhood\ deprivation_i + \varepsilon_i$

ACE-III

As these were simple linear regressions, associations for all ACE-III outcomes used a similar equation (3). Again, the parameter of interest is β_1, which is rescaled by the IQR in the model and so changes in outcome y_i was reported as a β and 95% confidence intervals, representing a mean change per IQR increase in exposure:

(3) $$\begin{aligned} y_i = \beta_0 + \beta_1 pollutant_i + \beta_2 sex_i + \beta_3 father's\ social\ class_i + \beta_4 coal\ index\ at\ birth_i \\ + \beta_5 black\ smoke_i + \beta_6 Sulphur\ Dioxide_i + \beta_7 childhood\ internalising\ problems_i \\ + \beta_8 childhood\ externalising\ problems_i + \beta_9 childhood\ cognition_i + \beta_{10} education_i \\ + \beta_{11} pack - years\ smoking_i + \beta_{12} adult\ social\ class_i \\ + \beta_{13} neighbourhood\ deprivation_i + \varepsilon_i \end{aligned}$$

Neuroimaging outcomes

Associations for hippocampal volume, brain volume and ventricular volume outcomes used a similar equation (4). As before, the parameter of interest is β_1 which is rescaled by the IQR in the model and so changes in outcome y_i was reported as a β and 95% confidence intervals, representing a mean change per IQR increase in exposure:

$$(4)\ y_i = \beta_0 + \beta_1 pollutant_i + \beta_2 sex_i + \beta_3 father's\ social\ class_i + \beta_4 coal\ index\ at\ birth_i + \beta_5 black\ smoke_i + \beta_6 Sulphur\ Dioxide_i + \beta_7 childhood\ internalising\ problems_i + \beta_8 childhood\ externalising\ problems_i + \beta_9 childhood\ cognition_i + \beta_{10} education_i + \beta_{11} pack - years\ smoking_i + \beta_{12} adult\ social\ class_i + \beta_{13} neighbourhood\ deprivation_i + \beta_{14} age\ at\ scan\ date_i + \beta_{15} total\ intracranial\ volume_i + \varepsilon_i$$

For white matter hyperintensities, the following equation generalised linear model (5) applied:

$$(5)\ \log(E[Y_i]) = \beta_0 + \boldsymbol{\beta_1} pollutant_i + \beta_2 sex_i + \beta_3 father's\ social\ class_i + \beta_4 coal\ index\ at\ birth_i + \beta_5 black\ smoke_i + \beta_6 Sulphur\ Dioxide_i + \beta_7 childhood\ internalising\ problems_i + \beta_8 childhood\ externalising\ problems_i + \beta_9 childhood\ cognition_i + \beta_{10} education_i + \beta_{11} pack - years\ smoking_i + \beta_{12} adult\ social\ class_i + \beta_{13} neighbourhood\ deprivation_i + \beta_{14} age\ at\ scan\ date_i + \beta_{15} total\ intracranial\ volume_i$$

With link: $g(\mu_i) = \log(\mu_i)$ and variance: $y_i \sim Gamma(\mu_i, \theta)$. The exponentiated log($[Y_i]$) is the estimate, with Y_i reported in the paper, such that it represents change in white matter hyperintensities (such as 1.04 = 4% change) per quartile (µg/m^3) increase in air pollutant levels.

Sensitivity Analyses – two pollutant models

In constructing two pollutant models, we assessed collinearity between pollutants, we examined Pearson's correlation coefficients between pollutants at each time-point and assessed multicollinearity using the variance inflation factor (VIF) for all models. We firstly ensured that no co-pollutant model had a VIF of around 10, which would indicate large multicollinearity, and if so, excluded that model if the standard error more than doubled.

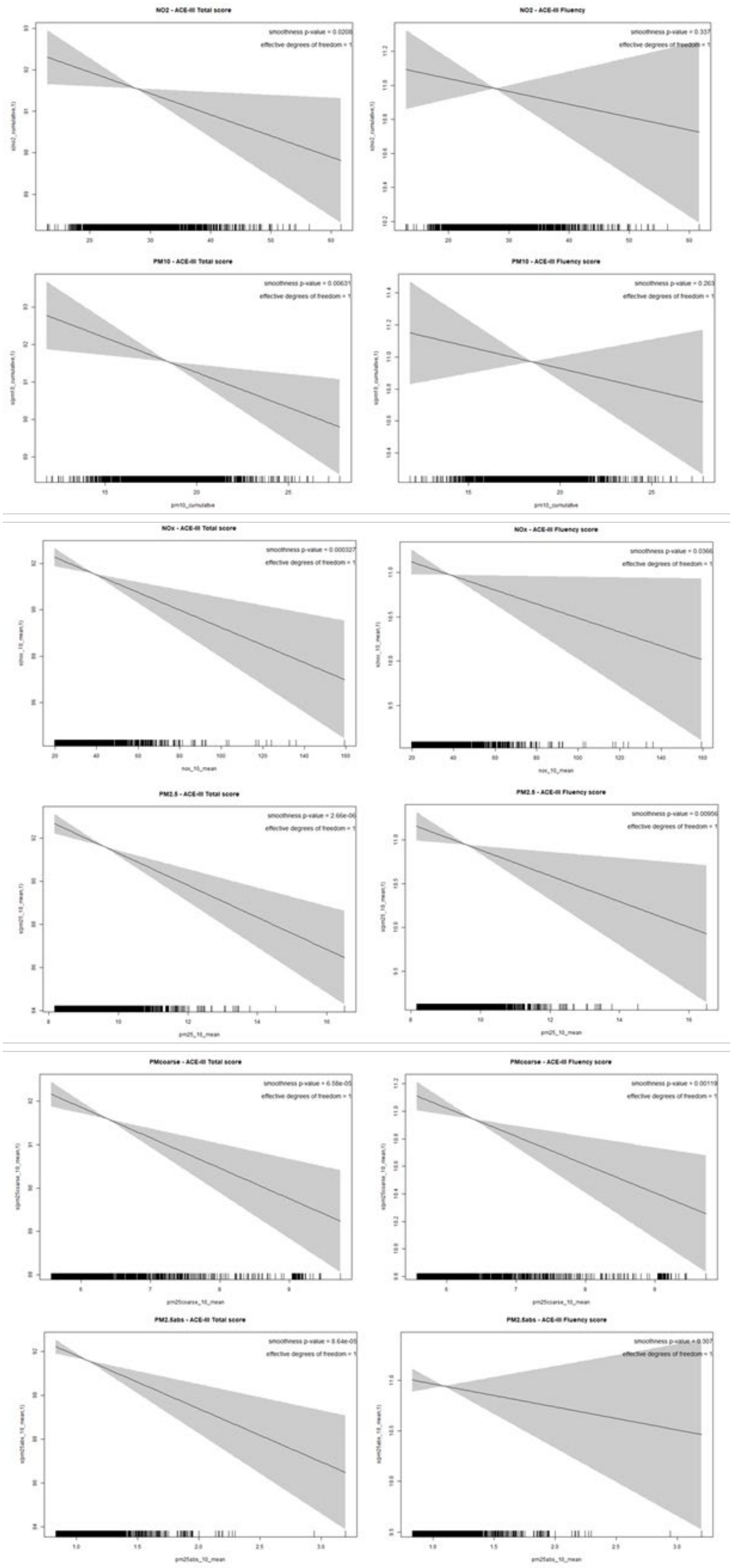
Generalised additive models

To examine non-linear relationships between exposure and outcome we ran generalised additive models, which estimate different distributions of the predictor variable and connect to the dependent variable via a link function.[25] These models were ran in R4.4.1 using mgcv[26] as STATA does not support GAMs. These models make no presumption that exposure-outcome associations are linear. We report the p-value of the smoothness term and effective degrees of freedom alongside visual representation of each of the exposure-outcome associations reported here. For multilevel models (NO_2 and PM_{10} and verbal memory and processing speed), only fixed effects were examined. We made assessments on linearity based on visual inspection, the total degrees of freedom and p-value of smoothness term. If a GAM indicated a non-linear association, we ran nested models with linear and smoothed terms and ran likelihood ratio tests to test model fit. We combined this with assessment of AIC to assess the model fit. Three exposure-outcome associations were investigated further. Examining nested models resulted in the following p-values and Akaike information criterion (AIC):

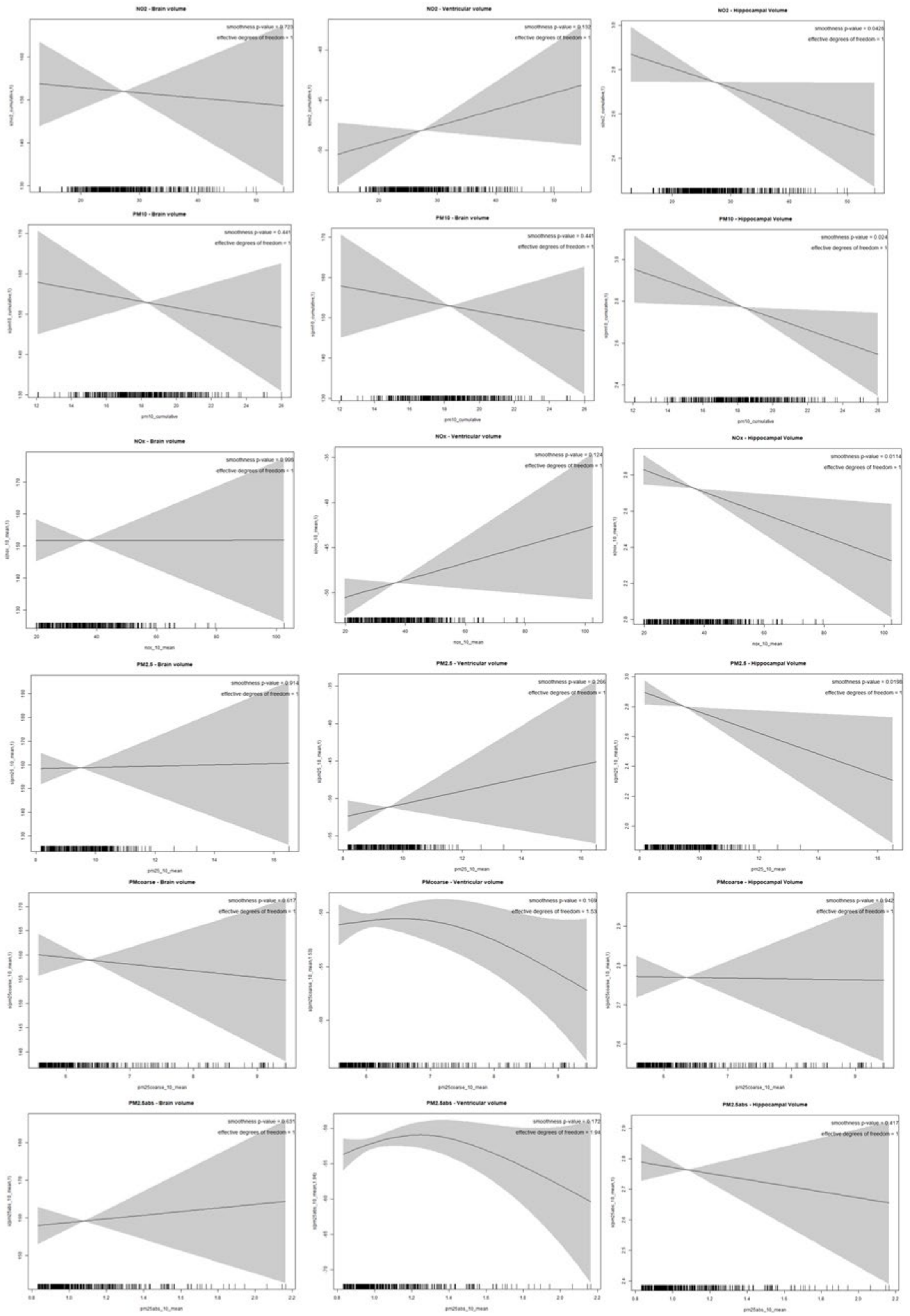
	LRT p-value	AIC
PM_{coarse} – ventricular volume	0.09	3211 (non-linear), 3212 (linear)
$PM_{2.5}$abs – ventricular volume	0.05	3211 (non-linear), 3214 (linear)
NO_2 – Processing speed	0.04*	50356 (non-linear), 50360 (linear)

*Supplementary Methods Table 2: Likelihood ratio tests and Akaike information criterion (AIC). * significant p<0.05.*

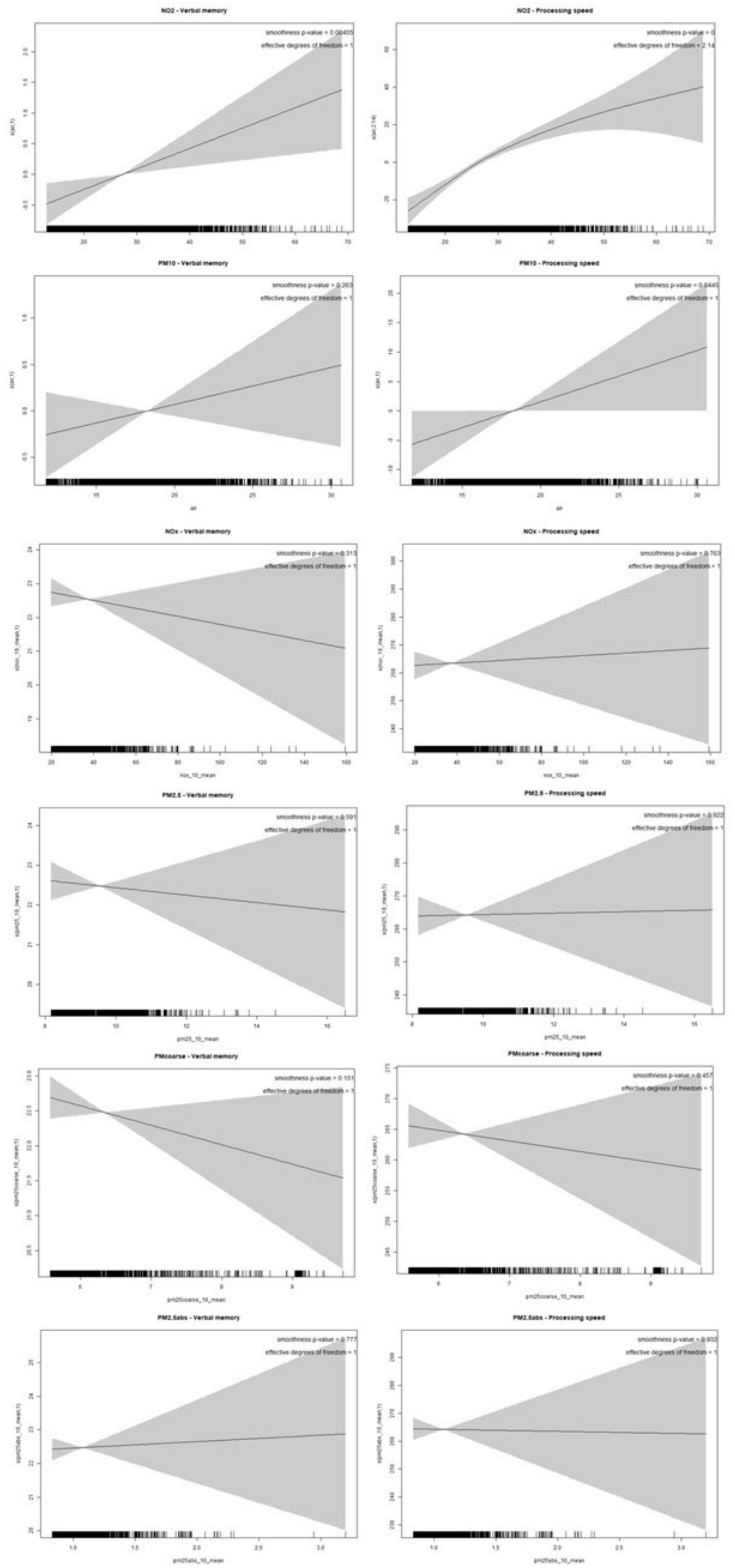
Based on the very similar performance of models and testing, all models were included as noted in the main paper, with linear associations between exposure and outcome, aside from white matter hyperintensities that followed prior methodology as noted in the Methods section.



Supplementary Methods Figure 1: General additive model for pollutants and ACE-III total score and Fluency.



Supplementary Methods Figure 2: General additive model for pollutants and brain volume, ventricular volume and hippocampal volume.



Supplementary Methods Figure 3: General additive model for pollutants and verbal memory and processing speed

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eTable 1: Strengthening the reporting of observational studies in epidemiology (STROBE) checklist

	Item No	Recommendation	Included?
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Birth cohort and population-based study referenced in abstract and title
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Study details in abstract.
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Background and rationale provided in introduction for all hypotheses.
Objectives	3	State specific objectives, including any prespecified hypotheses	Specified hypotheses in final paragraph of introduction.
Methods			
Study design	4	Present key elements of study design early in the paper	Cohort information provided in first paragraph of methods
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Cohort information provided in first paragraph of methods.
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Full reference to cohort papers provided for full detail.

		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	All variables defined in measures section of methods.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	All detail included for each variable, as well as reference for previous use if available.
Bias	9	Describe any efforts to address potential sources of bias	Examination of loss to follow-up explained in statistical analysis section.
Study size	10	Explain how the study size was arrived at	Available participant data broken down in results and methods.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Each main variable has explanation on coding and transformations, with justification for any transformations.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Included in statistical

			analyses section.
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	Multiple imputation with chained equations was used for analyses as outlined in methods.
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A referenced in cohort papers.
		(*e*) Describe any sensitivity analyses	Sensitivity analyses outlined in section "Sensitivity Analyses" in methods
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Reported in results section.
		(b) Give reasons for non-participation at each stage	Provided in cohort papers referenced in methods.
		(c) Consider use of a flow diagram	See Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	See Table 1.

		(b) Indicate number of participants with missing data for each variable of interest	To reference missing data a specific wave would have to be chosen. Full variables available in Table 1 and N included for the wave in which they were collected.
		(c) Summarise follow-up time (eg, mean and total amount)	Each data collection wave has follow-up time as per study design.
Outcome data	15*	Report numbers of outcome events or summary measures over time	Reported ACE-II and brain health markers in Table 1.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Models outlined in methods section. Multiple tables provided for all results.
		(*b*) Report category boundaries when continuous variables were categorized	NA
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA – reference to total score compared to coefficient seen in models.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Sensitivity analyses reported on in

			text and in Supplementary tables.
Discussion			
Key results	18	Summarise key results with reference to study objectives	Results outlined in terms of hypotheses in paragraph 1.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Limitations outlined in limitations section.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Results contextualised in existing evidence base.
Generalisability	21	Discuss the generalisability (external validity) of the study results	Reference to other studies, limitations and strengths of this study.
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Included after discussion.

eTable 2: Model performance for air pollution exposure models.

Year and Model	Air Pollution Variables	Model validation (r^2)	RMSE ($\mu g/m^3$)	Resolution
Black Smoke and SO_2 CHESS				
Age 16 (1962)	SO_2	0·71	44.8	1000metre x 1000metre
	BS	0·56	57.1	1000metre x 1000metre
Age 25 (1971)	SO_2	0·57	28.4	1000metre x 1000metre
	BS	0·41	28.8	1000metre x 1000metre
Age 36 (1982)	SO_2	0·26	18.9	1000metre x 1000metre
	BS	0·38	8.8	1000metre x 1000metre
Age 45 (1991)	SO_2	0·31	12.4	1000metre x 1000metre
	BS	0·34	5.9	1000metre x 1000metre
Age 45 (1991) Land use regression (NO_2)				
	NO_2	0·55	9.2	200metre x 200metre
Age 55 (2001) RGI				
	PM_{10}	0·37	4.10	100metre x 100metre
	NO_2	0·61	9.26	100metre x 100metre
Ages 60-64 (2010) ESCAPE				
	$PM_{2·5}$	0·71	1.4	100metre x 100metre
	PM_{coarse}	0·56	1.3	100metre x 100metre
	$PM_{2·5}$abs	0·92	0.2	100metre x 100metre
	PM_{10}	0·75	1.5	100metre x 100metre
	NO_x	0·78	16.2	100metre x 100metre
	NO_2	0·75	6.6	100metre x 100metre

SO_2 = Sulphur Dioxide, BS = Black Smoke, NO_2 = Nitrogen Dioxide, NO_x = Nitrogen oxides, PM_{10} = particulate matter 10µm or smaller, $PM_{2·5}$ = particulate matter 2·5µm or smaller, PM_{coarse} = particulate matter of size 2·5µm-10µm, $PM_{2·5}$abs = absorbance as a measure of black carbon absorption fraction, CHESS = Chronic Health Effects of Smoke and SO_2, ESCAPE = European Study of Cohorts for Air Pollution Effects, RGI = Ruimte voor Geoinformatie. RMSE = Root-mean-squared error.

eTable 3: Description of models used in analyses of the association between air pollution, cognition and brain health.

Air pollution exposure	Cognition or brain health outcomes	Covariates	Modelling framework
Objective 1: higher long-term exposure to NO_2, nitrogen oxide (NO_x), and particulate matter ($PM_{2·5}$, particulate matter smaller than 10µm (PM_{10}), particulate matter between 2·5 µm and 10 µm (PM_{coarse}) and particulate matter absorbance as a measure of black carbon absorption fraction ($PM_{2.5}abs$)) in mid-life to older age was associated with poorer processing speed and verbal memory			
NO_2 at ages 43, 53 and 60-64	Verbal memory and processing speed at ages 43, 53, 60-64 and 69	*Fully adjusted for: assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood, neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45*	Random intercept linear regression models between all exposures and outcomes utilising repeated measures in individuals over time
PM_{10} at ages 53 and 60-64	Verbal memory and processing speed at ages 43, 53, 60-64 and 69	*Fully adjusted for: assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood, neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45*	Random intercept linear regression models between all exposures and outcomes utilising repeated measures in individuals over time
NO_x, $PM_{2.5}$, PM_{coarse} and $PM_{2.5}abs$ at ages 60-64	Verbal memory and processing speed at age 69	*Fully adjusted for: assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood, neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45*	Linear regression models with each exposure and each outcome at each time-point independently
Objective 2: higher long-term exposure to NO_2, nitrogen oxide (NO_x), and particulate matter (PM2·5, particulate matter smaller than 10µm (PM_{10}), particulate matter between 2·5 µm and 10 µm (PM_{coarse}) and particulate matter absorbance as a measure of black carbon absorption fraction ($PM_{2·5}abs$)) in mid-life to older age was associated with poorer cognitive state and brain health.			
NO_2 mean exposure across ages 43, 53 and 60-64	Addenbrookes' cognitive examination – III (ACE-III) at age 69	*Fully adjusted for: assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood, neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45*	Linear regression models with each exposure and each outcome at each time-point independently

PM_{10} mean exposure across ages 53 and 60-64	Addenbrookes' cognitive examination – III (ACE-III) at age 69	*Fully adjusted for: assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood, neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45*	Linear regression models with each exposure and each outcome at each time-point independently
NO_x, $PM_{2.5}$, PM_{coarse} and $PM_{2.5}$abs at ages 60-64	Addenbrookes' cognitive examination – III (ACE-III) at age 69	*Fully adjusted for: assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood, neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45*	Linear regression models with each exposure and each outcome at each time-point independently
NO_2 mean exposure across ages 43, 53 and 60-64	Total brain volume, ventricular volume, hippocampal total volume, and white matter hyperintensities.	*Fully adjusted for: assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood, neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45*	Linear regression models with each exposure and each outcome at each time-point independently
PM_{10} mean exposure across ages 53 and 60-64	Total brain volume, ventricular volume, hippocampal total volume, and white matter hyperintensities.	*Fully adjusted for: assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood, neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45*	Linear regression models with each exposure and each outcome at each time-point independently
NO_x, $PM_{2.5}$, PM_{coarse} and $PM_{2.5}$abs at ages 60-64	Total brain volume, ventricular volume, hippocampal total volume, and white matter hyperintensities.	*Fully adjusted for: assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood, neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45*	Linear regression models with each exposure and each outcome at each time-point independently

NO_2 = nitrogen dioxide, PM_{10} = particulate matter 10µm or smaller, NO_x = nitrogen oxide, $PM_{2 \cdot 5}$ = particulate matter 2.5µm or smaller, PM_{coarse} = particulate matter of size 2.5µm-10µm. $PM_{2.5}$abs = absorbance as a measure of black carbon absorption fraction

eTable 4: Correlation coefficients for air pollutants (NO_2, PM_{10}, NO_x, $PM_{2·5}$, PM_{coarse}, $PM_{2·5}$abs, BS and SO_2) at each exposure time-point

	POLLUTANT												
	NO_2 (age 45)	NO_2 (age 55)	NO_2 (ages 60-64)	NO_2 mean exposure (ages 45-64)	PM_{10} (age 55)	PM_{10} (ages 60-64)	PM_{10} mean exposure (ages 55-64)	NO_x (Age 60-64	$PM_{2.5}$ (Age 60-64)	PM_{coarse} (Age 60-64)	$PM_{2·5}$abs (Age 60-64)	BS mean exposure (ages 16-45)	SO_2 mean exposure (ages 16-45)
NO_2 (age 45)	-												
NO_2 (age 55)	0.76	-											
NO_2 (age 60-64)	0.64	0.72	-										
NO_2 mean exposure (ages 45-64)	0.90	0.91	0.87	-									
PM_{10} (age 55)	0.67	0.94	0.65	0.84	-								
PM_{10} (age 60-64)	0.34	0.37	0.54	0.46	0.34	-							
PM_{10} mean exposure (ages 55-64)	0.50	0.77	0.66	0.72	0.80	0.73	-						
NO_x (age 60-64)	0.51	0.57	0.92	0.74	0.52	0.54	0.59	-					
$PM_{2.5}$ (age 60-64)	0.49	0.50	0.85	0.68	0.46	0.59	0.58	0.84	-				
PM_{coarse} (age 60-64)	0.12	0.18	0.18	0.18	0.14	0.76	0.48	0.64	0.58	-			
$PM_{2·5}$abs (age 60-64)	0.57	0.65	0.71	0.71	0.55	0.59	0.65	0.22	0.17	0.39	-		
BS mean exposure (ages 16-45)	0.27	0.16	0.17	0.19	0.11	0.09	0.10	0.14	0.15	0.13	0.05	-	
SO_2 mean exposure (ages 16-45)	0.57	0.44	0.35	0.46	0.37	0.18	0.22	0.26	0.25	0.33	0.11	0.76	-

NO_2 = nitrogen dioxide, PM_{10} = particulate matter 10µm or smaller, NO_x = nitrogen oxide, $PM_{2·5}$ = particulate matter 2·5µm or smaller, PM_{coarse} = particulate matter of size 2·5µm-10µm. $PM_{2·5}$abs = absorbance as a measure of black carbon absorption fraction. BS = Black Smoke. SO_2 = Sulphur Dioxide.

eTable 5: Differences between participants at age 69 with an ACE-III score recorded and those with missing data

Factor	Sample				Statistical test result
	ACE-III included		Missing ACE-III		
	N (%)	Mean/Median (SD/IQR)	N (%)	Mean/Median (SD/IQR)	
Mean NO_2 exposure (age 43 - 60-64) (median)	1745	26.5 (23.2, 31.1)	382	24.8 (21.6, 28.5)	Z=5.642, p < 0.0001
Education at age 26					
No qualification	499 (29.9)		132 (37.1)		$\chi 2$=7.528, p = 0.0232
Up to 'O' level	488 (29.2)		88 (24.7)		
'A' level or above	684 (40.9)		136 (38.2)		
Social class at age 53					
Professional and intermediate	789 (49.5)		161 (45.7)		$\chi 2$=4.627, p = 0.2012
Skilled (non-manual)	391 (24.5)		82 (23.3)		
Skilled (manual)	223 (14.0)		64 (18.2)		
Partly or unskilled	190 (11.9)		45 (12.8)		
Deprivation at age 60 (mean)	1630	15.4 (3.6)	358	15.2 (4.1)	t-test=0.981, p = 0.3266
Childhood cognition at age 15 (mean)	1513	0.2 (0.8)	315	0.06 (0.9)	t-test=2.796, p = 0.0052

NO_2 = Nitrogen Dioxide, $\chi 2$ = chi-square statistic, Addenbrookes' cognitive examination – III = ACE-III

eTable 6: Differences between participants in the Insight 46 sub study and participants who had an ACE-III score at age 69

	Sample				Statistical test result
Factor	Not in Insight-46		Included in Insight-46		
	N (%)	Mean/Median (SD/IQR)	N (%)	Mean/Median (SD/IQR)	
Addenbrooke's Cognitive Examination-III	1340	92 (88-96)	421	94 (91, 97)	Z=-7.133, $p < 0.0001$
Mean NO_2 exposure (ages 43 - 60-64) (median)	1328	26.5 (23.2, 31.3)	421	26.3 (23.0, 30.4)	Z=1.017, p = 0.3091
Education at age 26					
No qualification	436 (34.4)		64 (15.7)		$\chi2$=54.974, $p < 0.0001$
Up to 'O' level	359 (28.3)		130 (31.9)		
'A' level or above	472 (37.3)		214 (52.5)		
Social class at age 53					
Professional and intermediate	528 (44.3)		262 (64.5)		$\chi2$=55.778, $p < 0.0001$
Skilled (non-manual)	307 (25.8)		84 (20.7)		
Skilled (manual)	188 (15.8)		37 (9.1)		
Partly or unskilled	168 (14.1)		23 (5.7)		
Deprivation at age 60 (mean)	1215	15.6 (3.7)	419	14.7 (3.4)	t-test=4.210, $p < 0.0001$
Childhood cognition at age 15 (mean)	1126	0.093 (0.8)	391	0.502 (0.7)	t-test=-8.818, $p < 0.0001$

NO_2 = Nitrogen Dioxide, Addenbrookes' cognitive examination – III = ACE-III, $\chi2$ = chi-square statistics

eTable 7: Differences between participants in the included in ACE-III analysis and in Verbal Memory and Processing Speed analysis

	Sample			
Factor	ACE-III sample		Verbal Memory/ Processing speed Sample	
	N (%)	Mean/Median (SD/IQR)	N (%)	Mean/Median (SD/IQR)
Addenbrooke's Cognitive Examination-III	1761	93 (88-96)	1280	93 (89, 96)
Mean NO_2 exposure (ages 43 - 60-64) (median)	1749	26.5 (23.2, 31.1)	421	26.2 (22.9, 30.5)
Education at age 26	1675		1463	
No qualification	500 (29.9)		408 (27.9)	
Up to 'O' level	489 (29.2)		421 (28.8)	
'A' level or above	686 (41.0)		634 (43.3)	
Social class at age 53	1597		1478	
Professional and intermediate	790 (49.5)		746 (50.5)	
Skilled (non-manual)	391 (24.5)		350 (23.7)	
Skilled (manual)	225 (14.1)		212 (14.3)	
Partly or unskilled	191 (12.0)		170 (11.5)	
Deprivation at age 60 (mean)	1634	15.4 (3.6)	1524	15.3 (3.6)
Childhood cognition at age 15 (mean)	1517	0.20 (0.8)	1327	0.24 (0.8)

NO_2 = Nitrogen Dioxide, Addenbrookes' Cognitive Examination – III = ACE-III

eTable 8: Associations between mean exposure to NO_2 (at ages 45, 55 and 60-64), PM_{10} (at ages 55, 60-64), NO_x, $PM_{2.5}$, PM_{coarse} and $PM_{2.5}abs$ (at ages 60-64) and ACE-III continuous total and fluency sub-scale scores at age 69.

	Pollutant	N	Model 1		Model 2		Model 3		
Ages 45 to 60-64			**β**	**(95% CI)**	**β**	**(95% CI)**	**β**	**(95% CI)**	**VIF**
	NO_2	1749							
	Total score		**-0.405**	**-0.748, -0.062**	**-0.362**	**-0.669, -0.056**	**-0.589**	**-0.921, -0.257**	**1.73**
	Fluency		-0.060	-0.181, 0.062	-0.058	-0.174, 0.058	-0.118	-0.251, 0.014	**1.73**
Ages 55 to 60-64									
	PM_{10}	1731							
	Total score		**-0.480**	**-0.824, -0.136**	**-0.384**	**-0.691, -0.078**	**-0.442**	**-0.737, -0.147**	**1.67**
	Fluency		-0.070	-0.192, 0.052	-0.051	-0.167, 0.065	-0.082	-0.199, 0.035	**1.67**
Ages 60-64									
	NO_x	1607							
	Total score		**-0.609**	**-0.940, -0.277**	**-0.4399**	**-0.696, -0.102**	**-0.465**	**-0.747, -0.177**	**1.67**
	Fluency		**-0.126**	**-0.245, -0.008**	-0.084	-0.197, 0.030	-0.114	-0.229, 0.000	**1.67**
	$PM_{2.5}$	1483							
	Total score		**-0.932**	**-1.317, -0.546**	**-0.514**	**-0.864, -0.165**	**-0.558**	**-0.890, -0.227**	**1.70**
	Fluency		**-0.184**	**-0.324, -0.045**	-0.101	-0.236, 0.034	**-0.137**	**-0.273, -0.002**	**1.70**
	PM_{coarse}	1483							
	Total score		**-0.526**	**-0.783, -0.268**	**-0.411**	**-0.642, -0.181**	**-0.290**	**-0.505, -0.075**	**1.69**
	Fluency		**-0.154**	**-0.246, -0.061**	**-0.126**	**-0.215, -0.037**	**-0.107**	**-0.194, -0.020**	**1.69**
	$PM_{2.5}abs$	1483							
	Total score		**-0.657**	**-0.984, -0.330**	**-0.535**	**-0.832, -0238**	**-0.526**	**-0.818, -0.234**	**1.71**
	Fluency		-0.062	-0.180, 0.057	-0.038	-0.153, 0.077	-0.052	-0.171, 0.068	**1.71**

NO_2 = Nitrogen Dioxide, PM_{10} = particulate matter 10µm or smaller. NO_x = Nitrogen oxide, $PM_{2.5}$ = particulate matter size 2.5µm or smaller, PM_{coarse} = Particulate matter size 2.5µm-10µm. $PM_{2.5}abs$ = absorbance as a measure of black carbon absorption fraction. p-value <0.05 in bold. Model 1 = outcome and exposure. Model 2 = assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood and neighbourhood deprivation in adulthood. Model 3 = Model 2 + cognitive scores at age 15 and air pollution at birth and up to age 45. VIF = mean value for the variance inflation factor for model 3. β and 95% confidence intervals (CI) represent the mean difference in ACE-III score per quartile ($\mu g/m^3$) increase in air pollutant levels.

eTable 9: Associations between mean exposure to NO_2 (at ages 45, 55 and 60-64), PM_{10} (at ages 55, 60-64), NO_x, $PM_{2.5}$, PM_{coarse} and $PM_{2.5}abs$ (at ages 60-64) and neuroimaging outcomes at ages 69-71.

	Pollutant	N	Model 1		Model 2		Model 3		
Ages 45 to 60-64			**β**	**(95% CI)**	**β**	**(95% CI)**	**β**	**(95% CI)**	**VIF**
	NO_2	**453**							
	Brain volume		-0.882	-5.768, 4.003	-0.321	-5.156, 4.514	-1.395	-6.914, 4.124	1.76
	Ventricle volume		1.200	-0.362, 2.763	1.294	-0.290, 2.877	**2.259**	**0.457, 4.061**	1.76
	Hippocampal Volume		**-0.063**	**-0.125, -0.002**	-0.062	-0.124, 0.001	-0.060	-0.131, 0.011	1.76
	WMHV		1.005	0.896, 1.126	1.004	0.895, 1.126	1.023	0.901, 1.163	1.76
Ages 55 to 60-64									
	PM_{10}	**451**							
	Brain volume		-2.148	-7.614, 3.319	-0.502	-5.887, 4.883	-1.688	-7.323, 3.873	1.72
	Ventricle volume		1.158	-0.581, 2.897	1.238	-0.518, 2.994	**1.841**	**0.013, 3.669**	1.72
	Hippocampal Volume		**-0.079**	**-0.148, -0.010**	**-0.071**	**-0.141, -0.001**	-0.070	-0.142, 0.003	1.72
	WMHV		0.997	0.868, 1.145	0.981	0.854, 1.127	0.994	0.862, 1.146	1.72
Ages 60-64									
	NO_x	**414**							
	Brain volume		0.023	-6.412, 6.458	1.591	-4.707, 7.888	0.927	-5.631, 7.486	1.74
	Ventricle volume		1.605	-0.442, 3.651	1.681	-0.389, 3.752	2.141	-0.011, 4.293	1.74
	Hippocampal Volume		**-0.103**	**-0.182, -0.023**	**-0.093**	**-0.174, -0.012**	**-0.088**	**-0.172, -0.004**	1.74
	WMHV		0.939	0.801, 1.100	0.944	0.804, 1.108	0.957	0.811, 1.131	1.74
	$PM_{2.5}$	**391**							
	Brain volume		0.370	-6.220, 6.961	1.355	-5.082, 7.795	0.409	-6.379, 7.198	1.76
	Ventricle volume		1.180	-0.903, 3.264	1.188	-0.914, 3.300	1.621	-0.587, 3.830	1.76
	Hippocampal Volume		-0.096	-0.177, -0.015	-0.089	-0.17, -0.006	-0.085	-0.171, 0.000	1.76
	WMHV		0.967	0.820, 1.141	0.971	0.822, 1.148	0.981	0.825, 1.167	1.76
	PM_{coarse}	**391**							
	Brain volume		-1.051	-5.173, 3.070	-1.269	-5.297, 2.816	-1.711	-5.843, 2.422	1.74
	Ventricle volume		-0.859	-2.162, 0.443	-0.735	-2.08, 0.573	-0.593	-1.940, 0.754	1.74
	Hippocampal Volume		-0.002	-0.053, 0.049	-0.009	-0.06, 0.044	-0.010	-0.063, 0.042	1.74
	WMHV		0.954	0.866, 1.051	0.956	0.865, 1.055	0.956	0.866, 1.055	1.74

$PM_{2.5}$abs	**391**							
Brain volume		1.283	-3.960, 6.527	2.013	-3.275, 7.300	1.418	-4.245, 7.082	1.77
Ventricle volume		-0.100	-1.761, 1.560	0.141	-1.584, 1.867	0.358	-1.487, 2.204	1.77
Hippocampal Volume		-0.027	-0.091, 0.038	-0.027	-0.095, 0.041	-0.019	-0.091, 0.053	1.77
WMHV		0.946	0.834, 1.072	0.964	0.846, 1.099	0.962	0.837, 1.105	1.77

NO_x = Nitrogen oxide, $PM_{2.5}$ = particulate matter size 2.5µm or smaller, PM_{coarse} = Particulate matter size 2.5µm-10µm. NO_2 = Nitrogen Dioxide, PM_{10} = particulate matter 10µm or smaller. $PM_{2.5}$abs = absorbance as a measure of black carbon absorption fraction. WMHV = white matter hyperintensity volume. p-value <0.05 in bold. Model 1 = outcome, exposure and total intracranial volume. Model 2 = age at scan date, assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood and neighbourhood deprivation in adulthood. Model 3 = Model 2 + cognitive scores at age 15 and air pollution at birth and up to age 45. VIF = mean value for the variance inflation factor for model 3. All volumes in cm^3. β and 95% confidence intervals (CI) represent the mean difference in volume or exponential beta coefficient which represents change in white matter hyperintensity volume (such as 1.04 = 4% change) per quartile ($\mu g/m^3$) increase in air pollutant levels.

eTable 10: Extremes analysis (quartile 4 of exposure versus quartile 1-3 of exposure) of associations between exposure to NO_2 (ages 45 to 60-64) and PM_{10} (ages 53 to 60-64) and continuous verbal memory and processing speed (at age 43, 53, 60-64, 69 and ages 53, 60-64 and 69 respectively)

		Model 1		Model 2		Model 3	
Pollutant	**N**	**β**	**95% CI**	**β**	**95% CI**	**β**	**95% CI**
NO_2							
Verbal Memory	1534	0.090	-0.297, 0.476	0.131	-0.236, 0.498	0.101	-0.272, 0.475
Processing Speed	1534	0.033	-5.855, 5.921	3.488	-2.199, 9.176	2.677	-3.321, 8.675
PM_{10}							
Verbal Memory	1522	0.122	-0.305, 0.592	0.149	-0.258, 0.555	0.106	-0.298, 0.510
Processing Speed	1522	-6.348	-11.949, -0.746	-5.397	-10.908, 0.115	-5.527	-11.131, 0.078

NO_2 = Nitrogen Dioxide, PM_{10} = particulate matter 10µm or smaller. p-value <0.05 in bold. Model 1 = outcome and exposure. Model 2 = assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood and neighbourhood deprivation in adulthood. Model 3 = Model 2 + cognitive scores at age 15 and air pollution at birth and up to age 45. β and 95% confidence intervals (CI) represent the mean difference in verbal memory and processing speed score between the top quartile of exposure and lower three quartiles.

eTable 11: Extremes analysis (quartile 4 of exposure versus quartiles 1-3 of exposure) of associations between exposure to NO_x, $PM_{2.5}$, PM_{coarse} and $PM_{2.5}abs$ (at ages 60-64) and continuous verbal memory and processing speed (at age 69)

		Model 1		Model 2		Model 3	
Pollutant	**N**	**β**	**(95% CI)**	**β**	**(95% CI)**	**β**	**(95% CI)**
NO_x							
Verbal Memory	1415	0.091	-0.625, 0.808	0.232	-0.417, 0.880	0.087	-0.548, 0.722
Processing Speed	1415	1.376	-7.239, 9.991	3.016	-5.538, 11.570	0.458	-8.343, 9.260
$PM_{2.5}$							
Verbal Memory	1298	-0.703	-1.448, 0.041	-0.239	-0.924, 0.446	-0.473	-1.136, 0.190
Processing Speed	1298	6.582	-2.370, 15.535	8.446	-0.488, 17.380	7.553	-1.518, 16.623
PM_{coarse}							
Verbal Memory	1298	-0.856	-1.600, -0.111	-0.798	-1.478, -0.117	-0.732	-1.384, -0.080
Processing Speed	1298	-1.052	-10.011, 7.908	-1.078	-9.980, 7.825	-2.374	-11.305, 6.557
$PM_{2.5}abs$							
Verbal Memory	1298	-0.017	-0.762, 0.729	0.071	-0.618, 0.759	-0.041	-0.733, 0.652
Processing Speed	1298	-2.668	-11.627, 6.291	0.485	-8.524, 9.494	-1.666	-11.125, 7.792

NO_x = Nitrogen oxide, $PM_{2.5}$ = particulate matter size 2.5µm or smaller, PM_{coarse} = Particulate matter size 2.5µm-10µm. $PM_{2.5}abs$ = absorbance as a measure of black carbon absorption fraction. p-value <0.05 in bold and *. Model 1 = outcome and exposure. Model 2 = assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood and neighbourhood deprivation in adulthood. Model 3 = Model 2 + cognitive scores at age 15 and air pollution at birth and up to age 45. β and 95% confidence intervals (95% CI) represent the mean difference in verbal memory score or processing speed between the top quartile of exposure and lower three quartiles

eTable 12: Extremes analysis (quartile 4 of exposure versus quartile 1-3 of exposure) of associations to mean NO_2 (at ages 45, 55 and 60-64), PM_{10} (at ages 55 and 60-64), NO_x, $PM_{2.5}$, PM_{coarse} and $PM_{2.5}$abs (at ages 60-64) and ACE-III continuous total and sub-scale scores at age 69.

	Pollutant	N	Model 1		Model 2		Model 3	
Ages 45 to 60-64			**β**	**(95% CI)**	**β**	**(95% CI)**	**β**	**(95% CI)**
	NO_2	**1749**						
	Total score		**-0.749**	**-1.391, -0.106**	**-0.677**	**-1.247, -0.104**	**-0.999**	**-1.598, -0.399**
	Fluency		-0.082	-0.309, 0.146	-0.073	-0.288, 0.144	-0.155	-0.394, 0.083
Ages 55 to 60-64								
	PM_{10}	**1731**						
	Total score		**-0.513**	**-1.159, 0.132**	**-0.616**	**-1.192, -0.039**	**-0.679**	**-1.226, -0.133**
	Fluency		-0.168	-0.397, 0.060	-0.195	-0.413, 0.023	**-0.240**	**-0.458, -0.022**
Ages 60-64								
	NO_x	**1607**						
	Total score		**-0.859**	**-1.527, -0.191**	**-0.603**	**-1.200, -0.005**	**-0.644**	**-1.208, -0.080**
	Fluency		-0.096	-0.334, 0.143	-0.039	-0.267, 0.189	-0.064	-0.292, 0.164
	$PM_{2.5}$	**1483**						
	Total score		**-1.456**	**-2.137, -0.775**	**-0.716**	**-1.330, -0.101**	**-0.760**	**-1.336, -0.183**
	Fluency		-0.325	-0.571, -0.079	-0.175	-0.412, 0.062	-0.217	-0.452, 0.018
	PM_{coarse}	**1483**						
	Total score		**-0.772**	**-1.456, -0.088**	**-0.718**	**-1.328, -0.107**	-0.461	-1.029, 0.107
	Fluency		-0.196	-0.442, 0.051	-0.193	-0.428, 0.042	-0.152	-0.383, 0.078
	$PM_{2.5}$abs	**1483**						
	Total score		**-1.272**	**-1.954, -0.590**	-1.116	-1.737, 0.495	**-1.109**	**-1.716, -0.502**
	Fluency		-0.232	-0.477, 0.015	-0.206	-0.446, 0.034	**-0.253**	**-0.501, -0.005**

NO_x = Nitrogen oxide, $PM_{2.5}$ = particulate matter size 2.5µm or smaller, PM_{coarse} = Particulate matter size 2.5µm-10µm, NO_2 = Nitrogen Dioxide, PM_{10} = particulate matter 10µm or smaller. $PM_{2.5}$abs = absorbance as a measure of black carbon absorption fraction. p-value <0.05 in bold. Model 1 = outcome and exposure. Model 2 = assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood and neighbourhood deprivation in adulthood. Model 3 = Model 2 + cognitive scores at age 15 and air pollution at birth and up to age 45. β and 95% confidence intervals (CI) represent the mean difference in ACE-III score between the top quartile of exposure and lower three quartiles.

eTable 13: Extremes analysis (quartile 4 of exposure versus quartile 1-3 of exposure) of associations to mean NO_2 (at ages 45, 55 and 60-64), PM_{10} (at ages 55 and 60-64), NO_x, $PM_{2.5}$, PM_{coarse} and $PM_{2.5}$abs (at ages 60-64) and neuroimaging outcomes at ages 69-71.

	Pollutant	N	Model 1		Model 2		Model 3	
Ages 45 to 60-64			**β**	**(95% CI)**	**β**	**(95% CI)**	**β**	**(95% CI)**
	NO_2	**453**						
	Brain volume		3.913	-5.81, 13.635	7.008	-2.567, 16.584	7.328	-3.208, 17.863
	Ventricle volume		0.689	-2.429, 3.807	0.473	-2.681, 3.626	1.368	-2.096, 4.832
	Hippocampal Volume		-0.102	-0.224, 0.021	-0.085	-0.210, 0.039	-0.077	-0.214, 0.059
	WMHV		1.089	0.867, 1.369	1.086	0.860, 1.372	1.115	0.862, 1.442
Ages 55 to 60-64								
	PM_{10}	**451**						
	Brain volume		-1.305	-11.104, 8.494	1.386	-8.272, 11.044	-0.075	-10.059, 9.909
	Ventricle volume		0.394	-2.727, 3.515	0.246	-2.912, 3.405	0.814	-2.444, 4.071
	Hippocampal Volume		**-0.158**	**-0.280, -0.035**	**-0.151**	**-0.276, -0.026**	**-0.152**	**-0.281, -0.023**
	WMHV		0.839	0.668, 1.054	0.802	0.636, 1.012	0.808	0.638, 1.023
Ages 60-64								
	NO_x	**414**						
	Brain volume		2.409	-7.929, 12.748	5.373	-4.777, 15.523	4.844	-5.661, 15.348
	Ventricle volume		2.136	-1.155, 5.428	2.074	-1.271, 5419	2.655	-0.801, 6.112
	Hippocampal Volume		**-0.155**	**-0.283, -0.028**	-0.141	-0.272, -0.010	-0.137	-0.272, -0.002
	WMHV		0.953	0.751, 1.208	0.957	0.751, 1.220	0.971	0.756, 1.248
	$PM_{2.5}$	**391**						
	Brain volume		-7.610	-18.246, 3.026	-5.211	-15.672, 5.250	-6.377	-17.106, 4.353
	Ventricle volume		2.260	-1.108, 5.628	1.867	-1.555, 5.290	2.281	-1.223, 5.786
	Hippocampal Volume		**-0.170**	**-0.300, -0.040**	-0.153	-0.286, -0.020	-0.136	-0.272, 0.001
	WMHV		0.856	0.672, 1.090	0.854	0.666, 1.094	0.858	0.666, 1.106
	PM_{coarse}	**391**						
	Brain volume		-4.116	-14.785, 6.553	-3.236	-13.789, 7.317	-4.216	-14.914, 6.482
	Ventricle volume		-0.932	-4.311, 2.447	-0.563	-4.006, 2.880	-0.255	-3.747, 3.238
	Hippocampal Volume		0.047	-0.085, 0.178	0.033	-0.103, 0.168	0.034	-0.102, 0.170
	WMHV		0.920	0.720, 1.177	0.930	0.724, 1.194	0.931	0.725, 1.198

$PM_{2.5}$abs	**391**						
Brain volume		0.226	-10.436, 10.887	2.590	-8.126, 13.305	1.456	-9.936, 12.849
Ventricle volume		0.358	-3.018, 3.733	0.892	-2.608, 4.393	1.224	-2.492, 4.941
Hippocampal Volume		-0.091	-0.222, 0.040	-0.095	-0.232, 0.042	-0.092	-0.237, 0.052
WMHV		0.827	0.648, 1.056	0.866	0.670, 1.120	0.835	0.633, 1.102

NO_x = Nitrogen oxide, $PM_{2.5}$ = particulate matter size 2.5µm or smaller, PM_{coarse} = Particulate matter size 2.5µm-10µm, NO_2 = Nitrogen Dioxide, PM_{10} = particulate matter 10µm or smaller. $PM_{2.5}$abs = absorbance as a measure of black carbon absorption fraction. WMHV = white matter hyperintensity volume. p-value <0.05 in bold. Model 1 = outcome and exposure. Model 2 = assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood and neighbourhood deprivation in adulthood. Model 3 = Model 2 + cognitive scores at age 15 and air pollution at birth and up to age 45. All volumes in cm^3. β and 95% confidence intervals (CI) represent the mean difference in volume or exponential beta coefficient which represents change in white matter hyperintensity volume (such as 1.04 = 4% change) between the top quartile of exposure and lower three quartiles

eTable 14: Longitudinal associations between exposure to PM_{10} (at ages 55 and 60-64) with continuous verbal memory and processing speed at ages 53, 60-64 and 69 in fully adjusted models, further adjusted for co-pollutant exposure to NO_2 (at ages 55 and 60-64).

	N	Β	95% CI	VIF
Pollutant				
Verbal Memory				
PM_{10}	1522	-0.005	-0.161, 0.151	1.28
NO_2	1522	0.126	-0.036, 0.289	1.37
Processing Speed				
PM_{10}	1522	**-4.325**	**-6.489, -2.161**	1.28
NO_2	1522	**2.885**	**0.606, 5.163**	1.37

NO_2 = Nitrogen Dioxide, PM_{10} = particulate matter size 10µm or smaller. p-value <0.05 in bold and *. Fully adjusted model = outcome and exposure, assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood and neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45. NO_2 at age 55 is mean exposure across the two time-points available for PM_{10} (ages 55 and 60-64). VIF = variance inflation factor for each pollutant for fixed effects only. β and 95% confidence intervals (CI) represent the mean difference in score per quartile (µg/m3) increase in air pollutant levels.

eTable 15: Associations between exposure to NO_x, $PM_{2.5}$, PM_{coarse} and $PM_{2.5}$abs (at ages 60-64) and continuous verbal memory and processing speed (at age 69) in fully adjusted models, adjusted for co-pollutants

		Verbal Memory			Processing Speed		
Pollutant	N	β (95% CI)	β (95% CI)	N	β (95% CI)	β (95% CI)	VIF
$PM_{2.5}$ + NO_X	1298	0.672	**-0.710**	1298	-4.864	5.494	3.53, 3.58
		(-0.045, 1.388)	**(-1.327, -0.094)**		(-14.634, 4.906)	(-2.918, 13.907)	
PM_{coarse} + NO_X	1298	-0.072	-0.211	1298	-1.518	2.458	1.07, 1.17
		(-0.312, 0.169)	(-0.563, 0.140)		(-4.792, 1.756)	(-2.362, 7.278)	
$PM_{2.5}$abs + NO_X	1298	0.246	-0.386	1298	-1.646	3.060	1.80, 1.69
		(-0.144, 0.637)	(-0.809, 0.036)		(-6.990, 3.698)	(-2.732, 8.852)	

NO_2 = Nitrogen Dioxide, PM_{10} = particulate matter 10µm or smaller. NO_x = Nitrogen oxide, $PM_{2.5}$ = particulate matter size 2.5µm or smaller, PM_{coarse} = Particulate matter size 2.5µm-10µm. $PM_{2.5}$abs = absorbance as a measure of black carbon absorption fraction. p-value <0.05 in bold. Fully adjusted model = outcome and exposure, assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood and neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45. VIF = variance inflation factor for each pollutant. β and 95% confidence intervals (CI) represent the mean difference in verbal memory or processing speed scores per quartile (µg/m^3) increase in air pollutant levels.

eTable 16: Associations between mean exposure to air pollution at ages 55 and 60-64 (PM_{10} and NO_2) and ages 60-64 (NO_x, $PM_{2.5}$, PM_{coarse}, $PM_{2.5}abs$) with continuous ACE-III total score at age 69 in fully adjusted models, and further adjusted for co-pollutants.

		Outcome		
Pollutants		ACE-III Total score		VIF
	N	β (95% CI)	β (95% CI)	
Ages 55 – 60-64				
		Pollutant 1	Pollutant 2	
PM_{10} + NO_2	1731	-0.187	-0.339	2.75, 3.25
		(-0.660, 0.286)	(-0.826, 0.147)	
Ages 60-64				
$PM_{2.5}$ + NO_X	1483	-0.389	-0.181	3.43, 3.48
		(-0.969, 0.190)	(-0.691, 0.329)	
PM_{coarse} + NO_X	1483	**-0.233**	**-0.400**	1.08, 1.17
		(-0.452, -0.015)	**(-0.698, -0.103)**	
$PM_{2.5}abs$ + NO_X	1483	**-0.389**	-0.232	1.83, 1.73
		(-0.753, -0.026)	(-0.595, 0.130)	

NO_2 = Nitrogen Dioxide, PM_{10} = particulate matter 10µm or smaller. NO_x = Nitrogen oxide, $PM_{2.5}$ = particulate matter size 2.5µm or smaller, PM_{coarse} = Particulate matter size 2.5µm-10µm. $PM_{2.5}abs$ = absorbance as a measure of black carbon absorption fraction. p-value <0.05 in bold. Fully adjusted model = outcome, exposure, assigned sex at birth and father's social class, air pollution at birth and up to age 45, externalising and internalising scores at ages 13-15, cognitive scores at age 15, smoking, educational attainment, social class in adulthood and neighbourhood deprivation. NO_2 at age 55 is mean exposure across the two time-points available for PM_{10} (ages 55 and 60-64). VIF = variance inflation factor for each pollutant. β and 95% confidence intervals (CI) represent the mean difference in ACE-III score per quartile (µg/m^3) increase in air pollutant levels.

eTable 17: Associations between mean exposure to air pollution at ages 55 and 60-64 (PM_{10} and NO_2) and ages 60-64 (NO_x, $PM_{2.5}$, PM_{coarse}, $PM_{2.5}abs$) with neuroimaging outcomes at age 69-71 in fully adjusted models and further adjusted for co-pollutants.

		Brain Volume		Ventricular Volume		Total Hippocampal Volume		WMHV		VIF
Pollutants	N	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	
Ages 55 – 60-64										
		Pollutant 1	Pollutant 2	Pollutant 1	Pollutant 2	Pollutant 1	Pollutant 2	Pollutant 1	Pollutant 2	
PM_{10} and NO_2	451	-2.318 (-11.414, 6.777)	0.799 (-8.238, 9.835)	-0.620 (-3.558, 2.318)	**3.116 (0.188, 6.044)**	-0.030 (-0.148, 0.088)	-0.050 (-0.167, 0.067)	0.940 (0.739, 1.196)	1.066 (0.852, 1.333)	2.94, 3.31
Ages 60-64										
$PM_{2.5}$ and NO_X	391	0.229 (-11.266, 11.723)	0.224 (-11.218, 11.665)	-0.500 (-4.229, 3.229)	2.619 (-1.094, 6.332)	-0.017 (-0.162, 0.128)	-0.084 (-0.228, 0.061)	1.090 (0.785, 1.512)	0.884 (0.643, 1.217)	3.22, 3.23
PM_{coarse} and NO_X	391	-1.755 (-5.914, 2.404)	0.703 (-6.091, 7.496)	-0.741 (-2.089, 0.607)	2.341 (0.136, 4.545)	-0.004 (-0.057, 0.048)	**-0.097 (-0.183, -0.011)**	0.956 (0.866, 1.056)	0.951 (0.801, 1.129)	1.08, 1.14
$PM_{2.5}abs$ and NO_X	391	1.951 (-5.240, 9.143)	-1.035 (-9.614, 7.544)	-1.262 (-3.587, 1.064)	**3.149 (0.369, 5.929)**	0.051 (-0.040, 0.141)	**-0.135 (-0.244, -0.027)**	0.978 (0.820, 1.167)	0.966 (0.777, 1.200)	1.97, 1.81

NO_2 = Nitrogen Dioxide, PM_{10} = particulate matter 10µm or smaller. NO_x = Nitrogen oxide, $PM_{2.5}$ = particulate matter size 2.5µm or smaller, PM_{coarse} = Particulate matter size 2.5µm-10µm, $PM_{2.5}abs$ = absorbance as a measure of black carbon absorption fraction. WMHV = white matter hyperintensity volume. p-value <0.05 in bold. Fully adjusted model = outcome, exposure, assigned sex at birth and father's social class, air pollution at birth and up to age 45, externalising and internalising scores at ages 13-15, cognitive scores at age 15, smoking, educational attainment, social class in adulthood and neighbourhood deprivationNO_2 at age 55 is mean exposure across the two time points available for PM_{10} (age 55 and 60-64). VIF = variance inflation factor for each pollutant. β and 95% confidence intervals (CI) represent the mean difference in volume or exponential beta coefficient which represents change in white matter hyperintensity volume (such as 1.04 = 4% change) per quartile ($\mu g/m^3$) increase in air pollutant levels.

eTable 18: Complete case analysis of longitudinal associations between exposure to NO_2 (ages 45 to 60-64) and PM_{10} (ages 53 to 60-64) and continuous verbal memory and processing speed (at ages 43, 53, 60-64, 69 and ages 53, 60-64 and 69, respectively).

	N	MODEL 3	
Pollutant		**β**	**95% CI**
NO_2			
Verbal Memory	941	-0·144	-0·321, 0·033
Processing Speed	941	**-9·415**	**-12·239, -6·592**
PM_{10}			
Verbal Memory	912	-0·042	-0·243, 0·159
Processing Speed	912	**-5·908**	**-8·626, -3·189**

NO_2 = Nitrogen Dioxide, PM_{10} = particulate matter 10µm or smaller. p-value <0.05 in bold. All associations are fully adjusted or assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood and neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45. β and 95% confidence intervals (CI) represent the mean difference in ACE-III score per quartile (µg/m^3) increase in air pollutant levels.

eTable 19: Complete case analysis of prospective associations between exposure to NO_x, $PM_{2\cdot5}$, PM_{coarse} and $PM_{2\cdot5}abs$ (at ages 60-64) and continuous verbal memory and processing speed (at age 69).

Pollutant	N	Model 3 β	(95% CI)
NO_x			
Verbal Memory	849	-0·052	-0·484, 0·380
Processing Speed	849	2·171	-4·005, 8·347
$PM_{2\cdot5}$			
Verbal Memory	769	0·009	-0·507, 0·525
Processing Speed	769	0·506	-6·806, 7·818
PM_{coarse}			
Verbal Memory	769	-0·100	-0·336, 0·137
Processing Speed	769	0·469	-3·884, 4·822
$PM_{2\cdot5}abs$			
Verbal Memory	769	-0·052	-0·359, 0·255
Processing Speed	769	0·091	-5·560, 5·742

NO_x = Nitrogen oxide, $PM_{2.5}$ = particulate matter size 2.5µm or smaller, PM_{coarse} = Particulate matter size 2.5µm-10µm. $PM_{2.5}abs$ = absorbance as a measure of black carbon absorption fraction. p-value <0.05 in bold. All associations are fully adjusted or assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood and neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45. β and 95% confidence intervals (CI) represent the mean difference in ACE-III score per quartile (µg/m^3) increase in air pollutant levels.

eTable 20: Complete case analysis of associations between mean exposure to NO_2 (at ages 45, 55 and 60-64), PM_{10} (at ages 55, 60-64), NO_x, $PM_{2.5}$, PM_{coarse} and $PM_{2.5}$abs (at ages 60-64) and ACE-III continuous total and fluency sub-scale scores at age 69.

		N	Model 3	
Pollutant				
Ages 45 to 60-64			**β**	**(95% CI)**
	NO_2	987		
	Total score		-0.296	-0.739, 0.149
	Fluency		-0.103	-0.287, 0.080
Ages 55 to 60-64				
	PM_{10}	983		
	Total score		-0.364	-0.750, 0.022
	Fluency		-0.060	-0.219, 0.099
Ages 60-64				
	NO_x	863		
	Total score		-0.364	-0.741, 0.013
	Fluency		-0.078	-0.237, 0.080
	$PM_{2.5}$	788		
	Total score		-0.358	-0.786, 0.070
	Fluency		-0.089	-0.276, 0.098
	PM_{coarse}	788		
	Total score		**-0.340**	**-0.624, -0.056**
	Fluency		**-0.168**	**-0.292, -0.044**
	$PM_{2.5}$abs	788		
	Total score		-0.317	-0.696, 0.062
	Fluency		-0.126	-0.291, 0.040

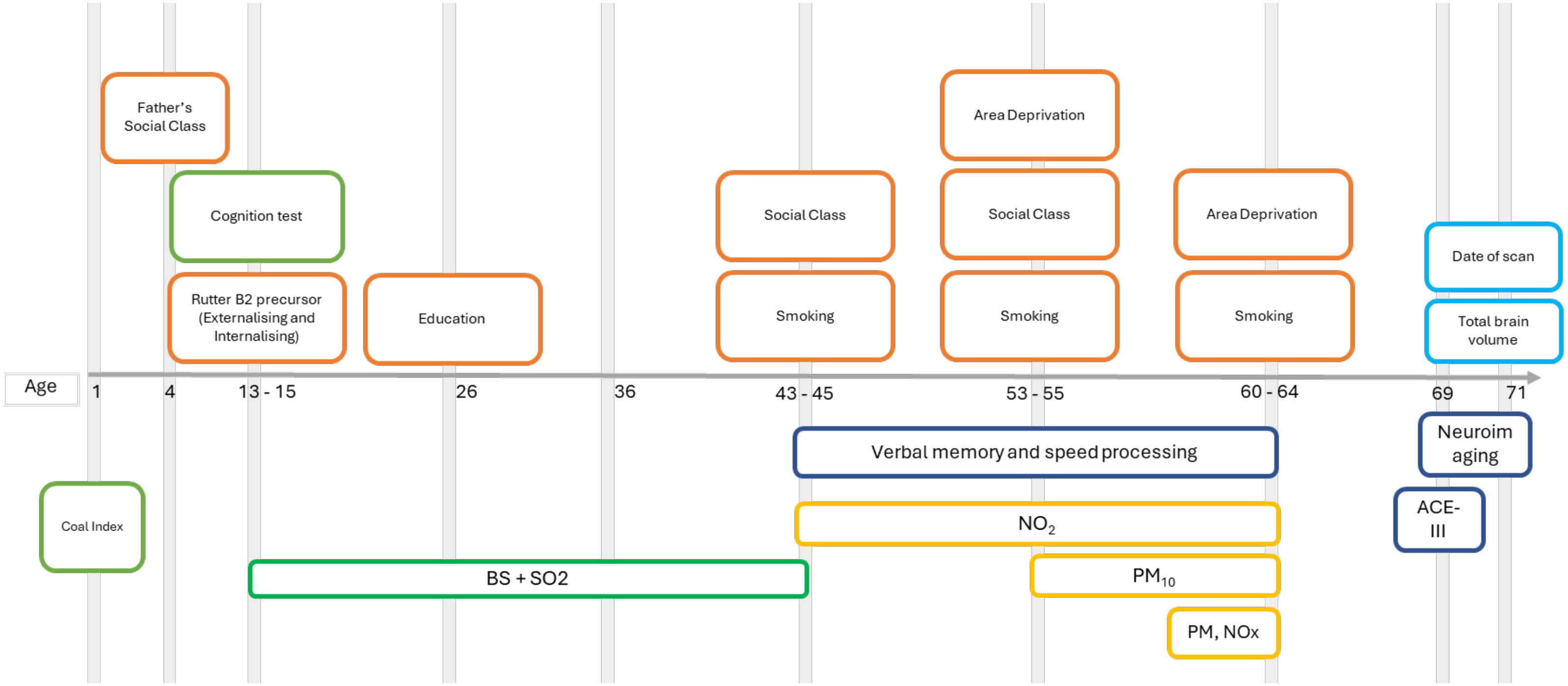
NO_2 = Nitrogen Dioxide, PM_{10} = particulate matter 10µm or smaller. NO_x = Nitrogen oxide, $PM_{2.5}$ = particulate matter size 2.5µm or smaller, PM_{coarse} = Particulate matter size 2.5µm-10µm. $PM_{2.5}$abs = absorbance as a measure of black carbon absorption fraction. p-value <0.05 in bold. All associations are fully adjusted or assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood and neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45. β and 95% confidence intervals (CI) represent the mean difference in ACE-III score per quartile (μg/m^3) increase in air pollutant levels.

eTable 21: Complete case analysis of associations between mean exposure to NO_2 (at ages 45, 55 and 60-64), PM_{10} (at ages 55, 60-64), NO_x, $PM_{2.5}$, PM_{coarse} and $PM_{2.5}$abs (at ages 60-64) and neuroimaging outcomes at ages 69-71.

	N	Model 3	
Pollutant			
Ages 45 to 60-64		**β**	**(95% CI)**
NO_2	**276**		
Brain volume		-2.569	-10.095, 4.956
Ventricle volume		2.187	-0.210, 4.583
Hippocampal Volume		-0.032	-0.125, 0.061
WMHV		1.124	0.955, 1.323
Ages 55 to 60-64			
PM_{10}	**287**		
Brain volume		0.348	-7.143, 7.838
Ventricle volume		1.622	-0.792, 4.038
Hippocampal Volume		-0.065	-0.160, 0.031
WMHV		1.072	0.891, 1.291
Ages 60-64			
NO_x	**264**		
Brain volume		2.032	-6.046, 10.109
Ventricle volume		1.850	-0.832, 4.532
Hippocampal Volume		-0.083	-0.195, 0.018
WMHV		1.086	0.881, 1.339
$PM_{2.5}$	**248**		
Brain volume		2.232	-5.905, 10.369
Ventricle volume		1.212	-1.465, 3.888
Hippocampal Volume		-0.081	-0.183, 0.021
WMHV		1.104	0.890, 1.369
PM_{coarse}	**248**		
Brain volume		-2.504	-8.116, 3.108
Ventricle volume		-0.318	-2.169, 1.533
Hippocampal Volume		-0.040	-0.110, 0.031
WMHV		0.893	0.779, 1.026

	$PM_{2.5}$abs	**248**		
	Brain volume		0.203	-6.794, 7.200
	Ventricle volume		0.868	-1.433, 3.169
	Hippocampal Volume		-0.039	-0.127, 0.049
	WMHV		1.054	0.886, 1.254

NO_x = Nitrogen oxide, $PM_{2.5}$ = particulate matter size 2.5µm or smaller, PM_{coarse} = Particulate matter size 2.5µm-10µm. NO_2 = Nitrogen Dioxide, PM_{10} = particulate matter 10µm or smaller. $PM_{2.5}$abs = absorbance as a measure of black carbon absorption fraction. WMHV = white matter hyperintensity volume. p-value <0.05 in bold. All models adjusted for age at scan date, assigned sex at birth, father's occupational social class, externalising and internalising scores at age 13-15, smoking status, educational attainment at age 26, occupational social class in adulthood and neighbourhood deprivation in adulthood, cognitive scores at age 15 and air pollution at birth and up to age 45. All volumes in cm^3. β and 95% confidence intervals (CI) represent the mean difference in volume or exponential beta coefficient which represents change in white matter hyperintensity volume (such as 1.04 = 4% change) per quartile ($\mu g/m^3$) increase in air pollutant levels.



eFigure 1 Timeline of measures used in this study. NO_2 = Nitrogen Dioxide, NO_x = Nitrogen oxides, SO_2 = sulphur dioxide, BS = black smoke, PM = PM_{10}, $PM_{2.5}$, PM_{coarse}, $PM_{2.5}$abs. PM_{10} = particulate matter 10µm or smaller, $PM_{2.5}$ = particulate matter 2.5µm or smaller, PM_{coarse} = particulate matter of size 2.5µm-10µm, $PM_{2.5}$abs = absorbance as a measure of black carbon absorption fraction. Yellow = main exposures. Green = prior exposure and childhood cognition. Orange = covariates. Dark blue = outcomes. Light blue = additional covariates for objective 2.