

Table S1. Baseline characteristics for included and excluded participants of the current study.

Characteristics *	Included Participants	Excluded Participants
No. of participants	263,095	239,080
Age, years (Mean (SD))	55.80 (8.05)	57.33 (8.07)
Sex, Female, n (%)	132,832 (50.49)	140,391 (58.72)
Ethnicity, White, n (%)	252,276 (95.89)	220,115 (93.15)
BMI level, n (%)		
Underweight	1,219 (0.47)	1,407 (0.59)
Normal	85,166 (32.51)	77,134 (32.54)
Overweight	112,844 (43.07)	99,143 (41.82)
Obese	62,770 (23.96)	59,392 (25.05)
Higher TDI, n (%)	46,839 (17.83)	53,472 (22.39)
Higher education, n (%)	135,217 (51.52)	98,241 (42.79)
Intake of alcohol, n (%)		
Never	17,775 (6.76)	22,810 (9.60)
Occasional	55,328 (21.03)	58,455 (24.60)
Moderate	131,943 (50.16)	112,667 (47.41)
Heavy	57,991 (22.05)	43,707 (18.39)
Smoking status, n (%)		
Never	1443,32 (54.86)	129,029 (54.17)
Previous	91,988 (34.96)	80,939 (33.98)
Current	26,775 (10.18)	26,167 (10.99)
Physical activity, n (%)		
Low	42,906 (18.59)	33,239 (19.40)
Moderate	93,850 (40.67)	70,083 (40.89)
High	93,994 (40.73)	68,053 (39.71)
APOE ε4 carrier, n (%)	72,981 (28.32)	65,447 (28.54)
Hypertension, n (%)	111,257 (42.29)	105,427 (44.10)
Diabetes, n (%)	14,463 (5.84)	15,627 (7.10)
PM_{2.5}, µg/m³ (Mean (SD))	9.96 (1.05)	10.03 (1.06)
PM₁₀, µg/m³ (Mean (SD))	19.27 (1.94)	19.38 (1.94)
NO₂, µg/m³ (Mean (SD))	28.98 (9.20)	29.18 (8.90)
NO_x, µg/m³ (Mean (SD))	43.59 (15.47)	44.70 (15.58)
Psychological score (Mean (SD))	8.10 (5.21)	8.13 (5.23)
Affective symptom score (Mean (SD))	1.49 (1.55)	1.49 (1.55)
Anxiety symptom score (Mean (SD))	1.77 (1.63)	1.82 (1.65)
Emotional instability symptom score (Mean (SD))	3.20 (2.37)	3.21 (2.36)

BMI, body mass index; TDI, Townsend deprivation index; *APOE*, apolipoprotein E PM_{2.5}, fine particulate matter with diameter < 2.5 µm; PM₁₀, particulate matter with diameter < 10 µm; NO₂, nitrogen dioxide; NO_x, nitrogen oxides; SD, standard deviation. * Percentages shown for available, non-missing data.

Table S2. The detailed definition of the 24 psychological factors in the UK biobank.

Psychological Factors	Field ID	Question	Answer Categories
Mood swings	1920	Does your mood often go up and down?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Miserableness	1930	Do you ever feel 'just miserable' for no reason?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Irritability	1940	Are you an irritable person?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Sensitivity hurt feelings	1950	Are your feelings easily hurt?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Fed up feelings	1960	Do you often feel 'fed-up'?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Nervous feelings	1970	Would you call yourself a nervous person?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Anxious feelings	1980	Are you a worrier?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Tense /highly strung	1990	Would you call yourself tense or 'highly strung'?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Worry too long	2000	Do you worry too long after an embarrassing experience?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Suffering from nerves	2010	Do you suffer from 'nerves'?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Loneliness and isolation	2020	Do you often feel lonely?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Guilty feelings	2030	Are you often troubled by feelings of guilt?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Risk taking	2040	Would you describe yourself as someone who takes risks?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Depressed mood	2050	Over the past two weeks, how	1. Not at all

		often have you felt down, depressed, or hopeless?	2. Several days 3. More than half the days 4. Nearly every day 5. Do not know 6. Prefer not to answer 1. Not at all
Unenthusiasm	2060	Over the past two weeks, how often have you had little interest or pleasure in doing things?	2. Several days 3. More than half the days 4. Nearly every day 5. Do not know 6. Prefer not to answer 1. Not at all
Tenseness	2070	Over the past two weeks, how often have you felt tense, fidgety, or restless?	2. Several days 3. More than half the days 4. Nearly every day 5. Do not know 6. Prefer not to answer 1. Not at all
Tiredness	2080	Over the past two weeks, how often have you felt tired or had little energy?	2. Several days 3. More than half the days 4. Nearly every day 5. Do not know 6. Prefer not to answer
Seen a doctor	2090	Have you ever seen a general practitioner (GP) for nerves, anxiety, tension or depression?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Seen a psychiatrist	2100	Have you ever seen a psychiatrist for nerves, anxiety, tension or depression?	1. Yes 2. No 3. Do not know 4. Prefer not to answer
Grief and stress	6145	In the last 2 years have you experienced any of the following?	1. Serious illness, injury, or assault to yourself 2. Serious illness, injury, or assault of a close relative 3. Death of a close relative 4. Death of a spouse or partner 5. Marital separation/divorce 6. Financial difficulties 7. None of the above 8. Prefer not to answer
Neuroticism score	20127	The score was generated by summarizing the number of Yes answers across these twelve neurotic behavior domains into a single integer score for each participant (0 to 12): 1. Does your mood often go up and down? 2. Do you ever feel 'just miserable' for no reason? 3. Are you an irritable person? 4. Are your feelings easily hurt? 5. Do you often feel 'fed-up'? 6. Would you call yourself a nervous person? 7. Are you a worrier? 8. Would you call yourself tense or 'highly strung'? 9. Do you worry too long after an	For each question, participants could answer: 1. Yes 2. No 3. Do not know 4. Prefer not to answer

		embarrassing experience? 10. Do you suffer from 'nerves'? 11. Do you often feel lonely? 12. Are you often troubled by feelings of guilt?	
Able to confide	2110	How often are you able to confide in someone close to you?	1. Almost daily 2. 2-4 times a week 3. About once a week 4. About once a month 5. Once every few months 6. Never or almost never 7. Do not know 8. Prefer not to answer
Frequency of friend/family visits	1031	How often do you visit friends or family or have them visit you?	1. Almost daily 2. 2-4 times a week 3. About once a week 4. About once a month 5. Once every few months 6. Never or almost never 7. Do not know 8. Prefer not to answer
Leisure/social activities	6160	Which of the following do you attend once a week or more often? (You can select more than one)	1. Sports club or gym 2. Pub or social club 3. Religious group 4. Adult education class 5. Other group activity 6. None of the abover 7. Prefer not to answer

Table S3. International Classification of Disease codes used to ascertain psychiatric disorders.

	ICD-9	ICD-10
Depression	296.2	F32, F32.0, F32.1, F32.2, F32.3, F32.8, F32.9, F33, F33.0, F33.1, F33.2, F33.3, F33.4, F33.8, F33.9
Anxiety	300.00, 300.01, 300.02, 300.09	F40, F40.1, F40.2, F40.8, F40.9, F41.0, F41.1, F41.2, F41.3, F41.8, F41.9
Bipolar affective disorder	296.8	F31, F31.0, F31.1, F31.2, F31.3, F31.4, F31.5, F31.6, F31.7, F31.8, F31.9

Table S4. The definitions of brain imaging phenotypes.

Brain Structure	Field ID
Volume of grey matter in amygdala (left and right)	25888 and 25889
Volume of grey matter in angular gyrus (left and right)	25822 and 25823
Volume of grey matter in brain-stem	25892
Volume of grey matter in caudate (left and right)	25880 and 25881
Volume of grey matter in central opercular cortex (left and right)	25864 and 25865
Volume of grey matter in cingulate gyrus, anterior division (left and right)	25838 and 25839
Volume of grey matter in cingulate gyrus, posterior division (left and right)	25840 and 25841
Volume of grey matter in crus i cerebellum (left and right)	25900 and 25902
Volume of grey matter in crus i cerebellum (vermis)	25901
Volume of grey matter in crus ii cerebellum (left and right)	25903 and 25905
Volume of grey matter in crus ii cerebellum (vermis)	25904
Volume of grey matter in cuneal cortex (left and right)	25844 and 25845
Volume of grey matter in frontal medial cortex (left and right)	25830 and 25831
Volume of grey matter in frontal operculum cortex (left and right)	25862 and 25863
Volume of grey matter in frontal orbital cortex (left and right)	25846 and 25847
Volume of grey matter in frontal pole (left and right)	25782 and 25783
Volume of grey matter in heschl's gyrus (includes h1 and h2) (left and right)	25870 and 25871
Volume of grey matter in hippocampus (left and right)	25886 and 25887
Volume of grey matter in i-iv cerebellum (left and right)	25893 and 25894
Volume of grey matter in ix cerebellum (left and right)	25915 and 25917
Volume of grey matter in ix cerebellum (vermis)	25916
Volume of grey matter in inferior frontal gyrus, pars opercularis (left and right)	25792 and 25793
Volume of grey matter in inferior frontal gyrus, pars triangularis (left and right)	25790 and 25791
Volume of grey matter in inferior temporal gyrus, anterior division (left and right)	25808 and 25809
Volume of grey matter in inferior temporal gyrus, posterior division (left and right)	25810 and 25811
Volume of grey matter in inferior temporal gyrus, temporooccipital part (left and right)	25812 and 25813
Volume of grey matter in insular cortex (left and right)	25784 and 25785
Volume of grey matter in intracalcarine cortex (left and right)	25828 and 25829
Volume of grey matter in juxtapositional lobule cortex (formerly supplementary motor cortex) (left and right)	25832 and 25833
Volume of grey matter in lateral occipital cortex, inferior division (left and right)	25826 and 25827
Volume of grey matter in lateral occipital cortex, superior division (left and right)	25824 and 25825
Volume of grey matter in lingual gyrus (left and right)	25852 and 25853
Volume of grey matter in middle frontal gyrus (left and right)	25788 and 25789
Volume of grey matter in middle temporal gyrus, anterior division (left and right)	25802 and 25803
Volume of grey matter in middle temporal gyrus, posterior division (left and right)	25804 and 25805
Volume of grey matter in middle temporal gyrus, temporooccipital part (left and right)	25806 and 25807
Volume of grey matter in occipital fusiform gyrus (left and right)	25860 and 25861
Volume of grey matter in occipital pole (left and right)	25876 and 25877
Volume of grey matter in pallidum (left and right)	25884 and 25885
Volume of grey matter in paracingulate gyrus (left and right)	25836 and 25837
Volume of grey matter in parahippocampal gyrus, anterior division (left and right)	25848 and 25849
Volume of grey matter in parahippocampal gyrus, posterior division (left and right)	25850 and 25851
Volume of grey matter in parietal operculum cortex (left and right)	25866 and 25867
Volume of grey matter in planum polare (left and right)	25868 and 25869
Volume of grey matter in planum temporale (left and right)	25872 and 25873
Volume of grey matter in postcentral gyrus (left and right)	25814 and 25815

Volume of grey matter in precentral gyrus (left and right)	25794 and 25795
Volume of grey matter in precuneous cortex (left and right)	25842 and 25843
Volume of grey matter in putamen (left and right)	25882 and 25883
Volume of grey matter in subcallosal cortex (left and right)	25834 and 25835
Volume of grey matter in superior frontal gyrus (left and right)	25786 and 25787
Volume of grey matter in superior parietal lobule (left and right)	25816 and 25817
Volume of grey matter in superior temporal gyrus, anterior division (left and right)	25798 and 25799
Volume of grey matter in superior temporal gyrus, posterior division (left and right)	25800 and 25801
Volume of grey matter in supracalcarine cortex (left and right)	25874 and 25875
Volume of grey matter in supramarginal gyrus, anterior division (left and right)	25818 and 25819
Volume of grey matter in supramarginal gyrus, posterior division (left and right)	25820 and 25821
Volume of grey matter in temporal fusiform cortex, anterior division (left and right)	25854 and 25855
Volume of grey matter in temporal fusiform cortex, posterior division (left and right)	25856 and 25857
Volume of grey matter in temporal occipital fusiform cortex (left and right)	25858 and 25859
Volume of grey matter in temporal pole (left and right)	25796 and 25797
Volume of grey matter in thalamus (left and right)	25878 and 25879
Volume of grey matter in v cerebellum (left and right)	25895 and 25896
Volume of grey matter in vi cerebellum (left and right)	25897 and 25899
Volume of grey matter in vi cerebellum (vermis)	25898
Volume of grey matter in viia cerebellum (left and right)	25909 and 25911
Volume of grey matter in viia cerebellum (vermis)	25910
Volume of grey matter in viib cerebellum (left and right)	25912 and 25914
Volume of grey matter in viib cerebellum (vermis)	25913
Volume of grey matter in viib cerebellum (left and right)	25906 and 25908
Volume of grey matter in viib cerebellum (vermis)	25907
Volume of grey matter in ventral striatum (left and right)	25890 and 25891
Volume of grey matter in x cerebellum (left and right)	25918 and 25920
Volume of grey matter in x cerebellum (vermis)	25919

Table S5. International Classification of Disease codes used to ascertain dementia and its subtypes.

	ICD-9	ICD-10
All-cause dementia	290.2, 290.3, 290.4, 291.2, 294.1, 331.0, 331.1, 331.2, 331.5	F00, F00.0, F00.1, F00.2, F00.9, F01, F01.0, F01.1, F01.2, F01.3, F01.8, F01.9, F02, F02.0, F02.1, F02.2, F02.3, F02.4, F02.8, F03, F05.1, F10.6, G30, G30.0, G30.1, G30.8, G30.9, G31.0, A81.0, G31.1, G31.8, I67.3
Alzheimer's dementia	331.0	F00, F00.0, F00.1, F00.2, F00.9, G30, G30.0, G30.1, G30.8, G30.9
Vascular dementia	290.4	F01, F01.0, F01.1, F01.2, F01.3, F01.8, F01.9, I67.3

Table S6. Associations of air pollution exposure with dementia risk stratified by age.

Outcomes	Air Pollution	Age Group	Hazard Ratios ^a	<i>p</i> -Value ^b	<i>p</i> for Interaction ^c
All-cause dementia	PM _{2.5}	<65	1.079 (1.017, 1.146)	0.012	0.708
		≥65	1.096 (1.040, 1.155)	0.001	
	PM ₁₀	<65	1.079 (1.019, 1.143)	0.010	0.574
		≥65	1.103 (1.048, 1.160)	<0.001	
	NO ₂	<65	1.091 (1.026, 1.160)	0.006	0.724
		≥65	1.075 (1.019, 1.135)	0.009	
	NO _x	<65	1.038 (0.988, 1.092)	0.141	0.568
		≥65	1.058 (1.014, 1.104)	0.009	
Alzheimer's dementia	PM _{2.5}	<65	1.075 (0.976, 1.185)	0.143	0.498
		≥65	1.117 (1.031, 1.211)	0.007	
	PM ₁₀	<65	1.056 (0.961, 1.161)	0.260	0.301
		≥65	1.108 (1.025, 1.198)	0.010	
	NO ₂	<65	1.076 (0.973, 1.189)	0.154	0.985
		≥65	1.075 (0.989, 1.168)	0.090	
	NO _x	<65	1.039 (0.958, 1.127)	0.356	0.396
		≥65	1.077 (1.009, 1.148)	0.025	
Vascular dementia	PM _{2.5}	<65	1.156 (1.015, 1.317)	0.029	0.569
		≥65	1.114 (1.001, 1.239)	0.047	
	PM ₁₀	<65	1.149 (1.010, 1.307)	0.034	0.754
		≥65	1.120 (1.013, 1.239)	0.027	
	NO ₂	<65	1.142 (0.994, 1.311)	0.060	0.733
		≥65	1.109 (0.993, 1.239)	0.067	
	NO _x	<65	1.134 (1.025, 1.254)	0.015	0.396
		≥65	1.086 (1.000, 1.178)	0.049	

PM_{2.5}, fine particulate matter with diameter < 2.5 µm; PM₁₀, particulate matter with diameter < 10 µm; NO₂, nitrogen dioxide; NO_x, nitrogen oxides. ^a Hazard ratios were associated with per IQR increase in air pollution levels. ^b Cox proportional hazard regression models were adjusted for age, sex, ethnicity, education level, Townsend deprivation index (TDI), body mass index (BMI), smoking status, alcohol consumption, physical activity, diabetes, hypertension, and *APOE* ε4 carrier status. ^c *p* for interaction for each subgroup was calculated to evaluate comparability through the multiplicative term in the model.

Table S7. Associations of air pollution exposure with dementia risk stratified by sex.

Outcomes	Air Pollution	Sex	Hazard Ratios ^a	<i>p</i> -Value ^b	<i>p</i> for Interaction ^c
All-cause dementia	PM _{2.5}	Female	1.123 (1.054, 1.196)	<0.001	0.093
		Male	1.065 (1.011, 1.120)	0.017	
	PM ₁₀	Female	1.135 (1.068, 1.207)	<0.001	0.053
		Male	1.066 (1.014, 1.120)	0.013	
	NO ₂	Female	1.090 (1.020, 1.166)	0.011	0.754
		Male	1.078 (1.023, 1.136)	0.005	
	NO _x	Female	1.061 (1.005, 1.119)	0.033	0.396
		Male	1.042 (0.999, 1.087)	0.057	
Alzheimer's dementia	PM _{2.5}	Female	1.190 (1.084, 1.306)	<0.001	0.004
		Male	1.034 (0.950, 1.126)	0.435	
	PM ₁₀	Female	1.152 (1.051, 1.263)	0.002	0.042
		Male	1.040 (0.958, 1.130)	0.350	
	NO ₂	Female	1.082 (0.978, 1.197)	0.127	0.905
		Male	1.076 (0.988, 1.173)	0.093	
	NO _x	Female	1.092 (1.009, 1.182)	0.028	0.301
		Male	1.041 (0.971, 1.116)	0.255	
Vascular dementia	PM _{2.5}	Female	1.047 (0.899, 1.219)	0.554	0.093
		Male	1.164 (1.054, 1.286)	0.003	
	PM ₁₀	Female	1.106 (0.956, 1.279)	0.176	0.569

	Male	1.141 (1.035, 1.257)	0.008	
	Female	1.059 (0.904, 1.241)	0.476	
NO ₂	Male	1.150 (1.034, 1.278)	0.010	0.189
	Female	1.037 (0.912, 1.180)	0.578	
NO _x	Male	1.127 (1.046, 1.214)	0.002	0.065

PM_{2.5}, fine particulate matter with diameter < 2.5 µm; PM₁₀, particulate matter with diameter < 10 µm; NO₂, nitrogen dioxide; NO_x, nitrogen oxides. ^a Hazard ratios were associated with per IQR increase in air pollution levels. ^b Cox proportional hazard regression models were adjusted for age, sex, ethnicity, education level, Townsend deprivation index (TDI), body mass index (BMI), smoking status, alcohol consumption, physical activity, diabetes, hypertension, and *APOE* ε4 carrier status. ^c *p* for interaction for each subgroup was calculated to evaluate comparability through the multiplicative term in the model.

Table S8. Associations of air pollution exposure with dementia risk stratified by *APOE* ε4 carrier's status.

Outcomes	Air Pollution	<i>APOE</i> ε4	Hazard Ratios ^a	<i>p</i> -Value ^b	<i>p</i> for Interaction ^c
All-cause dementia	PM _{2.5}	Non-carrier	1.119 (1.059, 1.183)	<0.001	0.020
		carrier	1.058 (0.999, 1.120)	0.054	
	PM ₁₀	Non-carrier	1.117 (1.058, 1.180)	<0.001	0.189
		carrier	1.069 (1.013, 1.128)	0.015	
	NO ₂	Non-carrier	1.121 (1.057, 1.190)	<0.001	0.053
		carrier	1.049 (0.990, 1.112)	0.102	
	NO _x	Non-carrier	1.064 (1.016, 1.114)	0.008	0.301
		carrier	1.034 (0.986, 1.084)	0.169	
	PM _{2.5}	Non-carrier	1.106 (1.002, 1.219)	0.045	0.823
		carrier	1.094 (1.008, 1.188)	0.031	
Alzheimer's dementia	PM ₁₀	Non-carrier	1.058 (0.959, 1.168)	0.257	0.301
		carrier	1.102 (1.021, 1.191)	0.013	
	NO ₂	Non-carrier	1.035 (0.931, 1.150)	0.523	0.189
		carrier	1.104 (1.016, 1.200)	0.019	
	NO _x	Non-carrier	1.054 (0.971, 1.144)	0.208	0.823
		carrier	1.065 (0.996, 1.138)	0.065	
	PM _{2.5}	Non-carrier	1.121 (0.999, 1.257)	0.052	0.654
		carrier	1.149 (1.017, 1.298)	0.025	
	PM ₁₀	Non-carrier	1.161 (1.040, 1.296)	0.008	0.396
		carrier	1.106 (0.984, 1.243)	0.092	
Vascular dementia	NO ₂	Non-carrier	1.229 (1.089, 1.388)	0.001	0.004
		carrier	1.027 (0.904, 1.167)	0.682	
	NO _x	Non-carrier	1.106 (1.013, 1.207)	0.025	0.985
		carrier	1.107 (1.005, 1.220)	0.039	

PM_{2.5}, fine particulate matter with diameter < 2.5 µm; PM₁₀, particulate matter with diameter < 10 µm; NO₂, nitrogen dioxide; NO_x, nitrogen oxides. ^a Hazard ratios were associated with per IQR increase in air pollution levels. ^b Cox proportional hazard regression models were adjusted for age, sex, ethnicity, education level, Townsend deprivation index (TDI), body mass index (BMI), smoking status, alcohol consumption, physical activity, diabetes, hypertension, and *APOE* ε4 carrier status. ^c *p* for interaction for each subgroup was calculated to evaluate comparability through the multiplicative term in the model.

Table S9. Associations between psychological factors and incident vascular dementia risk.

Psychological Factors	Hazard Ratios	<i>p</i> -Value ^a	Adjusted <i>p</i> -Value ^b
Mood swings	1.311 (1.115, 1.541)	0.001	0.003
Miserableness	1.160 (0.982, 1.370)	0.082	0.122
Irritability	1.090 (0.911, 1.305)	0.347	0.374
Sensitivity hurt feelings	1.005 (0.856, 1.181)	0.950	0.950
Fed up feelings	1.257 (1.064, 1.485)	0.007	0.016
Nervous feelings	1.264 (1.047, 1.526)	0.015	0.026
Anxious feelings	1.137 (0.968, 1.336)	0.118	0.149
Tense /highly strung	1.181 (0.959, 1.456)	0.118	0.149
Worry too long	0.859 (0.728, 1.014)	0.072	0.116
Suffering from nerves	1.353 (1.120, 1.635)	0.002	0.004
Loneliness and isolation	1.615 (1.329, 1.962)	<0.001	<0.001
Guilty feelings	0.867 (0.714, 1.053)	0.151	0.173
Risk taking	1.086 (0.910, 1.297)	0.358	0.374
Depressed mood	1.570 (1.303, 1.892)	<0.001	<0.001
Unenthusiasm	1.433 (1.182, 1.737)	<0.001	0.001
Tenseness	1.484 (1.241, 1.773)	<0.001	<0.001
Tiredness	1.417 (1.204, 1.668)	<0.001	<0.001
Seen a doctor	1.471 (1.244, 1.739)	<0.001	<0.001
Seen a psychiatrist	1.790 (1.452, 2.206)	<0.001	<0.001
Grief and stress	1.364 (1.162, 1.602)	<0.001	0.001
Neuroticism score	1.236 (1.048, 1.457)	0.012	0.022
Able to confide	1.233 (1.051, 1.447)	0.010	0.020
Frequency of friend/family visits	0.889 (0.756, 1.044)	0.151	0.173
Leisure/social activities	1.160 (0.975, 1.381)	0.094	0.132

^a Cox proportional hazard regression models were adjusted for age, sex, ethnicity, education level, Townsend deprivation index (TDI), body mass index (BMI), smoking status, alcohol consumption, physical activity, diabetes, hypertension, and *APOE* ε4 carrier status. ^b *p*-value was corrected using false discovery rate (FDR) method.

Table S10. Associations between psychological factors and incident Alzheimer's dementia risk.

Psychological Factors	Hazard Ratios	<i>p</i> -Value ^a	Adjusted <i>p</i> -Value ^b
Mood swings	1.199 (1.061, 1.354)	0.004	0.028
Miserableness	0.967 (0.851, 1.098)	0.604	0.691
Irritability	0.940 (0.815, 1.084)	0.392	0.588
Sensitivity hurt feelings	0.959 (0.850, 1.082)	0.499	0.677
Fed up feelings	1.040 (0.915, 1.183)	0.548	0.691
Nervous feelings	1.078 (0.932, 1.247)	0.310	0.573
Anxious feelings	1.182 (1.047, 1.334)	0.007	0.042
Tense /highly strung	1.024 (0.869, 1.206)	0.776	0.835
Worry too long	0.857 (0.758, 0.970)	0.014	0.051
Suffering from nerves	1.069 (0.918, 1.244)	0.389	0.588

Loneliness and isolation	1.377 (1.182, 1.603)	<0.001	0.001
Guilty feelings	1.009 (0.879, 1.158)	0.897	0.897
Risk taking	1.038 (0.907, 1.189)	0.586	0.691
Depressed mood	1.205 (1.037, 1.400)	0.015	0.051
Unenthusiasm	1.360 (1.171, 1.580)	<0.001	0.001
Tenseness	1.182 (1.027, 1.361)	0.020	0.054
Tiredness	1.170 (1.036, 1.322)	0.011	0.051
Seen a doctor	1.090 (0.957, 1.242)	0.194	0.423
Seen a psychiatrist	1.187 (0.990, 1.424)	0.064	0.154
Grief and stress	0.984 (0.870, 1.113)	0.800	0.835
Neuroticism score	1.060 (0.935, 1.201)	0.362	0.588
Able to confide	1.157 (1.026, 1.303)	0.017	0.051
Frequency of friend/family visits	0.960 (0.851, 1.083)	0.508	0.677
Leisure/social activities	1.075 (0.940, 1.228)	0.292	0.573

^a Cox proportional hazard regression models were adjusted for age, sex, ethnicity, education level, Townsend deprivation index (TDI), body mass index (BMI), smoking status, alcohol consumption, physical activity, diabetes, hypertension, and *APOE* $\epsilon 4$ carrier status. ^b *p*-value was corrected using false discovery rate (FDR) method.

Table S11. Factor loading in confirmatory factor analysis for latent variable of air pollution, psychological factors, and brain structure.

Latent Variable	Factor	Loading	<i>p</i> -Value
Air pollution	PM _{2.5}	0.907	< 1.00×10 ⁻¹³
	PM ₁₀	0.542	< 1.00×10 ⁻¹³
	NO ₂	0.966	< 1.00×10 ⁻¹³
	NO _x	0.952	< 1.00×10 ⁻¹³
Psychological factors	Neuroticism score	0.876	< 1.00×10 ⁻¹³
	Mood swings	0.691	< 1.00×10 ⁻¹³
	Fed up feelings	0.677	< 1.00×10 ⁻¹³
	Miserableness	0.639	< 1.00×10 ⁻¹³
	Depressed mood	0.575	< 1.00×10 ⁻¹³
	Anxious feelings	0.559	< 1.00×10 ⁻¹³
	Guilty feelings	0.528	< 1.00×10 ⁻¹³
	Tenseness	0.524	< 1.00×10 ⁻¹³
	Sensitivity hurt feelings	0.523	< 1.00×10 ⁻¹³
	Unenthusiasm	0.506	< 1.00×10 ⁻¹³
	Irritability	0.495	< 1.00×10 ⁻¹³
	Nervous feelings	0.494	< 1.00×10 ⁻¹³
	Worry too long	0.491	< 1.00×10 ⁻¹³
	Tense /highly strung	0.487	< 1.00×10 ⁻¹³
	Loneliness and isolation	0.458	< 1.00×10 ⁻¹³
	Suffering from nerves	0.443	< 1.00×10 ⁻¹³
	Tiredness	0.422	< 1.00×10 ⁻¹³
	Seen a doctor	0.385	< 1.00×10 ⁻¹³
	Seen a psychiatrist	0.267	< 1.00×10 ⁻¹³
	Able to confide	0.182	< 1.00×10 ⁻¹³
	Grief and stress	0.126	< 1.00×10 ⁻¹³
	Leisure/social activities	0.060	< 1.00×10 ⁻¹³
Brain structure	Frequency of friend/family visits	0.039	4.39×10 ⁻⁷
	Risk taking	0.038	4.44×10 ⁻⁷
	Frontal pole (right)	0.857	< 1.00×10 ⁻¹³
	Frontal pole (left)	0.852	< 1.00×10 ⁻¹³

Precuneous cortex (right)	0.769	$< 1.00 \times 10^{-13}$
Precuneous cortex (left)	0.756	$< 1.00 \times 10^{-13}$
Frontal orbital cortex (right)	0.725	$< 1.00 \times 10^{-13}$
Central opercular cortex (left)	0.718	$< 1.00 \times 10^{-13}$
Precentral gyrus (left)	0.706	$< 1.00 \times 10^{-13}$
Precentral gyrus (right)	0.692	$< 1.00 \times 10^{-13}$
Temporal pole (right)	0.672	$< 1.00 \times 10^{-13}$
Temporal pole (left)	0.671	$< 1.00 \times 10^{-13}$
Temporal fusiform cortex, posterior division (left)	0.665	$< 1.00 \times 10^{-13}$
Lateral occipital cortex, superior division (right)	0.659	$< 1.00 \times 10^{-13}$
Lateral occipital cortex, superior division (left)	0.657	$< 1.00 \times 10^{-13}$
Amygdala (right)	0.654	$< 1.00 \times 10^{-13}$
Temporal fusiform cortex, posterior division (right)	0.653	$< 1.00 \times 10^{-13}$
Postcentral gyrus (left)	0.617	$< 1.00 \times 10^{-13}$
Cuneal cortex (right)	0.596	$< 1.00 \times 10^{-13}$
Occipital pole (left)	0.594	$< 1.00 \times 10^{-13}$
Occipital fusiform gyrus (left)	0.585	$< 1.00 \times 10^{-13}$
Frontal medial cortex (right)	0.521	$< 1.00 \times 10^{-13}$

PM_{2.5}, fine particulate matter with diameter $< 2.5 \mu\text{m}$; PM₁₀, particulate matter with diameter $< 10 \mu\text{m}$; NO₂, nitrogen dioxide; NO_x, nitrogen oxides.

Table S12. The Mendelian randomization estimates of bidirectional associations among psychiatric disorders, brain imaging-derived phenotypes, and dementia.

Exposure	Outcome	No. of SNPs	OR or β and 95% CI	<i>p</i> Value
Psychiatric disorders		Brain IDPs		
Anxiety disorders	GM in Hippocampus (left)	5	0.22 (0.09, 0.35)	9.83×10^{-4}
	GM in Hippocampus (right)	5	0.23 (0.07, 0.40)	5.53×10^{-3}
	GM in Postcentral Gyrus (left)	5	0.15 (0.02, 0.28)	2.44×10^{-2}
	GM in Pallidum (right)	5	-0.15 (-0.28, -0.02)	2.74×10^{-2}
	GM in in Brain-Stem	5	0.15 (0.01, 0.29)	4.16×10^{-2}
Major Depressive Disorder	GM in Precentral Gyrus (left)	5	0.16 (0.00, 0.31)	4.30×10^{-2}
	GM in Lateral Occipital Cortex, superior division (right)	72	0.08 (0.01, 0.16)	3.15×10^{-2}
	GM in Lateral Occipital Cortex, superior division (left)	72	0.07 (0.01, 0.14)	3.17×10^{-2}
	GM in V Cerebellum (right)	72	-0.09 (-0.17, -0.01)	3.58×10^{-2}
	GM in VI Cerebellum (vermis)	72	-0.09 (-0.18, 0.00)	4.67×10^{-2}
Anorexia Nervosa	GM in Superior Temporal Gyrus, anterior division (right)	5	0.05 (0.01, 0.09)	1.92×10^{-2}
	GM in Middle Frontal Gyrus (left)	5	0.05 (0.00, 0.09)	3.21×10^{-2}
	GM in Planum Polare (right)	5	0.05 (0.00, 0.09)	3.65×10^{-2}
	GM in Inferior Frontal Gyrus, pars opercularis (left)	5	0.05 (0.00, 0.09)	4.09×10^{-2}
	GM in Supramarginal Gyrus, anterior division (right)	5	-0.05 (-0.11, 0.00)	4.36×10^{-2}
Bipolar disorder	GM in Parietal Operculum Cortex (right)	5	-0.04 (-0.09, 0.00)	4.81×10^{-2}
	GM in Supracalcarine Cortex (left)	5	-0.04 (-0.09, 0.00)	4.91×10^{-2}
	GM in Lateral Occipital Cortex, inferior division (left)	108	0.05 (0.02, 0.08)	2.57×10^{-4}
	GM in X Cerebellum (right)	108	-0.05 (-0.08, -0.01)	9.74×10^{-3}
	GM in Subcallosal Cortex (right)	108	0.04 (0.00, 0.07)	2.60×10^{-2}
	GM in Middle Temporal Gyrus, temporooccipital part (right)	108	0.03 (0.00, 0.06)	2.89×10^{-2}
	GM in Middle Temporal Gyrus, posterior division (right)	108	0.03 (0.00, 0.06)	3.18×10^{-2}
	GM in Postcentral Gyrus (left)	108	-0.03 (-0.07, 0.00)	3.39×10^{-2}
	GM in Inferior Temporal Gyrus, temporooccipital part (right)	108	0.03 (0.00, 0.06)	4.14×10^{-2}
	GM in Cingulate Gyrus, posterior division (right)	108	0.03 (0.00, 0.07)	4.58×10^{-2}
Schizophrenia	GM in Lateral Occipital Cortex, superior division (left)	108	0.03 (0.00, 0.06)	4.86×10^{-2}
	GM in Juxtapositional Lobule Cortex (left)	290	0.02 (0.01, 0.04)	1.10×10^{-2}
	GM in Superior Parietal Lobule (left)	290	0.02 (0.00, 0.04)	1.52×10^{-2}
	GM in Precuneous Cortex (right)	290	0.02 (0.00, 0.04)	4.34×10^{-2}
Psychiatric disorders		Dementia		
Bipolar disorder	All-cause dementia	103	1.05 (1.01, 1.10)	1.76×10^{-2}

Schizophrenia	All-cause dementia	285	1.07 (1.04, 1.10)	1.39×10^{-5}
Brain IDPs	Psychiatric disorders			
GM in Crus II Cerebellum (vermis)	Anxiety disorders	35	0.92 (0.85, 1.00)	4.95×10^{-2}
GM in Caudate (right)	Anxiety disorders	35	1.12 (1.03, 1.22)	8.59×10^{-3}
GM in Thalamus (right)	Anxiety disorders	28	1.17 (1.06, 1.30)	3.11×10^{-3}
GM in Thalamus (left)	Anxiety disorders	38	1.10 (1.01, 1.19)	2.24×10^{-2}
GM in Heschl's Gyrus (right)	Anxiety disorders	15	1.21 (1.04, 1.40)	1.18×10^{-2}
GM in Cuneal Cortex (right)	Anxiety disorders	9	1.23 (1.03, 1.46)	1.94×10^{-2}
GM in Paracingulate Gyrus (left)	Anxiety disorders	15	0.79 (0.67, 0.93)	5.11×10^{-3}
GM in Superior Temporal Gyrus, posterior division (left)	Anxiety disorders	6	0.71 (0.55, 0.94)	1.47×10^{-2}
GM in IX Cerebellum (left)	Anorexia Nervosa	41	1.26 (1.02, 1.57)	3.27×10^{-2}
GM in VIIb Cerebellum (left)	Anorexia Nervosa	42	1.27 (1.05, 1.55)	1.61×10^{-2}
GM in Parahippocampal Gyrus, posterior division (left)	Anorexia Nervosa	15	0.71 (0.51, 0.98)	3.95×10^{-2}
GM in Paracingulate Gyrus (left)	Anorexia Nervosa	13	1.54 (1.05, 2.28)	2.83×10^{-2}
GM in Amygdala (left)	Bipolar disorder	15	0.86 (0.76, 0.98)	2.43×10^{-2}
GM in Heschl's Gyrus (left)	Bipolar disorder	13	0.72 (0.54, 0.95)	1.99×10^{-2}
GM in Cingulate Gyrus, anterior division (left)	Bipolar disorder	9	1.24 (1.04, 1.48)	1.92×10^{-2}
GM in Paracingulate Gyrus (left)	Bipolar disorder	12	1.25 (1.06, 1.46)	5.96×10^{-3}
GM in Supramarginal Gyrus, anterior division (left)	Bipolar disorder	5	1.22 (1.03, 1.45)	2.07×10^{-2}
GM in Inferior Temporal Gyrus, posterior division (right)	Bipolar disorder	9	1.20 (1.00, 1.43)	4.79×10^{-2}
GM in Ventral Striatum (right)	Schizophrenia	31	1.14 (1.01, 1.28)	3.20×10^{-2}
GM in Ventral Striatum (left)	Schizophrenia	34	1.14 (1.02, 1.27)	2.24×10^{-2}
GM in amygdala (right)	Schizophrenia	15	0.86 (0.76, 0.97)	1.72×10^{-2}
GM in amygdala (left)	Schizophrenia	17	0.87 (0.77, 0.98)	2.73×10^{-2}
GM in putamen (right)	Schizophrenia	31	1.14 (1.01, 1.29)	3.07×10^{-2}
GM in putamen (left)	Schizophrenia	40	1.12 (1.02, 1.24)	2.37×10^{-2}
GM in Caudate (right)	Schizophrenia	32	1.19 (1.04, 1.35)	8.76×10^{-3}
GM in Caudate (left)	Schizophrenia	34	1.21 (1.06, 1.37)	3.44×10^{-3}
GM in Supracalcarine Cortex (left)	Schizophrenia	21	1.15 (1.01, 1.31)	3.69×10^{-2}
GM in Central Opercular Cortex (left)	Schizophrenia	9	0.77 (0.67, 0.88)	1.66×10^{-4}

GM in Frontal Operculum Cortex (right)	Schizophrenia	11	0.90 (0.81, 1.00)	4.63×10^{-2}
GM in Frontal Operculum Cortex (left)	Schizophrenia	10	0.80 (0.70, 0.91)	6.59×10^{-4}
GM in Occipital Fusiform Gyrus (left)	Schizophrenia	9	1.18 (1.05, 1.32)	5.42×10^{-3}
GM in Temporal Occipital Fusiform Cortex (left)	Schizophrenia	14	1.11 (1.01, 1.23)	3.46×10^{-2}
GM in Temporal Fusiform Cortex, anterior division (left)	Schizophrenia	2	0.75 (0.58, 0.97)	3.03×10^{-2}
GM in Parahippocampal Gyrus, posterior division (right)	Schizophrenia	22	1.18 (1.00, 1.39)	4.81×10^{-2}
GM in Juxtapositional Lobule Cortex (right)	Schizophrenia	5	0.74 (0.63, 0.88)	5.64×10^{-4}
GM in Juxtapositional Lobule Cortex (left)	Schizophrenia	2	0.54 (0.37, 0.80)	1.83×10^{-3}
GM in Supramarginal Gyrus, posterior division (left)	Schizophrenia	6	0.72 (0.60, 0.86)	2.45×10^{-4}
GM in Inferior Temporal Gyrus, anterior division (right)	Schizophrenia	6	0.79 (0.68, 0.91)	1.15×10^{-3}
GM in Middle Temporal Gyrus, temporooccipital part (right)	Schizophrenia	5	1.22 (1.02, 1.45)	2.71×10^{-2}
GM in Superior Frontal Gyrus (right)	Schizophrenia	6	0.79 (0.65, 0.97)	2.30×10^{-2}
GM in Insular Cortex (right)	Schizophrenia	32	0.85 (0.77, 0.93)	1.02×10^{-3}
Brain IDPs	Dementia			
GM in Heschl's Gyrus (right)	All-cause dementia	15	1.34 (1.16, 1.55)	8.73×10^{-5}
GM in Caudate (left)	All-cause dementia	33	1.22 (1.10, 1.35)	1.46×10^{-4}
GM in VI Cerebellum (vermis)	All-cause dementia	31	0.83 (0.76, 0.91)	6.34×10^{-5}
GM in IX Cerebellum (left)	All-cause dementia	41	1.12 (1.04, 1.22)	5.02×10^{-3}
GM in IX Cerebellum (right)	All-cause dementia	38	1.15 (1.05, 1.25)	1.87×10^{-3}
GM in Middle Frontal Gyrus (right)	All-cause dementia	13	0.75 (0.64, 0.89)	1.03×10^{-3}
GM in Middle Temporal Gyrus, posterior division (left)	All-cause dementia	8	1.36 (1.10, 1.68)	5.23×10^{-3}
GM in Superior Parietal Lobule (left)	All-cause dementia	5	1.51 (1.19, 1.92)	8.22×10^{-4}

GM in Paracingulate Gyrus (right)	All-cause dementia	4	0.59 (0.43, 0.82)	1.39×10^{-3}
GM in Cingulate Gyrus, anterior division (right)	All-cause dementia	9	1.48 (1.24, 1.77)	1.57×10^{-5}
GM in Cingulate Gyrus, posterior division (right)	All-cause dementia	12	1.34 (1.09, 1.64)	4.99×10^{-3}

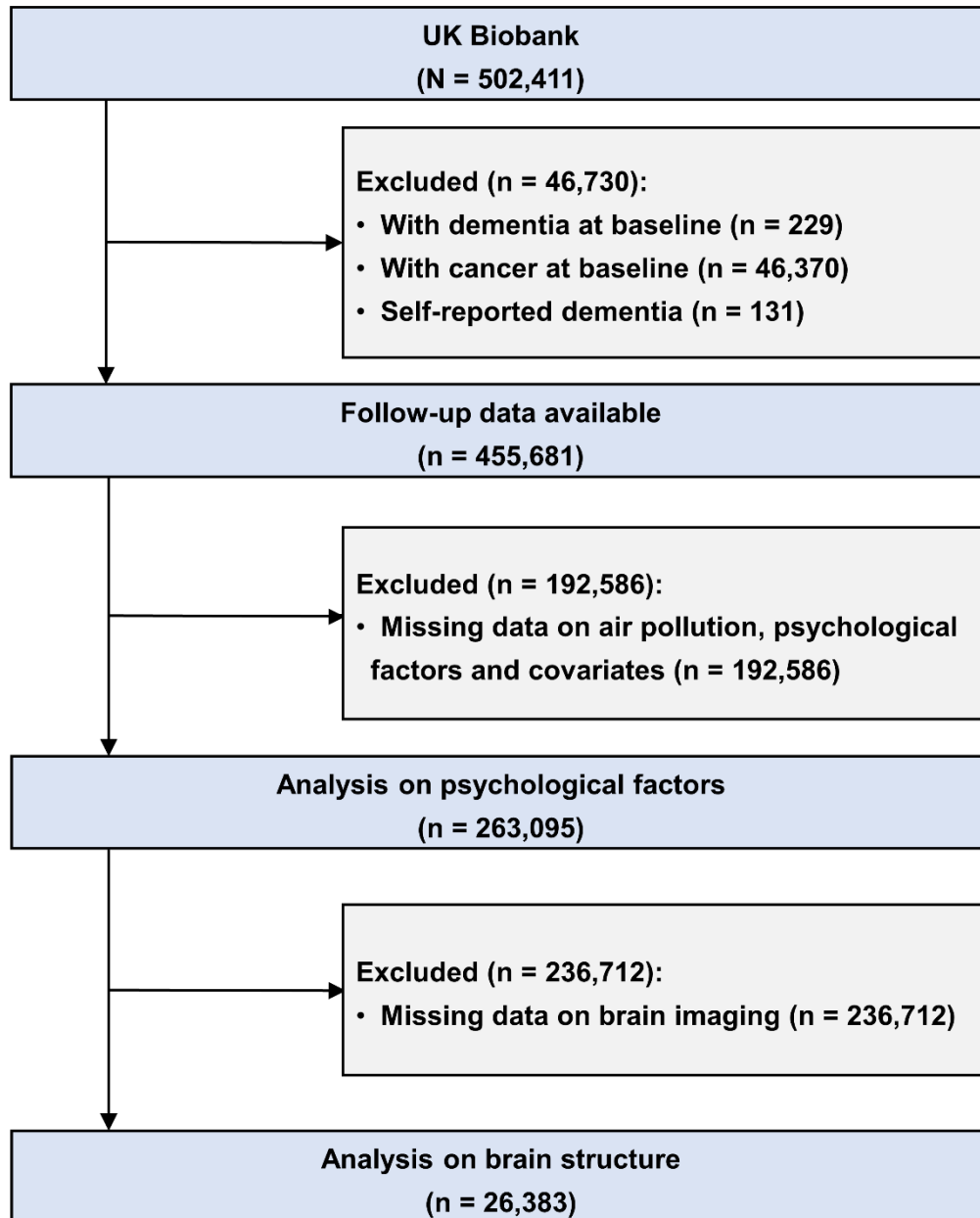


Figure S1. The flowchart of the UK biobank participants included and excluded in the current analysis.

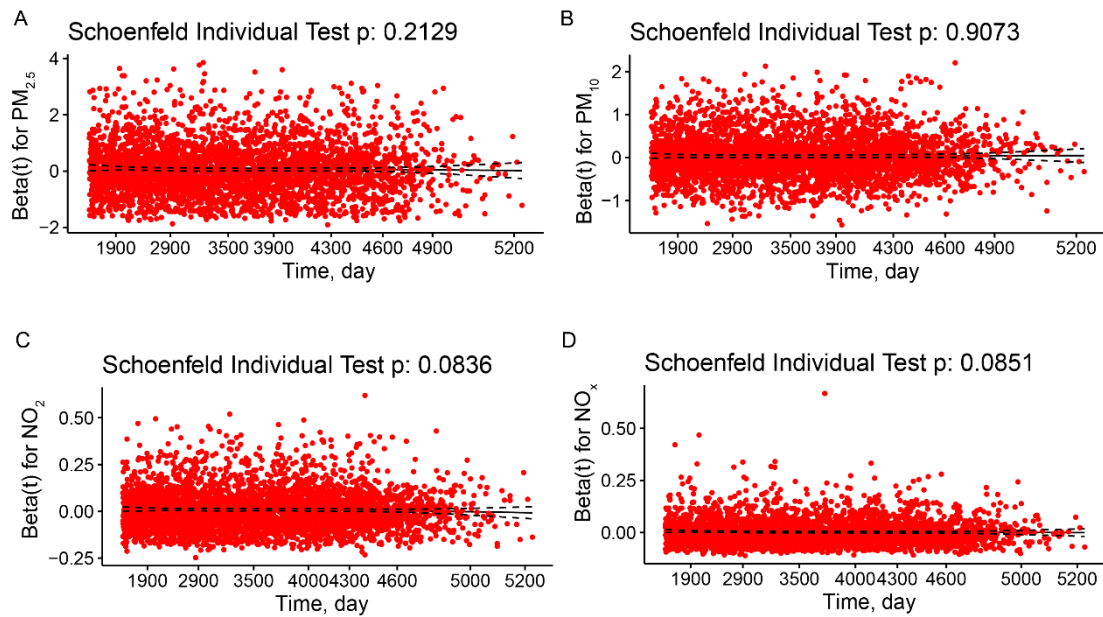


Figure S2. Diagnostic plot for cox model proportional hazards assumption.

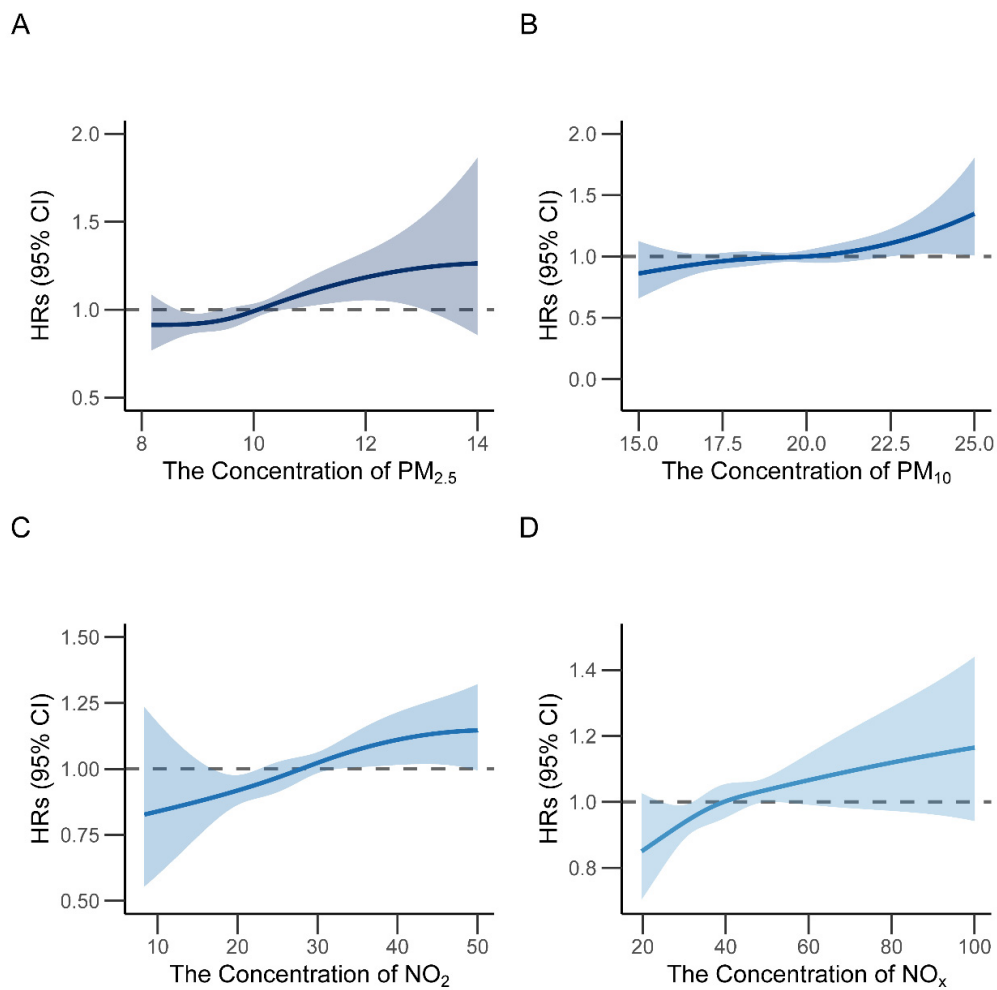


Figure S3. The exposure-response relationship between air pollution exposure and Alzheimer's dementia. $PM_{2.5}$, fine particulate matter with diameter $< 2.5 \mu m$; PM_{10} , particulate matter with diameter

< 10 μm ; NO_2 , nitrogen dioxide; NO_x , nitrogen oxides. HRs, hazard ratios; CIs, confidence intervals. Models adjusted for age, sex, ethnicity, education level, Townsend deprivation index (TDI), body mass index (BMI), smoking status, alcohol consumption, physical activity, diabetes, hypertension, and *APOE* $\epsilon 4$ carrier status.

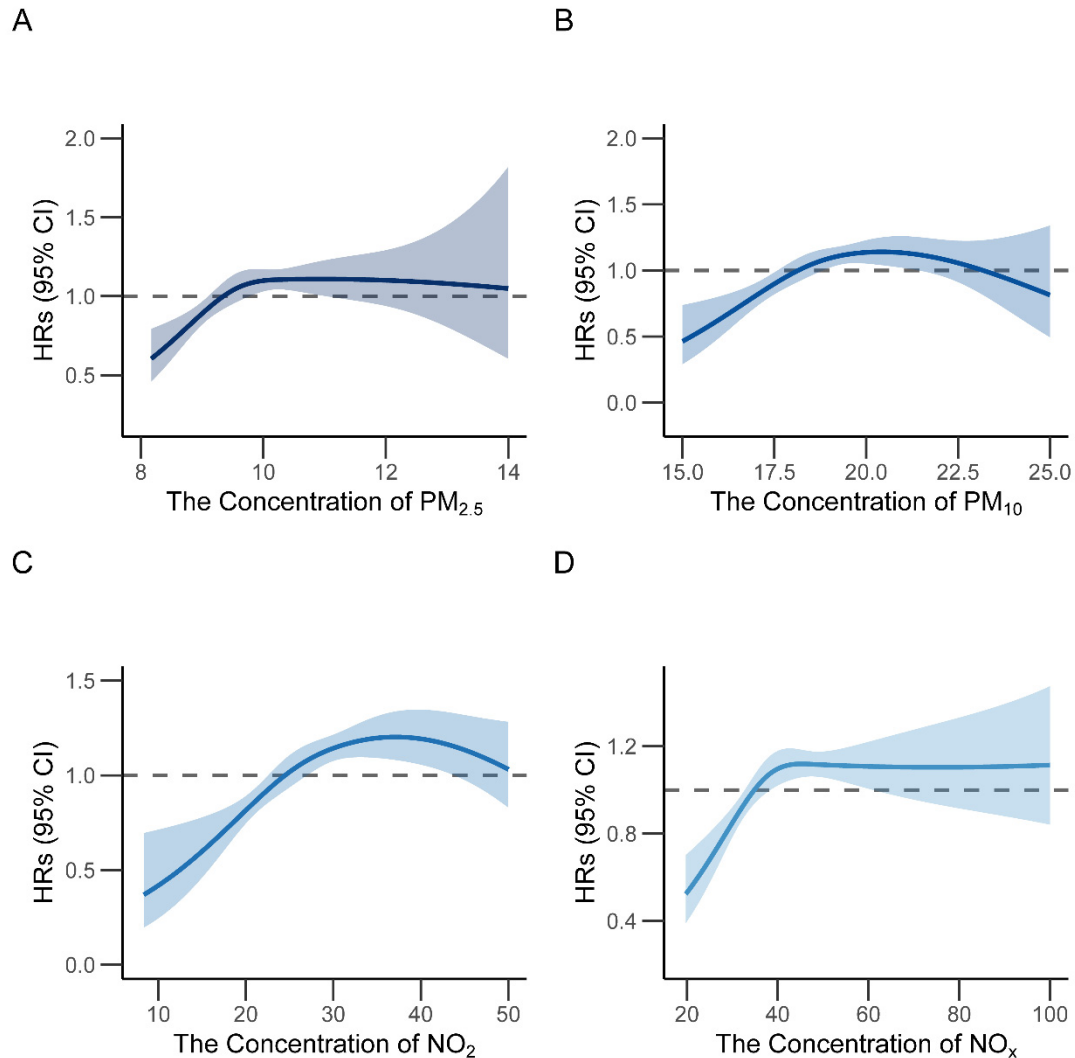


Figure S4. The exposure-response relationship between air pollution exposure and vascular dementia. $\text{PM}_{2.5}$, fine particulate matter with diameter < 2.5 μm ; PM_{10} , particulate matter with diameter < 10 μm ; NO_2 , nitrogen dioxide; NO_x , nitrogen oxides. HRs, hazard ratios; CIs, confidence intervals. Models adjusted for age, sex, ethnicity, education level, Townsend deprivation index (TDI), body mass index (BMI), smoking status, alcohol consumption, physical activity, diabetes, hypertension, and *APOE* $\epsilon 4$ carrier status.

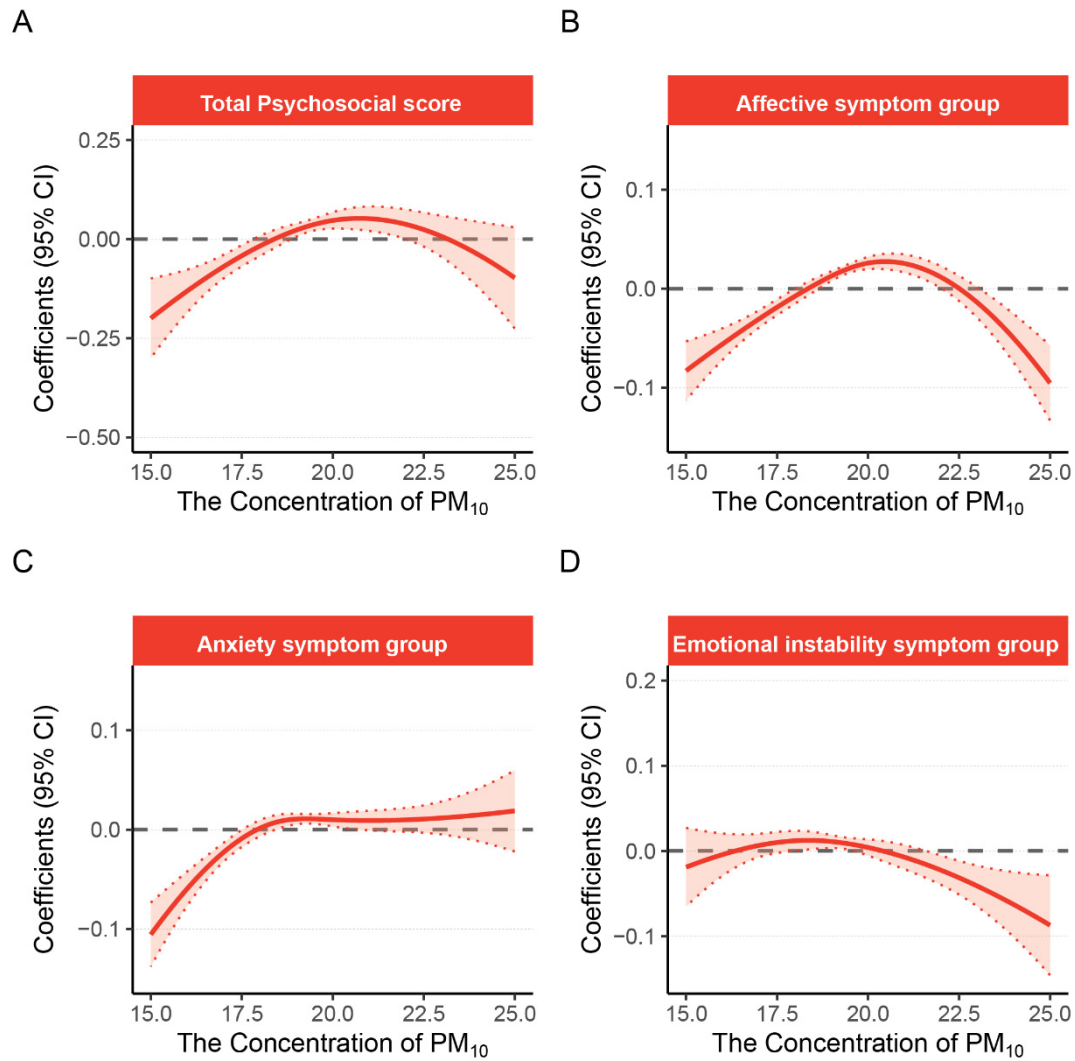


Figure S5. The exposure-response relationship between PM_{10} exposure and psychological group scores. PM_{10} , particulate matter with diameter $< 10 \mu m$; HRs, CIs, confidence intervals. Models adjusted for age, sex, ethnicity, education level, Townsend deprivation index (TDI), body mass index (BMI), smoking status, alcohol consumption, physical activity, diabetes, and hypertension.

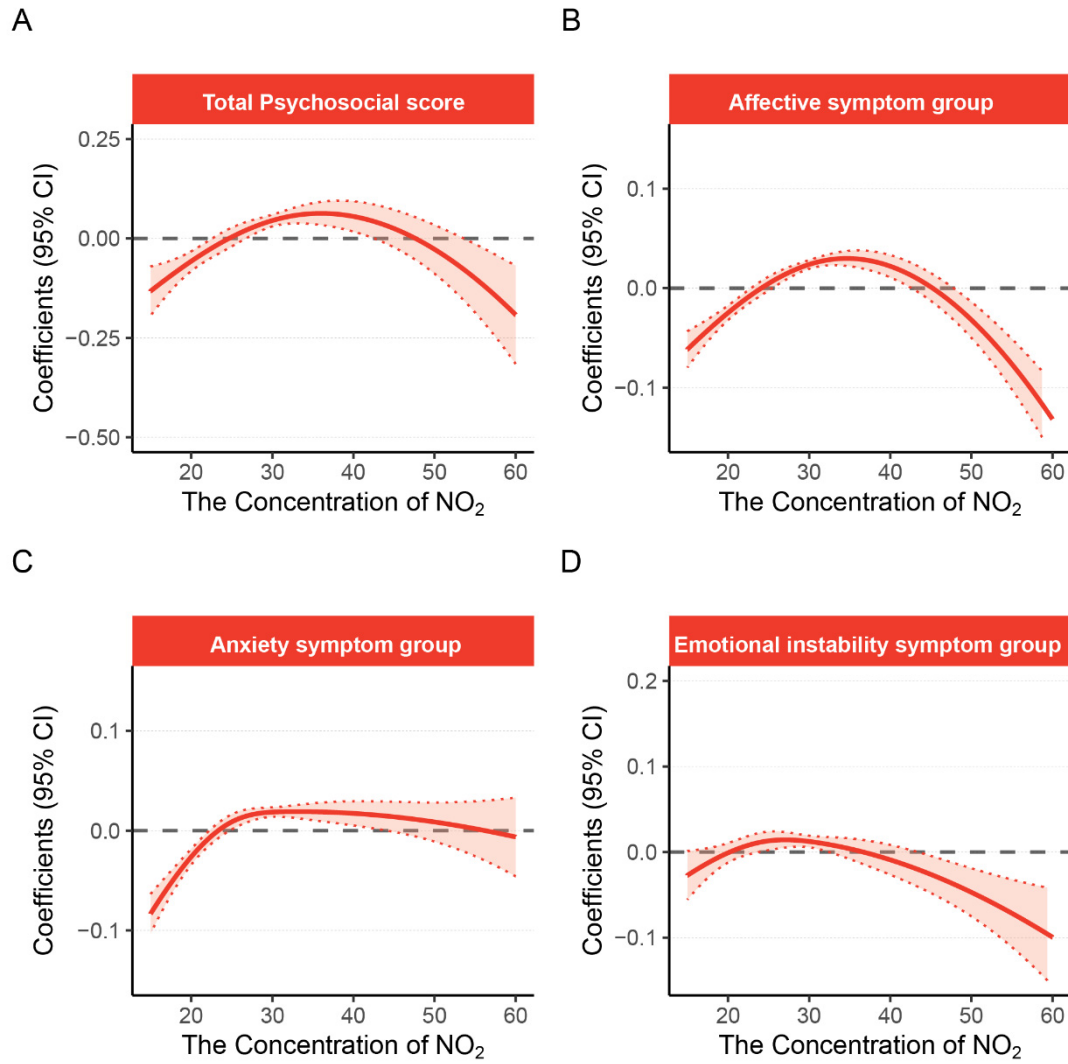


Figure S6. The exposure-response relationship between NO_2 exposure and psychological group scores. NO_2 , nitrogen dioxide; CIs, confidence intervals. Models adjusted for age, sex, ethnicity, education level, Townsend deprivation index (TDI), body mass index (BMI), smoking status, alcohol consumption, physical activity, diabetes, and hypertension.

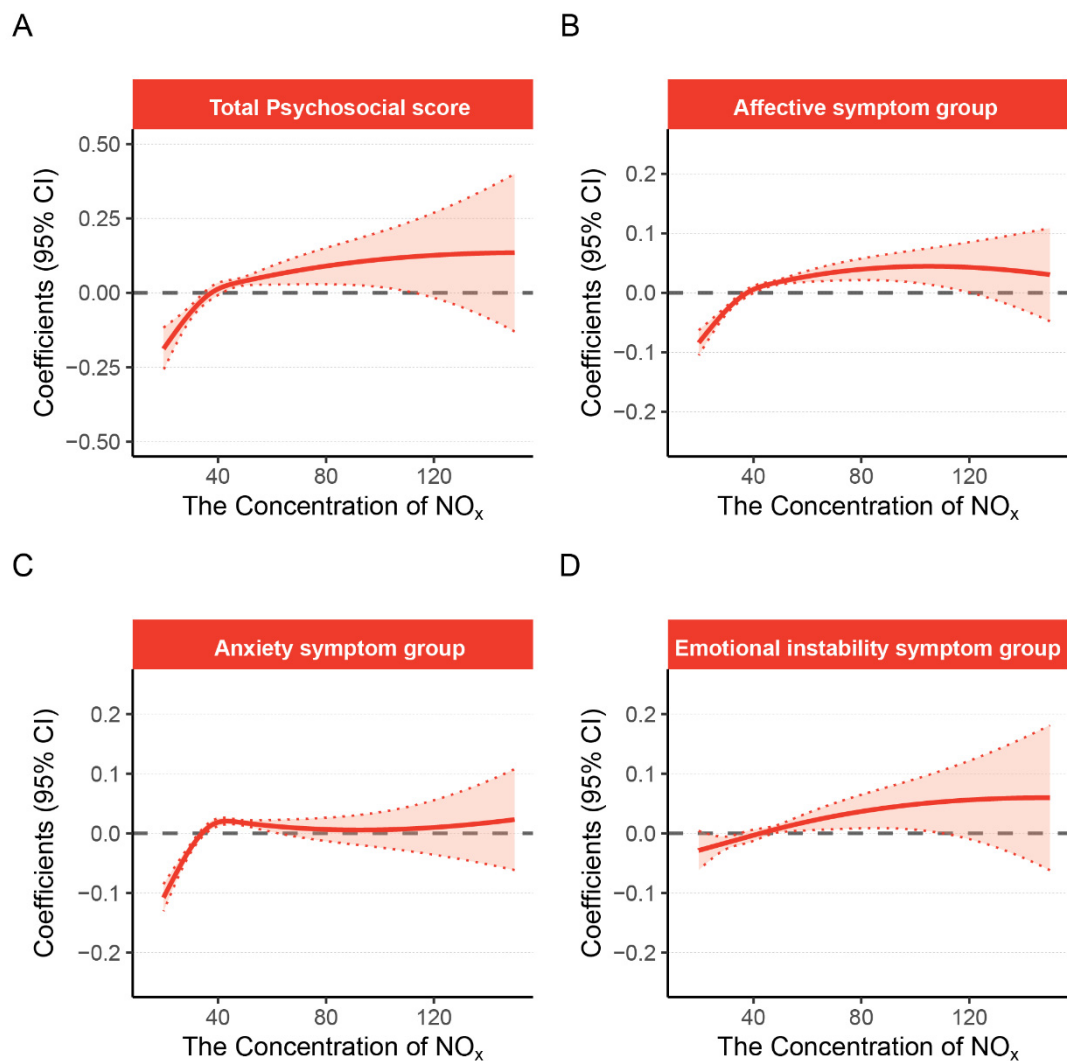


Figure S7. The exposure-response relationship between NO_x exposure and psychological group scores. NO_x , nitrogen oxides; CIs, confidence intervals. Models adjusted for age, sex, ethnicity, education level, Townsend deprivation index (TDI), body mass index (BMI), smoking status, alcohol consumption, physical activity, diabetes, and hypertension.

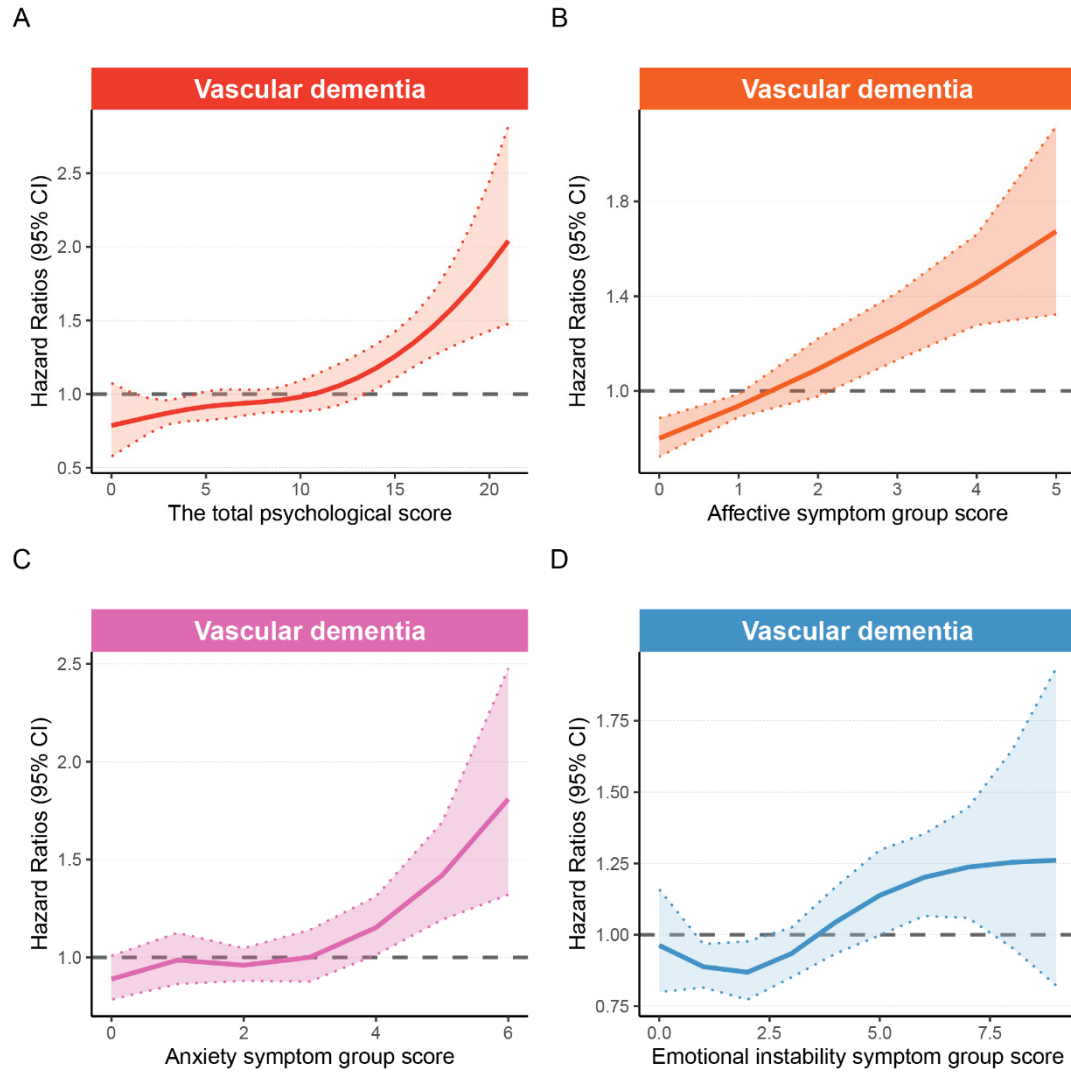


Figure S8. The exposure-response relationship between psychological group score and vascular dementia. HRs, hazard ratios; CIs, confidence intervals. Models adjusted for age, sex, ethnicity, education level, Townsend deprivation index (TDI), body mass index (BMI), smoking status, alcohol consumption, physical activity, diabetes, hypertension, and *APOE* $\epsilon 4$ carrier status.

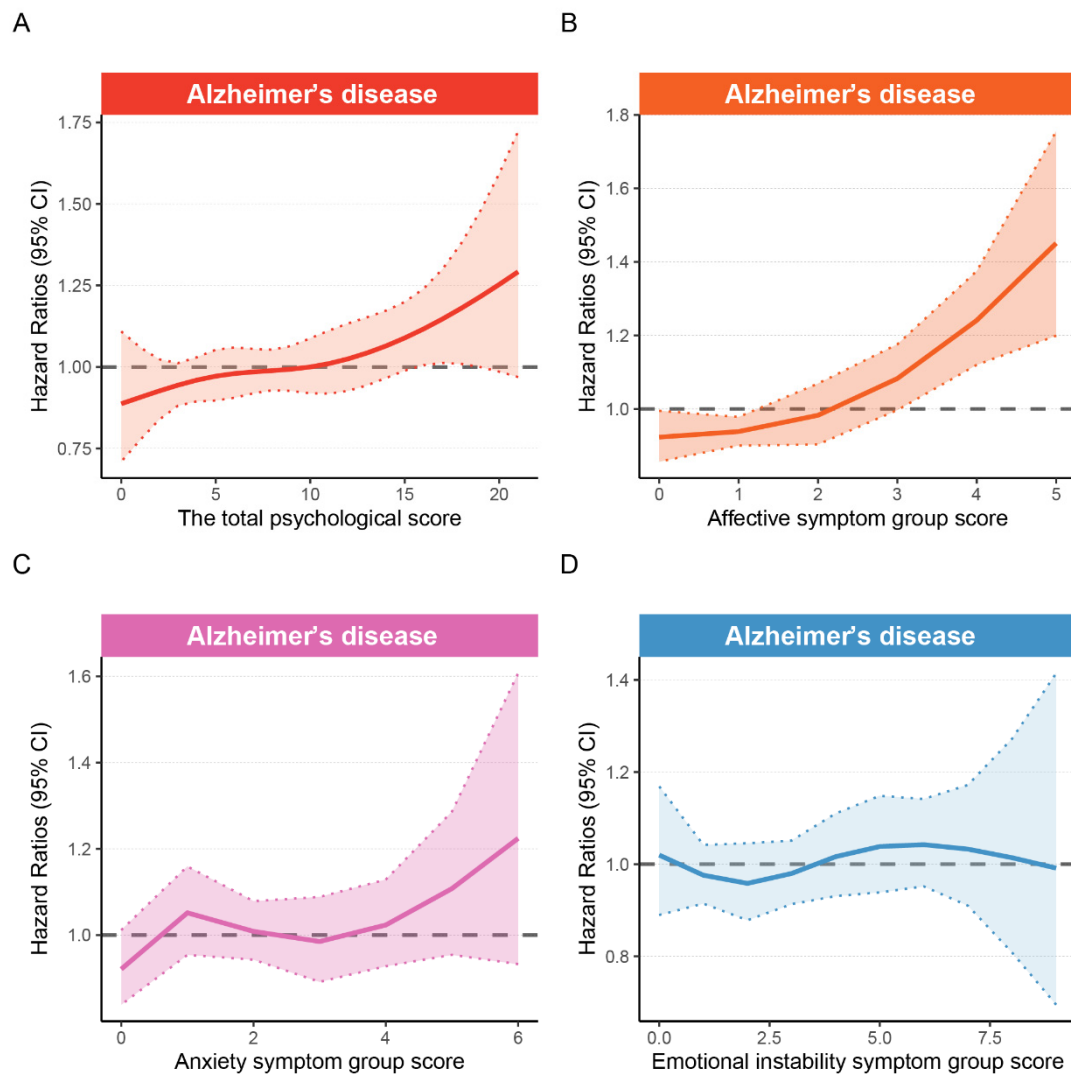


Figure S9. The exposure-response relationship between psychological group score and Alzheimer's dementia. HRs, hazard ratios; CIs, confidence intervals. Models adjusted for age, sex, ethnicity, education level, Townsend deprivation index (TDI), body mass index (BMI), smoking status, alcohol consumption, physical activity, diabetes, hypertension, and *APOE* $\epsilon 4$ carrier status.

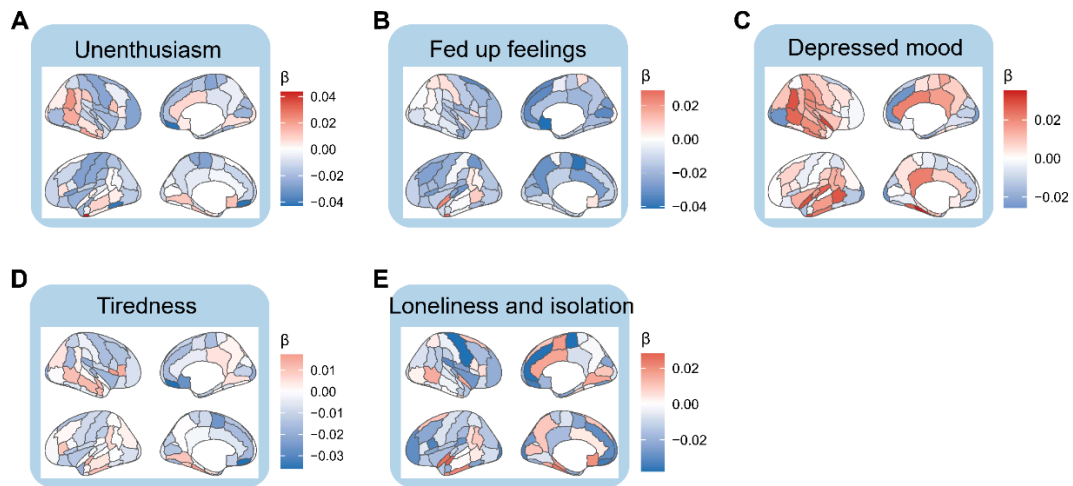


Figure S10. The association of affective symptom factors with brain structures. Tested using a linear regression model. Data are presented as β values.

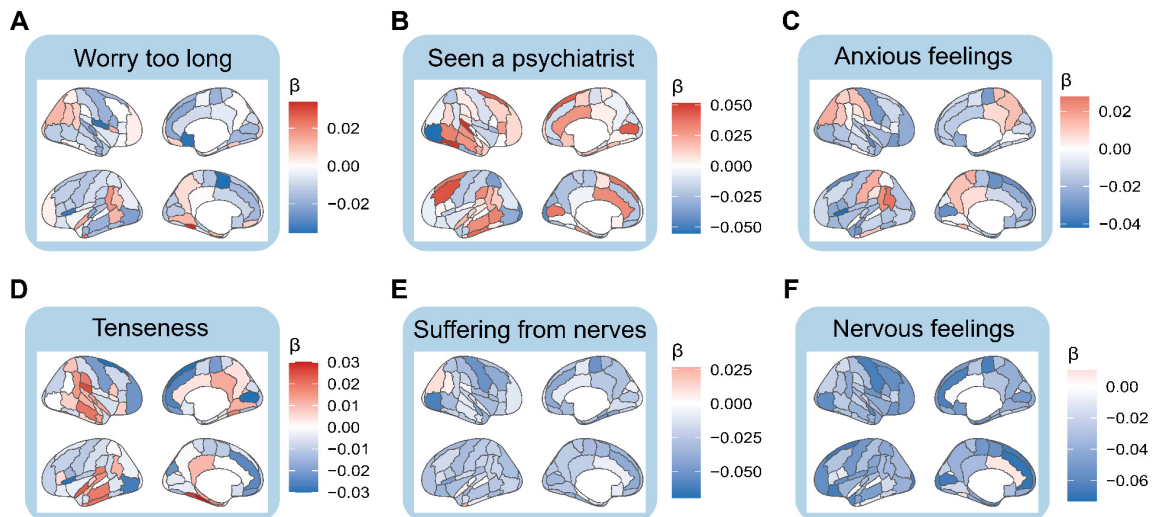


Figure S11. The association of anxiety symptom factors with brain structures. Tested using a linear regression model. Data are presented as β values.

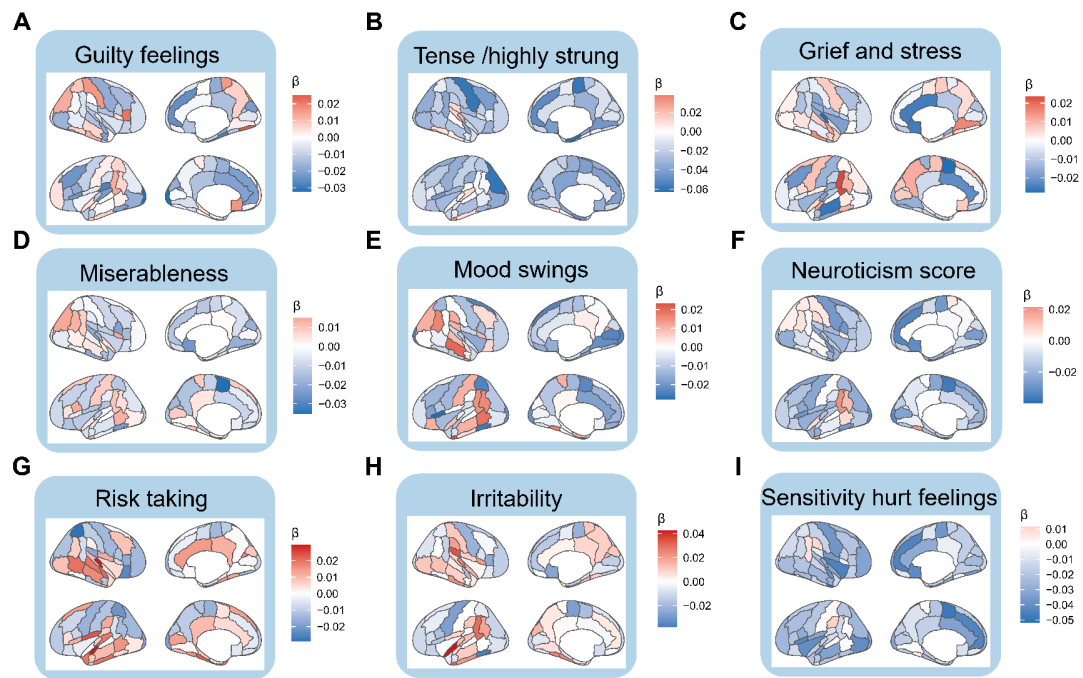


Figure S12. The association of emotional instability symptom factors with brain structures. Tested using a linear regression model. Data are presented as β values.

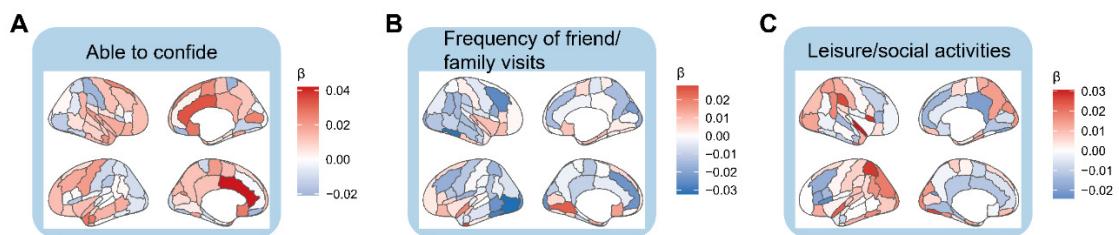


Figure S13. The association of other psychological factors with brain structures. Tested using a linear regression model. Data are presented as β values.