eTable 1. STROBE checklist

	Item No.	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1 and 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4, 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5, 6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5, 6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	

Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5, 6
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	5, 6
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	9

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Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5, 6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7, 8
		(*b*) Describe any methods used to examine subgroups and interactions	7, 8
		(*c*) Explain how missing data were addressed	5, 7, 8
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	7, 8
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	9, 10
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	Not done
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9, 10
		(b) Indicate number of participants with missing data for each variable of interest	9, 10
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	9, 10
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	9
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	-
		Cross-sectional study—Report numbers of outcome events or summary measures	-

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	9, 10
		(*b*) Report category boundaries when continuous variables were categorized	7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-

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Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7,8, 11
Key results	18	Summarise key results with reference to study objectives	12
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	15, 16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15, 16
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
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	17

eTable 2 Decomposition of the association between NOx and incident dementia into pathways involving homocysteine (Panel A) and methionine (Panel B)

PANEL A: Homocysteine

	Proportions	P-value	95% CI
Proportion attributable to direct effect	69.7%	0.103	-14.2%; 100%
Proportion attributable to interaction	23.5%	0.588	-61.6%; 100%
Proportion attributable to mediation	7.9%	0.036	0.5%;15.4%
Overall proportion eliminated*	30.3%	0.478	-53.5%; 100%

PANEL B: Methionine

	Proportions	P-value	95% CI
Proportion attributable to direct effect	39.7%	0.000	9.4%; 69.9%
Proportion attributable to interaction	-38.9%	0.009	-68.1%; -9.8%
Proportion attributable to mediation	-1.3%	0.695	-7.6%; 5.1%
Overall proportion eliminated*	-39.7%	0.010	-69.9%; -9.4%

Results are derived from Cox regression models with four-way decomposition by levels of homocysteine (cut-off: 15 µmol/L) and methionine (cut-off: 20.7 µmol/L).

Model adjusted for age, sex, education, socioeconomic position, retirement age, smoking, physical activity, creatinine, year of assessment and use of supplements.

*This proportion includes the effect attributed to both interaction and mediation.

eTable 3 Decomposition of the association between $PM_{2.5}$ (Panel A) and NOx (Panel B) and incident dementia into pathways involving Met:tHcy

PANEL A: $PM_{2.5}$

	Proportions	P-value	95% CI
Proportion attributable to direct effect	44.5%	0.000	5.9%;83.0%
Proportion attributable to interaction	-45.4%	0.019	-83.3%;-7.5%
Proportion attributable to mediation	1.7%	0.576	-4.1%;7.5%
Overall proportion eliminated*	-44.5%	0.024	-83.0%;-5.9%

PANEL B: NOx

	Proportions	P-value	95% CI
Proportion attributable to direct effect	52.1%	0.000	7.1%;97.1%
Proportion attributable to interaction	-56.2%	0.012	-99.9%;-12.5%
Proportion attributable to mediation	6.6%	0.101	-12.9%;14.5%
Overall proportion eliminated*	-52.1%	0.023	-97.1%;-7.1%

Results are derived from Cox regression models with four-way decomposition by levels of methionine to homocysteine ratio (cutoff: 1.47 µmol/L).
Models are adjusted for age, sex, education, socioeconomic position, retirement age, smoking, physical activity, creatinine, year of assessment and use of supplements.

*This proportion includes the effect attributed to both interaction and mediation.

eTable 4 Decomposition of the association between NOx and incident dementia into pathways involving homocysteine (Panel A) and methionine (Panel B) after excluding incident cardiovascular diseases

PANEL A: Homocysteine

	Proportions	**P-value**	**95% CI**
Proportion attributable to direct effect	92.6%	0.088	-13.6%;98.8%
Proportion attributable to interaction	2.2%	0.967	-0.5%;9.2%
Proportion attributable to mediation	5.3%	0.137	-0.2%;12.2%
Overall proportion eliminated*	7.4%	0.891	-98.8%; 100%

PANEL B: Methionine

	Proportions	**P-value**	**95% CI**
Proportion attributable to direct effect	39.3%	0.000	11.3%;67.3%
Proportion attributable to interaction	-39.1%	0.004	-66.0%;-12.1%
Proportion attributable to mediation	-0.4%	0.903	-0.6%;6.1%
Overall proportion eliminated*	-39.3%	0.006	-67.3%;-11.3%

Results are derived from Cox regression model with four-way decomposition by levels of homocysteine (cut-off: 15 µmol/L) and methionine (cut-off: 20.7 µmol/L).

Models adjusted for age, sex, education, socioeconomic position, retirement age, smoking, physical activity, creatinine, year of assessment, use of supplements and cardiovascular diseases at baseline.

*This proportion includes the effect attributed to both interaction and mediation.

eTable 5. Hazard ratios (HR) of dementia with 95% confidence intervals (CI) by $PM_{2.5}$ and NOx by sex and *APOE* genotype

	HR (95%CI) for dementia		**HR (95%CI) for dementia**	
	Females	Males	*APOEε4* non carriers	*APOEε4* carriers
1µg/m3 increase of $PM_{2.5}$	1.87 (1.61-2.16)	1.66 (1.32-2.09)	1.78 (1.53-2.00)	1.83 (1.48-2.26)
10 µg/m3 increase of NOx	1.03 (1.02-1.04)	1.03 (1.01-1.05)	1.03 (1.01-1.04)	1.03 (1.01-1.05)

Estimates are hazard ratios derived from Cox proportional hazard models according to $PM_{2.5}$ and NOx levels five years before baseline assessment. Models are adjusted for age, education, smoking, socio-economic status, retirement age, smoking, physical activity.

p for interaction with sex: $PM_{2.5}$: 0.399 and NOx: 0.891

p for interaction with *APOE*: $PM_{2.5}$: 0.840 and NOx: 0.863

eTable 6. Decomposition of the association between $PM_{2.5}$ and incident dementia into pathways involving homocysteine (Panel A) and methionine (Panel B)

PANEL A: Homocysteine

	Proportions	P-value	95% CI
Proportion attributable to direct effect	47.1%	0.041	2.0%;92.3%
Proportion attributable to interaction	49.5%	0.033	4.0%;94.9%
Proportion attributable to mediation	6.1%	0.016	1.1%;11.8%
Overall proportion eliminated*	52.8%	0.022	7.7%;97.9%

PANEL B: Methionine

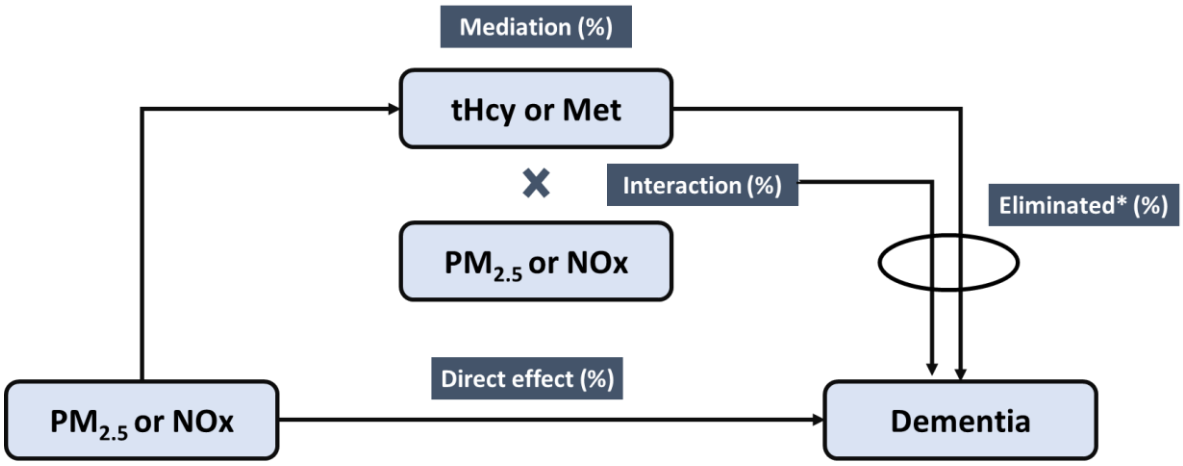
	Proportions	P-value	95% CI
Proportion attributable to direct effect	100%	0.000	98.8%;100%
Proportion attributable to interaction	-23.1%	0.073	-48.3%; 2.1%
Proportion attributable to mediation	-2.2%	0.320	-6.6%; 2.1%
Overall proportion eliminated*	-24.3%	0.062	-49.8%; 1.1%

Results are derived from Cox regression model with four-way decomposition by levels of homocysteine (cut-off: 15 µmol/L) and methionine (cut-off: 20.7 µmol/L).

Models adjusted for age, sex, education, socioeconomic position, retirement age, smoking, physical activity, creatinine, year of assessment, use of supplements **and food intake of vitamin B12 and folate**.

*This proportion includes the effect attributed to both interaction and mediation.

eFigure 1. Four different pathways models according to the levels of air pollution and biomarkers



Abbreviations: tHcy: total homocysteine Met: methionine

*This proportion includes the effect attributed to both interaction and mediation.