Supplementary materials

Text

Table of contents

Text S1. The model assumptions of causal mediation analyses

We used PROC CAUCALMED in SAS to perform causal mediation analyses. The methods for causal mediation analysis yield valid inferences for natural direct and natural indirect effects under the assumptions that the measured covariates control for confounding of the (1) exposure – outcome, (2) mediator – outcome, and (3) exposure – mediator relations, and (4) that none of the mediator – outcome confounders are affected by the exposure [1,2]. In addition, this method has been widely applied in epidemiological research [3,4]. In this study, the model assumptions included no unmeasurable confounders of the associations between residential greenness and epilepsy incidence, between air pollutants and epilepsy incidence, between residential greenness and air pollutants, and that residential greenness did not cause any confounder of the association between air pollutants and epilepsy incidence.

Reference

1. Pearl J. Interpretation and identification of causal mediation. *Psychol Methods* 2014; **19**(4): 459-81.
2. Valeri L, VanderWeele TJ. SAS macro for causal mediation analysis with survival data. *Epidemiology* 2015; **26**(2): e23-4.
3. Qin XD, Zhou Y, Bloom MS, et al. Prenatal Exposure to PFAS, Associations with Preterm Birth and Modification by Maternal Estrogen Levels: The Maoming Birth Study. *Environ Health Perspect* 2023; **131**(11): 117006.
4. Zhang B, Langa KM, Weuve J, et al. Hypertension and Stroke as Mediators of Air Pollution Exposure and Incident Dementia. *JAMA network open* 2023; **6**(9): e2333470.

Text S2 Measurement of time-varying residential greenness and air pollution

Average residential greenness exposures for each participant during follow-up were estimated from the same data sources as the main analysis. We also captured data from the Department for Environment, Food and Rural Affairs (DEFRA) on average annual concentrations of air pollutants from 2006 to 2021. DEFRA provided high-resolution data on near-surface air pollution in the UK (https://uk-air.defra.gov.uk/), which was widely used in existing publications [1-3]. This platform generates annual concentration maps of air pollutants at a 1 × 1 km resolution by utilizing an air dispersion model. This model integrates data from the National Atmospheric Emissions Inventory, measurements of secondary inorganic aerosol, and models for sources such as dust resuspension. DEFRA conducted a series of comparisons of simulated and measured annual average air pollutants to ensure the reliability of the model. The result suggested great model's performance, which can be available at https://uk-air.defra.gov.uk/data/pcm-data. According to a unique code (ukgridcode) for each 1 × 1 km cell in the annual concentration map, we estimated NO_2, NO_x, $PM_{2.5}$, and PM_{10} concentrations based on the postcode of dynamic residential addresses during follow-up in the UK Biobank, which has been published in the *European Heart Journal* [3].

To construct the 1-year time-varying variable, each observation was divided into multiple records by year (from wide data to long data) to analyze the Cox model with time-varying variables. For example, participant No.X was followed up from June 14, 2006 to June 31, 2021. Table A1 presents the wide data of participant No.X, which is transformed to long data of 16 records by year, as shown in Table A2. The long data were used to calculate the time-varying Cox model.

Table A1. Wide data of included participants (Example).

ID	Start time	End time	Average concentration of residential greenness and air pollution			
			2006	2007	…	2021
No.X	2006-06-14	2021-06-31	C1	C2	…	C16
…	…	…	…	…	…	…

Note: C1, C2 and C3 denote the air pollutant concentrations for the corresponding years.

Table A2. Long data of included participants (Example).

No. of records	ID	Start time	End time	Concentration of residential greenness and air pollution
1	No.X	2006-04-10	2006-12-31	C1
2	No.X	2006-12-31	2007-12-31	C2
3	No.X	2007-12-31	2008-12-31	C3
…	…	…	…	…
16	No.X	2019-12-31	2020-12-31	C16
17	No.X	2020-12-31	2021-06-31	C17

Reference

1. Hill W, Lim EL, Weeden CE, et al. Lung adenocarcinoma promotion by air pollutants. *Nature*. 2023;616(7955):159-167.
2. Wu Y, Zhang S, Qian SE, et al. Ambient air pollution associated with incidence and dynamic progression of type 2 diabetes: a trajectory analysis of a population-based cohort. *BMC Med*. 2022;20(1):375.
3. Ma Y, Li D, Cui F, et al. Air pollutants, genetic susceptibility, and abdominal aortic aneurysm risk: a prospective study. *Eur Heart J*. 2024.

Table S1. Codes used in the UK Biobank to exclude identifiable secondary causes of epilepsy at baseline.

Medical condition	Self-reported medical condition codes (Field 20002)	UK Biobank ICD-9 code	UK Biobank ICD-10 code	First occurrences	Operative procedures - OPCS4 (Field 41272)
Head injury	'1266','1433','1626'	"800","8000","8001","8002","8003","801","8010","8011","803","8030","8031","920","9209","925","9259"	"S00","S000","S007","S008","S009","S01","S010","S017","S018","S019","S02","S020","S0200","S0201","S021","S027","S0270","S0271","S028","S0280","S0281","S029","S0290","S0291","S033","S04","S040","S041","S042","S043","S045","S048","S049","S06","S060","S0600","S0601","S062","S0620","S0621","S063","S0630","S0631","S064","S0640","S0641","S065","S0650","S0651","S066","S0660","S0661","S067","S0670","S068","S0680","S0681","S069","S0690","S0691","S07","S070","S079","S08","S080","S088","S089","S09","S090","S091","S097","S098","S099"	-	-
Brain infection diseases including encephalitis, meningitis, and cerebral parasitic disease	'1245','1246','1247'	"013","0130","045","0459","047","0479","048","0489","049","0490","0531","0543","0721","138","1389","1390","320","3202","3204","3205","3207","321","3215","3216","3217","322","3220","3229","323","3232","3234","3236","3239","324","3240"	"A17","A170","A178","A39","A390","A391","A392","A394","A398","A399","A80","A803","A809","A81","A810","A812","A818","A819","A82","A821","A83","A838","A839","A84","A841","A849","A85","A850","A858","A86","A87","A870","A871","A872","A878","A879","A88","A881","A888","A89","B010","B011","B020","B021","B022","B220","G00","G000","G001","G002","G003","G008","G009","G01","G02","G020","G021","G03","G030","G031","G032","G038","G039","G04","G040","G042","G048","G049","G05","G050","G051","G052","G058","G06","G060","G061","G062","G07","G08","G09"	130992,130993,130994,130995,130996,130997,130998,130999,131000,131001,131002,131003,131004,131005,131006,131007,131008,131009,131010,131011,130140,130141,130142,130143,130144,130145,130146,130147,130148,130149	-
Benign and malignant tumors of brain and meninges	20002: "1659","1238"; 20001: "1031","1032";	"191","1913","1916","1919","1983",'225','2251','2252','2253','2254','2370','2371','2375','2377','2396','2397'	"C70","C700","C701","C709","C71","C710","C711","C712","C713","C714","C715","C716","C717","C718","C719",'C722','C723','C724','C725','C728','C751','C753','C793','C794','D32','D320','D321','D329','D33','D330','D331','D332','D333','D334','D337','D339','D352','D354','D42','D420','D421','D429','D43','D430','D431','D432','D433','D434','D437','D439','D443','D445'	-	-

Brain surgery	-	-	-	-	"A01","A011","A012","A013","A018","A019","A02","A021","A022","A023","A024","A025","A026","A027","A028","A029","A03","A031","A032","A033","A034","A038","A039","A04","A041","A042","A043","A044","A045","A046","A048","A049","A05","A051","A052","A053","A054","A058","A059","A06","A061","A062","A063","A064","A068","A069","A07","A071","A072","A073","A074","A075","A076","A077","A078","A079","A08","A081","A082","A083","A084","A085","A086","A088","A089","A09","A091","A092","A093","A094","A095","A098","A099","A10","A101","A102","A103","A104","A105","A106","A107","A108","A109","A11","A111","A112","A113","A114","A118","A119","A12","A121","A122","A123","A124","A125","A128","A129","A13","A131","A132","A133","A134","A138","A139","A14","A141","A142","A143","A144","A145","A148","A149","A16","A161","A168","A169","A17","A171","A172","A178","A179","A18","A181","A188","A189","A20","A201","A202","A203","A208","A209","A22","A221","A222","A223","A228","A229","A38","A381","A382","A383","A384","A385","A386","A388","A389","A39","A391","A392","A393","A394","A395","A398","A399","A40","A401","A408","A409","A41","A411","A412","A418","A419","A42","A421","A422","A428","A429","A51","A511","A512","A513","A514","A515","A518","A519","A531","B02","B021","B022","B023","B028","B029","B01","B011","B012","B013","B014","B018","B019","B04","B041","B042","B043","B044","B045","B048","B049","B06","B061","B068","B069","O05","O051","O052","O053","O058","O059","O28","O281","O288","O289","O33","O331","O338","O339","V01","V011","V012","V013","V014","V015","V016","V017","V018","V019","V02","V021","V022","V023","V028","V029","V03","V031","V032","V033","V034","V035","V036","V037","V038","V039","V04","V041","V048","V049","V05","V051","V052","V053","V054","V055","V056","V057","V058","V059","V12","V121","V122","V123","V124","V125","V128","V129","Y462","Y463","Y464","Y465","Y466","Y467","Y468","Y469","Y472","Y473","Y474","Y475","Y476","Y478","Y479","Z01","Z011","Z012","Z013","Z014","Z015","Z016","Z017","Z018","Z019","Z02","Z021","Z022","Z023","Z024","Z028","Z029","Z05","Z051","Z052","Z053","Z054","Z055","Z056","Z057","Z058","Z059"

Table S2. Codes used to identify epilepsy including incident and baseline cases.

Medical condition	First occurrences	Antiepileptic Drugs	ICD-9 code	ICD-10 code
Epilepsy	131048,131049,131050 ,131051	"1140909812","1140910706","1141181616","1140872132","1140872098","2038460076","1140872160","1140872150","1140872064","2038459704","1141175204","1140872280","2018602634","1141168436","1140872290","1140923484","1140872228","1141171932","1141200004","1140879744","1140856468","1140872198","1140872200","2038459704","1140872072","1141171932","1141171940","1140872290","1140872302"	345	G40 and G41

Table S3. Summary results of SNPs used for epilepsy PRS in the study.

Chr	Locus	lead SNP	Effect allele	Other allele	EAF	P value	Beta	SE	Genes
1	1q43	rs876793	T	C	0.67	2.64E-09	-0.05735	0.00964	RYR2/CHRM3
2	2p16.1	rs11688767	A	T	0.53	6.58E-21	0.08399	0.00895	BCL11A
2	2q12.1	rs62151809	T	C	0.43	1.28E-11	0.06126	0.00905	POU3F3
2	2q24.3	rs11890028	T	G	0.72	1.73E-08	0.05652	0.01003	SCN1A
2	2q32.2	rs6721964	A	G	0.66	6.54E-10	-0.05850	0.00947	GLS
3	3p22.3	rs9861238	A	G	0.41	1.33E-10	-0.05838	0.00909	STAC
3	3p21.31	rs739431	A	G	0.84	4.82E-10	0.07610	0.01223	CACNA2D2
4	4p15.1	rs1463849	A	G	0.59	4.38E-11	-0.05993	0.00909	PCDH7
5	5q22.3	rs4596374	T	C	0.55	2.91E-12	-0.06284	0.00900	KCNN2
5	5q31.2	rs2905552	C	G	0.48	2.49E-10	-0.05664	0.00895	SPOCK1
6	6q22.33	rs13219424	T	C	0.30	3.87E-08	-0.05453	0.00992	PTPRK
7	7p14.1	rs37276	T	G	0.26	1.29E-08	-0.05891	0.01036	SUGCT
9	9q21.32	rs2780103	T	C	0.26	4.34E-12	-0.07235	0.01045	RMI1
10	10q24.32	rs11191156	A	G	0.67	4.41E-14	-0.07173	0.00950	KCNIP2
16	16p13.3	rs62014006	T	G	0.47	4.22E-09	0.05313	0.00904	RBFOX1
17	17p13.1	rs2585398	A	C	0.53	1.84E-10	-0.05802	0.00910	ARHGEF15
17	17q21.32	rs16955463	T	G	0.25	2.30E-09	-0.06168	0.01032	CDK5RAP3
19	19p13.3	rs75483641	T	C	0.14	4.85E-10	-0.07973	0.01281	AP3D1
21	21q21.1	rs1487946	A	G	0.59	4.41E-08	0.05001	0.00914	TMPRSS15
21	21q22.1	rs7277479	A	G	0.36	8.94E-12	-0.06352	0.00931	GRIK1
22	22q13.32	rs469999	A	G	0.31	2.65E-10	-0.06175	0.00977	FAM19A5

Abbreviations: SNP, single nucleotide polymorphism; EAF, effect allele frequency; PRS, polygenic risk score; SE, standard error.

Table S4. Detailed food frequency questionnaires used to calculate diet score.

Diet component	Field code	Food frequency questionnaire	Types of variables	Health diet
Vegetables	1289	"On average how many heaped tablespoons of COOKED vegetables would you eat per DAY (tablespoons/day)? (Do not include potatoes; put '0' if you do not eat any)"	Continuous	≥ 4 tablespoons/day
Fresh fruits	1309	"About how many pieces of FRESH fruit would you eat per DAY (pieces/day)? (Count one apple, one banana, 10 grapes etc as one piece; put '0' if you do not eat any)"	Continuous	≥ 3 pieces/day
Fish	1329	"How often do you eat oily fish? (Oily fish include: Salmon Anchovies, Trout Swordfish, Mackerel Bloater, Herring Cacha, Sardines Carp, Pilchards Hilsa, Kipper Jack fish, Eel Katla, Whitebait Orange roughy, Tuna (fresh only) Pangas, and Sprats)"	Categorical	≥ 2 times a week
Unprocessed red meat	1369	"How often do you eat beef? (Do not count processed meats)"	Categorical	< 2 times a week
	1379	"How often do you eat lamb/mutton? (Do not count processed meats)"	Categorical	< 2 times a week
	1389	"How often do you eat pork? (Do not count processed meats such as bacon or ham)"	Categorical	< 2 times a week
Processed meat	1349	"How often do you eat processed meats (such as bacon, ham, sausages, meat pies, kebabs, burgers, chicken nuggets)?"	Categorical	< 2 times a week

Categorical variables included never, less than once a week, once a week, 2-4 times a week, 5-6 times a week, and once or more daily.

Table S5. The detailed codes of major diseases at recruitment.

Diseases	ICD-9	ICD-10	OPCS-4	Self-reported fields	Examination
Hypertension	401, 402, 403, 404, 405	I10, I11, I12, I13, I15, O10, O11	-	6150, 2966, 6153, 6177, 20002	4079, 4080, 93, 94
Diabetes	250	E10-E14	-	2443, 2976, 6153, 6177, 20002	30740, 30750
Cardiovascular diseases (CVD)	410, 411, 412, 413, 414, 428, 429, 430, 431, 434, 436	I20-I25, I48, I50, I60, I61, I63, I64	K40-K46, K49, K50, K621, K622, K623, K75, A052-A054, A103, L343, L351, L353, L354	6150, 3894, 4056, 20004, 20002	-
Cancer	140-172, 174-208	C00-C43, C45-C97	-	20001, 40005, 40006, 40013	-

Abbreviations: ICD, International Classification of Diseases; OPCS, Office of Population Censuses and Surveys Classification of Interventions and Procedures.

Table S6. Comparisons of baseline characteristics participants in this study.

Characteristics	Total (n=502479)	Main analysis (n=437526)	Genetic analysis (n=307877)	Life expectancy analysis (n=8345)
Age at recruitment (years)	56.53 ± 8.10	56.58 ± 8.09	56.86 ± 8.01	56.89 ± 7.93
Sex (Male, %)	229113 (45.6)	198782 (45.4)	140310 (45.6)	3738 (44.8)
Body mass index (BMI, kg/m^2)	27.43 ± 4.80	27.41 ± 4.78	27.37 ± 4.73	28.59 ± 5.59
Missing	3104 (0.6)	2492 (0.6)	893 (0.3)	177 (2.1)
Ethnicity (White, %)	472672 (94.1)	410364 (93.8)	307877 (100.0)	7926 (95.0)
Missing	2776 (0.6)	2422 (0.6)	-	51 (0.6)
Education level, n (%)				
College or University degree	161152 (32.1)	138236 (31.6)	96504 (31.3)	2039 (24.4)
Non-college or other professional	245927 (48.9)	217371 (49.7)	156094 (50.7)	4011 (48.1)
None of the above	85268 (17.0)	72783 (16.6)	52276 (17.0)	2060 (24.7)
Missing	10132 (2.0)	9136 (2.1)	3003 (1.0)	235 (2.8)
Employment status, n (%)				
Employed	287131 (57.1)	251764 (57.5)	176001 (57.2)	3075 (36.8)
Retired	166978 (33.2)	146016 (33.4)	106815 (34.7)	3101 (37.2)
Unemployed, home maker, or other	45420 (9.0)	37147 (8.5)	24151 (7.8)	2110 (25.3)
Missing	2950 (0.6)	2599 (0.6)	910 (0.3)	59 (0.7)
Drinking status, n (%)				
Never	22384 (4.5)	19296 (4.4)	9568 (3.1)	620 (7.4)
Previous	18102 (3.6)	14727 (3.4)	10000 (3.2)	896 (10.7)
Current	460341 (91.6)	402105 (91.9)	288055 (93.6)	6779 (81.2)
Missing	1652 (0.3)	1398 (0.3)	254 (0.1)	50 (0.6)
Smoking status, n (%)				
Never	273507 (54.4)	239095 (54.6)	166016 (53.9)	4114 (49.3)
Previous	173050 (34.4)	151513 (34.6)	109776 (35.7)	2906 (34.8)
Current	52974 (10.5)	44384 (10.1)	30977 (10.1)	1246 (14.9)
Missing	2948 (0.6)	2534 (0.6)	1108 (0.4)	79 (0.9)
Physical activity (MET)				
≤Median	201333 (40.1)	174608 (39.9)	123573 (40.1)	3630 (43.5)
>Median	201031 (40.0)	175773 (40.2)	126085 (41.0)	2585 (31.0)
Missing	100115 (19.9)	87145 (19.9)	58219 (18.9)	2130 (25.5)
Healthy diet score, n (%)				
0–1	112168 (22.3)	96020 (21.9)	68585 (22.3)	1816 (21.8)
2-3	314538 (62.6)	274920 (62.8)	194903 (63.3)	5143 (61.6)
4-5	64424 (12.8)	56961 (13.0)	39207 (12.7)	1069 (12.8)
Missing	11349 (2.3)	9625 (2.2)	5182 (1.7)	317 (3.8)
Hypertension, n (%)	275698 (54.9)	239824 (54.8)	169487 (55.1)	4937 (59.2)
Diabetes, n (%)	31371 (6.2)	26941 (6.2)	17145 (5.6)	993 (11.9)
Cardiovascular disease, n (%)	49594 (9.9)	40360 (9.2)	28551 (9.3)	1828 (21.9)
Cancer, n (%)	41749 (8.3)	35977 (8.2)	25866 (8.4)	813 (9.7)

Mean values (standard deviation) for normal continuous variables and n (%) for categorical variables.

Table S7. Adjusted HRs (95% CIs) of the risk of incident epilepsy by residential greenness and air pollution for several sensitivity analysis.

Residential greenness	Cases	Person-years	HRs (95%CIs)	Air pollution	Cases	Person-years	HRs (95%CIs)
Participants with complete covariates (n=339822)							
$NDVI_{300m}$, per IQR increment	1783	3920416	**0.93 (0.88, 0.98)**	NO_2, per IQR increment	1783	3920416	**1.10 (1.04, 1.16)**
$NDVI_{500m}$, per IQR increment	1783	3920416	**0.93 (0.88, 0.99)**	NO_x, per IQR increment	1783	3920416	**1.05 (1.01, 1.11)**
$NDVI_{1000m}$, per IQR increment	1783	3920416	**0.93 (0.88, 0.99)**	$PM_{2.5}$, per IQR increment	1783	3920416	**1.09 (1.03, 1.15)**
$NDVI_{1500m}$, per IQR increment	1783	3920416	**0.93 (0.88, 0.98)**	PM_{10}, per IQR increment	1783	3920416	**1.06 (1.00, 1.12)**
Repairing missing covariates with the multiple imputation method							
$NDVI_{300m}$, per IQR increment	2448	5050121	**0.92 (0.88, 0.97)**	NO_2, per IQR increment	2448	5050121	**1.08 (1.03, 1.14)**
$NDVI_{500m}$, per IQR increment	2448	5050121	**0.93 (0.88, 0.97)**	NO_x, per IQR increment	2448	5050121	**1.05 (1.01, 1.09)**
$NDVI_{1000m}$, per IQR increment	2448	5050121	**0.93 (0.88, 0.97)**	$PM_{2.5}$, per IQR increment	2448	5050121	**1.09 (1.04, 1.14)**
$NDVI_{1500m}$, per IQR increment	2448	5050121	**0.92 (0.88, 0.97)**	PM_{10}, per IQR increment	2448	5050121	**1.05 (1.00, 1.10)**
Excluding events occurred in the first two-year of follow-up (n=435209)							
$NDVI_{300m}$, per IQR increment	2198	5047444	**0.92 (0.87, 0.97)**	NO_2, per IQR increment	2198	5047444	**1.07 (1.01, 1.12)**
$NDVI_{500m}$, per IQR increment	2198	5047444	**0.93 (0.88, 0.98)**	NO_x, per IQR increment	2198	5047444	**1.04 (1.00, 1.09)**
$NDVI_{1000m}$, per IQR increment	2198	5047444	**0.93 (0.88, 0.98)**	$PM_{2.5}$, per IQR increment	2198	5047444	**1.08 (1.03, 1.14)**
$NDVI_{1500m}$, per IQR increment	2198	5047444	**0.93 (0.88, 0.97)**	PM_{10}, per IQR increment	2198	5047444	**1.05 (1.00, 1.11)**
Restricting analyses to those living at the same address >5 years (n=353786)							
$NDVI_{300m}$, per IQR increment	1972	4081235	**0.92 (0.87, 0.98)**	NO_2, per IQR increment	1972	4081235	**1.07 (1.02, 1.13)**
$NDVI_{500m}$, per IQR increment	1972	4081235	**0.93 (0.88, 0.99)**	NO_x, per IQR increment	1972	4081235	1.04 (0.99, 1.09)
$NDVI_{1000m}$, per IQR increment	1972	4081235	**0.93 (0.88, 0.99)**	$PM_{2.5}$, per IQR increment	1972	4081235	**1.09 (1.03, 1.15)**
$NDVI_{1500m}$, per IQR increment	1972	4081235	**0.92 (0.87, 0.98)**	PM_{10}, per IQR increment	1972	4081235	1.04 (0.98, 1.10)
Considering the competitive risk of death (death cases=26731)							
$NDVI_{300m}$, per IQR increment	2448	5050121	**0.92 (0.88, 0.97)**	NO_2, per IQR increment	2448	5050121	**1.08 (1.03, 1.14)**
$NDVI_{500m}$, per IQR increment	2448	5050121	**0.93 (0.88, 0.97)**	NO_x, per IQR increment	2448	5050121	**1.05 (1.01, 1.09)**
$NDVI_{1000m}$, per IQR increment	2448	5050121	**0.93 (0.88, 0.97)**	$PM_{2.5}$, per IQR increment	2448	5050121	**1.09 (1.04, 1.14)**
$NDVI_{1500m}$, per IQR increment	2448	5050121	**0.92 (0.88, 0.97)**	PM_{10}, per IQR increment	2448	5050121	**1.05 (1.00, 1.10)**
Further adjusting for hypertension, diabetes, cardiovascular disease, and cancer at baseline							
$NDVI_{300m}$, per IQR increment	2448	5050121	**0.92 (0.88, 0.97)**	NO_2, per IQR increment	2448	5050121	**1.08 (1.03, 1.14)**
$NDVI_{500m}$, per IQR increment	2448	5050121	**0.93 (0.89, 0.98)**	NO_x, per IQR increment	2448	5050121	**1.05 (1.00, 1.09)**
$NDVI_{1000m}$, per IQR increment	2448	5050121	**0.93 (0.89, 0.98)**	$PM_{2.5}$, per IQR increment	2448	5050121	**1.08 (1.03, 1.14)**

$NDVI_{1500m}$, per IQR increment	2448	5050121	**0.93 (0.88, 0.97)**	PM_{10}, per IQR increment	2448	5050121	**1.05 (1.00, 1.10)**
Employing time-varying Cox models to account for exposure variation during follow-up							
$NDVI_{300m}$, per IQR increment	2448	5050121	**0.90 (0.89, 0.92)**	NO_2, per IQR increment	2448	5050121	**1.05 (1.03, 1.07)**
$NDVI_{500m}$, per IQR increment	2448	5050121	**0.91 (0.89, 0.92)**	NO_x, per IQR increment	2448	5050121	**1.03 (1.01, 1.04)**
$NDVI_{1000m}$, per IQR increment	2448	5050121	**0.88 (0.86, 0.89)**	$PM_{2.5}$, per IQR increment	2448	5050121	**1.17 (1.16, 1.19)**
$NDVI_{1500m}$, per IQR increment	2448	5050121	**0.87 (0.85, 0.88)**	PM_{10}, per IQR increment	2448	5050121	**1.20 (1.19, 1.23)**
Including participants with brain injury, infection, benign and malignant tumors, and surgery at baseline							
$NDVI_{300m}$, per IQR increment	2605	5189429	**0.91 (0.87, 0.96)**	NO_2, per IQR increment	2605	5189429	**1.09 (1.04, 1.14)**
$NDVI_{500m}$, per IQR increment	2605	5189429	**0.92 (0.88, 0.97)**	NO_x, per IQR increment	2605	5189429	**1.05 (1.01, 1.09)**
$NDVI_{1000m}$, per IQR increment	2605	5189429	**0.92 (0.88, 0.97)**	$PM_{2.5}$, per IQR increment	2605	5189429	**1.09 (1.04, 1.14)**
$NDVI_{1500m}$, per IQR increment	2605	5189429	**0.91 (0.87, 0.96)**	PM_{10}, per IQR increment	2605	5189429	**1.06 (1.01, 1.11)**
Including participants with brain injury, infection, benign and malignant tumors, and surgery at baseline*							
$NDVI_{300m}$, per IQR increment	2605	5189429	**0.92 (0.87, 0.96)**	NO_2, per IQR increment	2605	5189429	**1.09 (1.04, 1.14)**
$NDVI_{500m}$, per IQR increment	2605	5189429	**0.92 (0.88, 0.97)**	NO_x, per IQR increment	2605	5189429	**1.05 (1.01, 1.09)**
$NDVI_{1000m}$, per IQR increment	2605	5189429	**0.92 (0.88, 0.97)**	$PM_{2.5}$, per IQR increment	2605	5189429	**1.09 (1.04, 1.14)**
$NDVI_{1500m}$, per IQR increment	2605	5189429	**0.91 (0.87, 0.96)**	PM_{10}, per IQR increment	2605	5189429	**1.06 (1.01, 1.11)**

Model was adjusted for age at recruitment, BMI, sex, ethnicity, education level, employment status, smoking status, drinking status, MET, and healthy diet score. * Model was additionally adjusted for baseline brain injury, infection, benign and malignant tumors, and surgery. Abbreviations: HRs, hazard ratios; CIs, confidence intervals; $NDVI_{300m}$, normalized difference vegetation index within 300m buffer; $NDVI_{500m}$, normalized difference vegetation index within 500m buffer; $NDVI_{1000m}$, normalized difference vegetation index within 1000m buffer; $NDVI_{1500m}$, normalized difference vegetation index within 1500m buffer, $PM_{2.5}$, fine particulate matter with diameter <2.5μm; PM_{10}, particulate matter with diameter <10μm; NO_2, nitrogen dioxide; NO_x, nitrogen oxides.

Table S8. Adjusted HRs (95%CIs) of the risk of incident epilepsy by residential greenness and air pollution further adjusted for noise pollution.

Exposure	Model 1	Model 2	Model 3	Model 4	Model 5
NO_2, per IQR increment	**1.09 (1.03, 1.14)**	**1.09 (1.03, 1.14)**	**1.09 (1.03, 1.14)**	**1.09 (1.03, 1.14)**	**1.09 (1.03, 1.14)**
NO_x, per IQR increment	**1.07 (1.02, 1.12)**	**1.07 (1.02, 1.12)**	**1.07 (1.02, 1.12)**	**1.07 (1.02, 1.12)**	**1.07 (1.02, 1.12)**
$PM_{2.5}$, per IQR increment	**1.10 (1.05, 1.16)**	**1.10 (1.05, 1.16)**	**1.10 (1.05, 1.16)**	**1.10 (1.05, 1.16)**	**1.10 (1.05, 1.16)**
PM_{10}, per IQR increment*	1.05 (1.00, 1.10)	1.05 (1.00, 1.10)	1.05 (1.00, 1.10)	1.05 (1.00, 1.10)	1.05 (1.00, 1.10)
$NDVI_{300m}$, per IQR increment	**0.92 (0.88, 0.97)**	**0.92 (0.88, 0.97)**	**0.92 (0.88, 0.97)**	**0.92 (0.88, 0.97)**	**0.92 (0.88, 0.97)**
$NDVI_{500m}$, per IQR increment	**0.93 (0.88, 0.97)**	**0.93 (0.88, 0.97)**	**0.93 (0.88, 0.97)**	**0.93 (0.88, 0.97)**	**0.93 (0.88, 0.97)**
$NDVI_{1000m}$, per IQR increment	**0.93 (0.88, 0.97)**	**0.93 (0.88, 0.97)**	**0.93 (0.88, 0.97)**	**0.93 (0.88, 0.97)**	**0.93 (0.88, 0.97)**
$NDVI_{1500m}$, per IQR increment	**0.92 (0.88, 0.97)**	**0.92 (0.88, 0.97)**	**0.92 (0.88, 0.97)**	**0.92 (0.88, 0.97)**	**0.92 (0.88, 0.97)**

Model 1was adjusted for age at recruitment, BMI, sex, ethnicity, education level, employment status, smoking status, drinking status, MET, healthy diet score, and average daytime sound level of noise pollution. Model 2 was adjusted for age at recruitment, BMI, sex, ethnicity, education level, employment status, smoking status, drinking status, MET, healthy diet score, and average evening sound level of noise pollution. Model 3 was adjusted for age at recruitment, BMI, sex, ethnicity, education level, employment status, smoking status, drinking status, MET, healthy diet score, and average night-time sound level of noise pollution. Model 4 was adjusted for age at recruitment, BMI, sex, ethnicity, education level, employment status, smoking status, drinking status, MET, healthy diet score, and average 16-hour sound level of noise pollution. Model 5 was adjusted for age at recruitment, BMI, sex, ethnicity, education level, employment status, smoking status, drinking status, MET, healthy diet score, and average 24-hour sound level of noise pollution. * $P_{FDR\text{-}adjusted} > 0.05$. Bold text indicates $P_{FDR\text{-}adjusted} < 0.05$. Abbreviations: HRs, hazard ratios; CIs, confidence intervals; $NDVI_{300m}$, normalized difference vegetation index within 300m buffer; $NDVI_{500m}$, normalized difference vegetation index within 500m buffer; $NDVI_{1000m}$, normalized difference vegetation index within 1000m buffer; $NDVI_{1500m}$, normalized difference vegetation index within 1500m buffer, $PM_{2.5}$, fine particulate matter with diameter <2.5μm; PM_{10}, particulate matter with diameter <10μm; NO_2, nitrogen dioxide; NO_x, nitrogen oxides.

Table S9. E-value (CI) of the risk of incident epilepsy by residential greenness and air pollution.

Exposure	HRs (95%CIs)	$P_{FDR\text{-}adjusted}$	E-value (CI)
$NDVI_{300m}$, per IQR increment	**0.92 (0.88, 0.97)**	**0.003**	**1.39 (1.23)**
$NDVI_{500m}$, per IQR increment	**0.93 (0.88, 0.97)**	**0.003**	**1.37 (1.19)**
$NDVI_{1000m}$, per IQR increment	**0.93 (0.88, 0.97)**	**0.003**	**1.37 (1.19)**
$NDVI_{1500m}$, per IQR increment	**0.92 (0.88, 0.97)**	**0.003**	**1.39 (1.22)**
NO_2, per IQR increment	**1.08 (1.03, 1.14)**	**0.003**	**1.38 (1.21)**
NO_x, per IQR increment	**1.05 (1.01, 1.09)**	**0.018**	**1.28 (1.11)**
$PM_{2.5}$, per IQR increment	**1.09 (1.04, 1.14)**	**0.002**	**1.41 (1.25)**
PM_{10}, per IQR increment	1.05 (1.00, 1.10)	0.064	1.27 (1.00)

Model was adjusted for age at recruitment, BMI, sex, ethnicity, education level, employment status, smoking status, drinking status, MET, and healthy diet score. E-value (CI) was computed using the adjusted HR (95% CI). Multiple testing was controlled by the false discovery rate (FDR) correction, with two-sided FDR-adjusted *P*-value ≤ 0.05 considered statistically significant. Abbreviations: HRs, hazard ratios; CIs, confidence intervals; $NDVI_{300m}$, normalized difference vegetation index within 300m buffer; $NDVI_{500m}$, normalized difference vegetation index within 500m buffer; $NDVI_{1000m}$, normalized difference vegetation index within 1000m buffer; $NDVI_{1500m}$, normalized difference vegetation index within 1500m buffer, $PM_{2.5}$, fine particulate matter with diameter <2.5μm; PM_{10}, particulate matter with diameter <10μm; NO_2, nitrogen dioxide; NO_x, nitrogen oxides.

Table S10. PAR% (95% CIs) and HRs (95% CIs) of incident epilepsy from residential greenness and air pollution.

Exposure	Reference	HRs (95% CIs)	PAR% (95% CIs)
$NDVI_{300m}$	Q4	**1.17 (1.06, 1.29)**	**24.3% (11.0%, 36.7%)**
$NDVI_{500m}$	Q4	**1.13 (1.03, 1.24)**	**19.4% (5.5%, 32.6%)**
$NDVI_{1000m}$	Q4	**1.17 (1.06, 1.29)**	**24.1% (10.7%, 36.6%)**
$NDVI_{1500m}$	Q4	**1.16 (1.06, 1.28)**	**23.1% (9.7%, 35.7%)**
NO_2	Q1	**1.14 (1.04, 1.25)**	**20.5% (6.7%, 33.6%)**
NO_x	Q1	**1.14 (1.04, 1.26)**	**20.8% (7.0%, 33.8%)**
$PM_{2.5}$	Q1	**1.11 (1.01, 1.22)**	**16.2% (1.9%, 29.9%)**
PM_{10}	Q1	**1.11 (1.01, 1.22)**	**16.1% (1.9%, 29.7%)**

Model was adjusted for age at recruitment, BMI, sex, ethnicity, education level, employment status, smoking status, drinking status, MET, and healthy diet score. Abbreviations: PAR%, population attributable risk percent; Q, quartile; $PM_{2.5}$, fine particulate matter with diameter <2.5 μm; PM_{10}, particulate matter with diameter <10 μm; NO_2, nitrogen dioxide; NO_x, nitrogen oxides.

Table S11. Adjusted HRs (95% CIs) of the risk of incident epilepsy by genetic risk score (n=307877).

PRS	Cases	Person-years	HRs (95%CIs)
Continuous	1717	3555691.00	**1.68 (1.30, 2.15)**
Low	495	1185951.00	Ref.
Medium	579	1184778.00	**1.17 (1.04, 1.32)**
High	643	1184963.00	**1.30 (1.15, 1.46)**
P for trend	-	-	**<0.001**

Model was adjusted for age at recruitment, BMI, sex, education level, employment status, smoking status, drinking status, MET, healthy diet score, genotyping batch, and the first ten genetic principal components. Abbreviations: HRs, hazard ratios; CIs, confidence intervals; PRS, polygenic risk score.

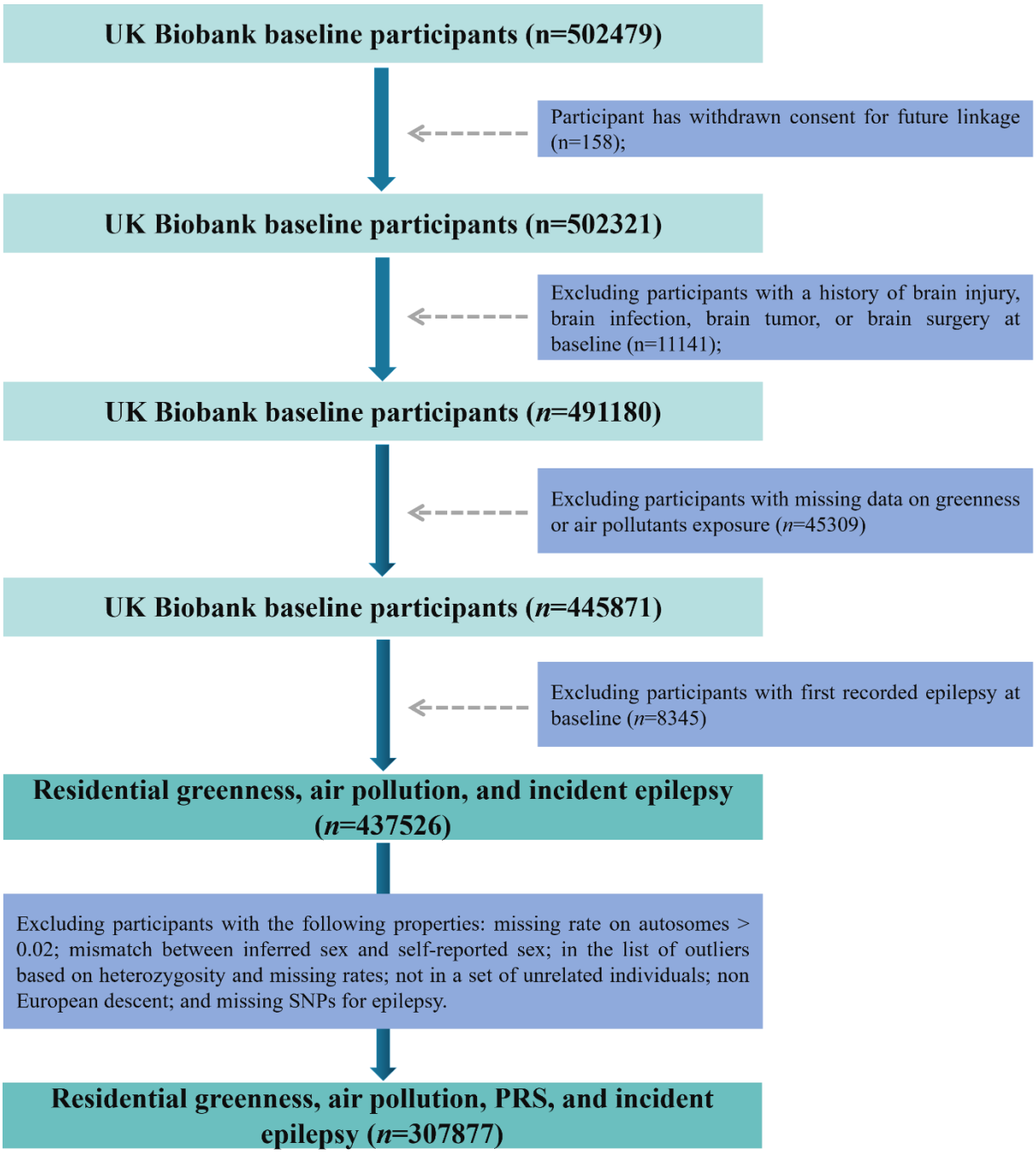
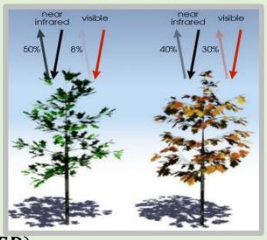


Figure S1. The flowchart for the participant inclusion and exclusion.

1. Obtain NDVI data

Global MOD13Q1 data are provided every 16 days at 250-meter spatial resolution as a gridded level-3 product in the Sinusoidal projection. (https://modis.gsfc.nasa.gov/data/dataprod/mod13.php)



$$NDVI = \frac{(NIR-RED)}{(NIR+RED)}$$, range from -1 to 1

2. Data pre-processing

Google Earth Engine is used for data quality control.

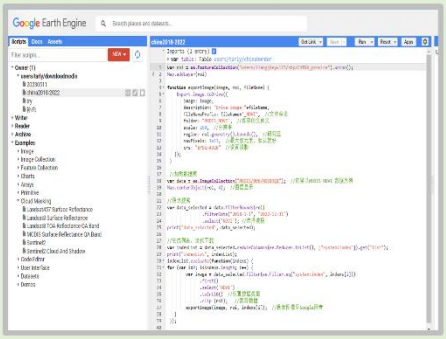


Table 1. MOD13Q1/A1 Pixel Reliablity

Rank Key	Summary QA	Description
-1	Fill/No Data	Not Processed
0	Good Data	Use with confidence
1	Marginal data	Useful, but look at other QA information
2	Snow/Ice	Target covered with snow/ice
3	Cloudy	Target not visible, covered with cloud

3. Individual exposure assessment

Figure S2. The overall process of greenness exposure assessment.

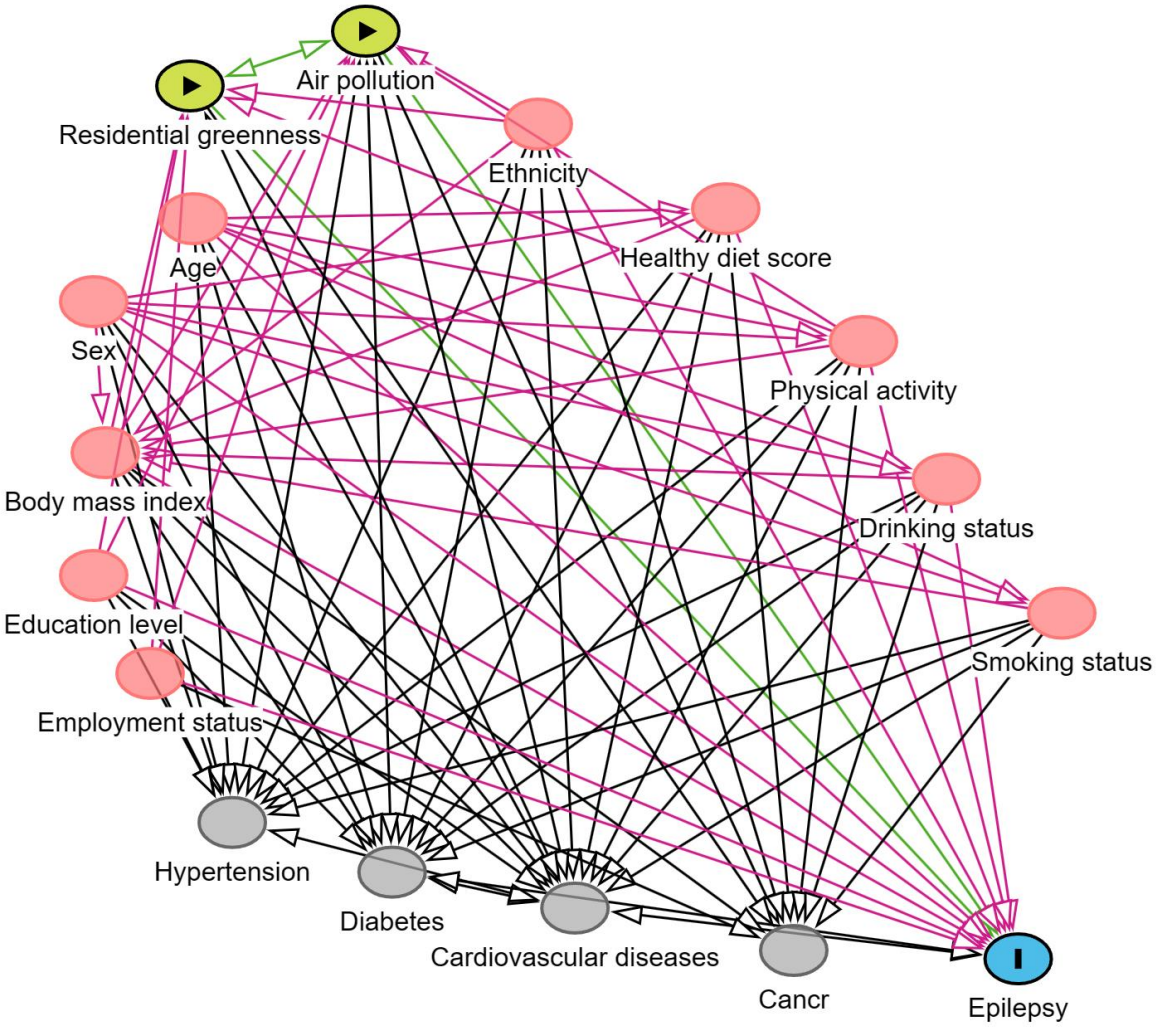


Figure S3. The directed acyclic graphs for the effect of the residential greenness and air pollution on epilepsy.

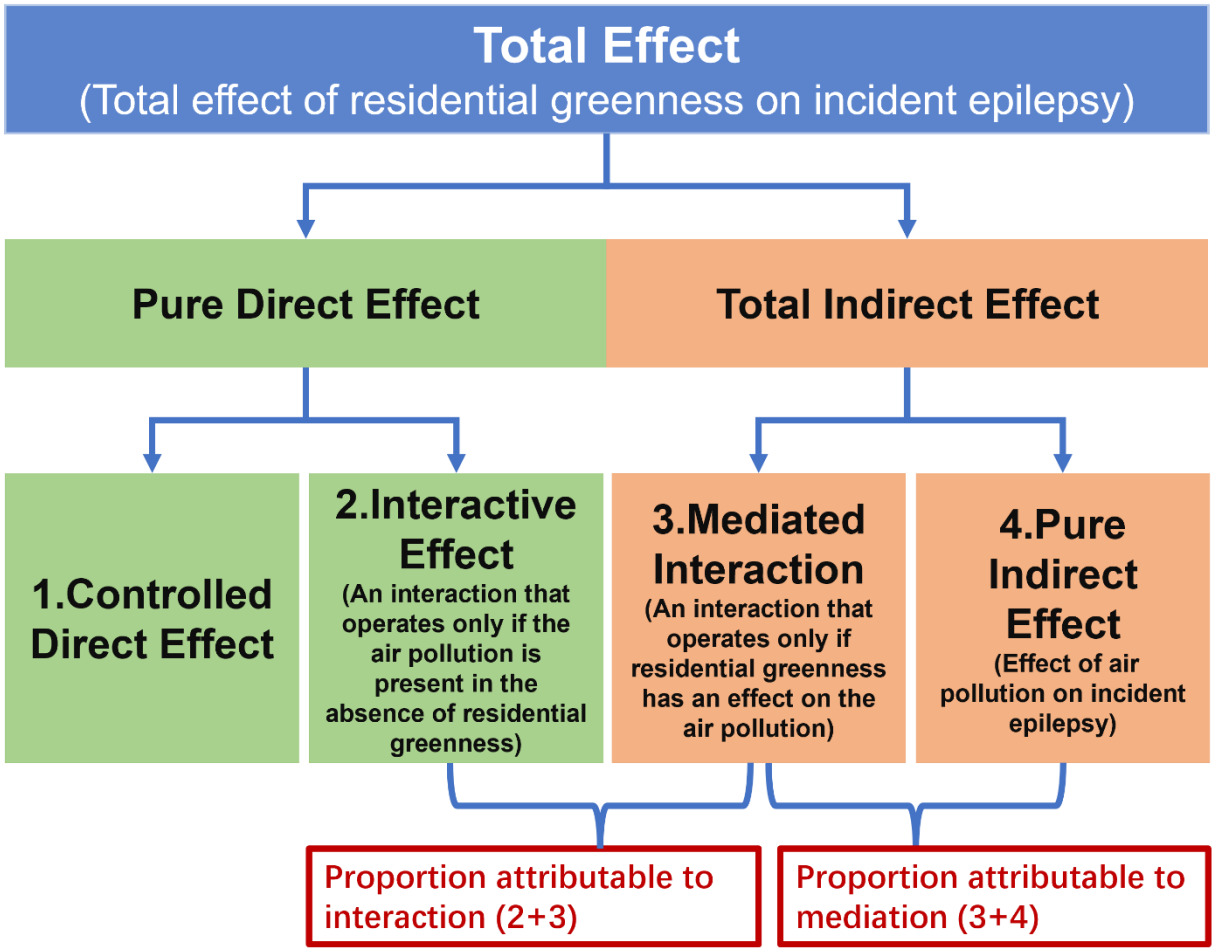


Figure S4. Causal mediation analysis encompassing decompositions for both mediation and interaction.

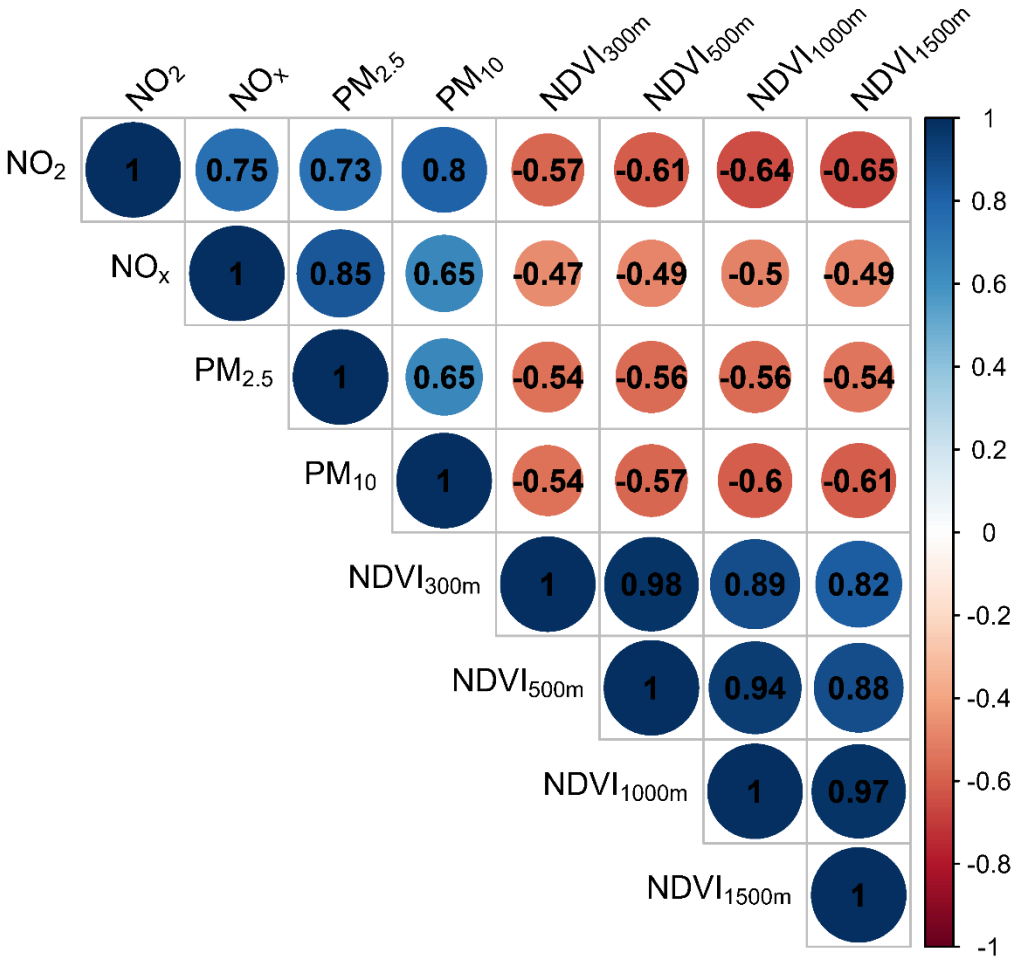


Figure S5. Pearson's correlation matrix among residential greenness and air pollution. Correlation map shows the Pearson correlation coefficients between each air pollutants. The size of the dots and the depth of the color represent the strength of the correlation coefficients. Abbreviations: $NDVI_{300m}$, normalized difference vegetation index within 300m buffer; $NDVI_{500m}$, normalized difference vegetation index within 500m buffer; $NDVI_{1000m}$, normalized difference vegetation index within 1000m buffer; $NDVI_{1500m}$, normalized difference vegetation index within 1500m buffer, $PM_{2.5}$, fine particulate matter with diameter <2.5μm; PM_{10}, particulate matter with diameter <10μm; NO_2, nitrogen dioxide; NO_x, nitrogen oxides.

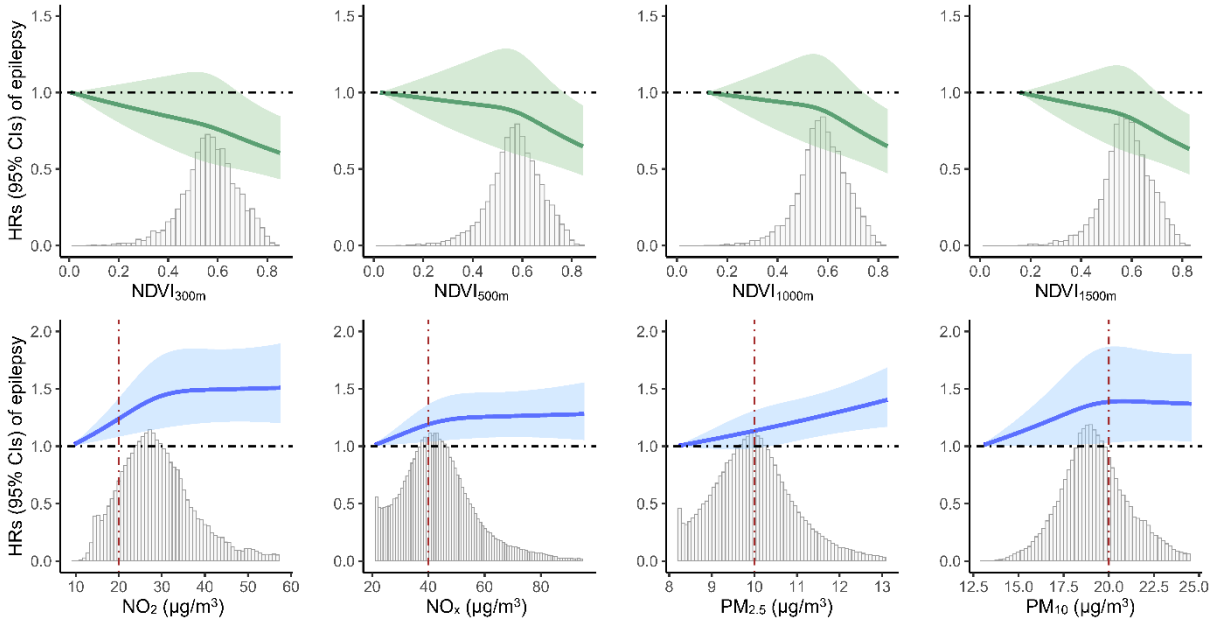


Figure S6. Exposure-response relationships of residential greenness and air pollution with the risk of incident epilepsy. Model was adjusted for age at recruitment, sex, ethnicity, BMI, education level, employment status, smoking status, drinking status, MET, and healthy diet score. The *P* values for overall associations were 0.003, 0.005, 0.005, 0.003, <0.001, 0.014, 0.001, and 0.069 for $NDVI_{300m}$, $NDVI_{500m}$, $NDVI_{1000m}$, $NDVI_{1500m}$, NO_2, NO_x, $PM_{2.5}$, and PM_{10}, respectively. The *P* values for non-linear associations were 0.488, 0.199, 0.190, 0.284, 0.036, 0.078, 0.996, and 0.161 for $NDVI_{300m}$, $NDVI_{500m}$, $NDVI_{1000m}$, $NDVI_{1500m}$, NO_2, NO_x, $PM_{2.5}$, and PM_{10}, respectively. Abbreviations: HRs, hazard ratios; CIs, confidence intervals; $NDVI_{300m}$, normalized difference vegetation index within 300m buffer; $NDVI_{500m}$, normalized difference vegetation index within 500m buffer; $NDVI_{1000m}$, normalized difference vegetation index within 1000m buffer; $NDVI_{1500m}$, normalized difference vegetation index within 1500m buffer, $PM_{2.5}$, fine particulate matter with diameter <2.5μm; PM_{10}, particulate matter with diameter <10μm; NO_2, nitrogen dioxide; NO_x, nitrogen oxides.

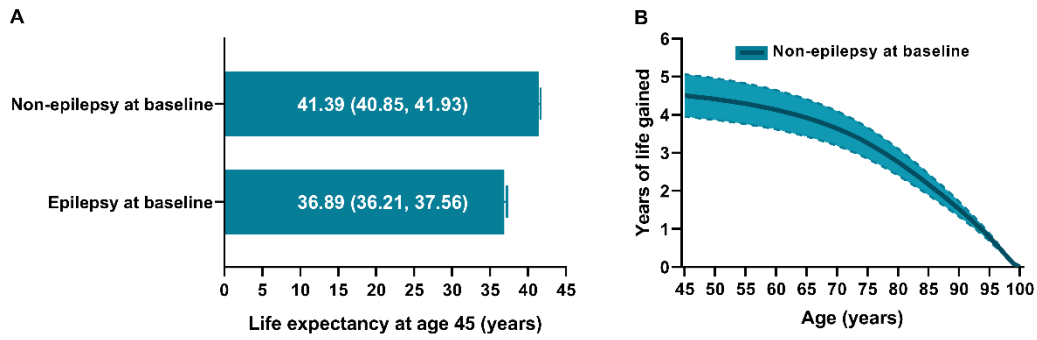


Figure S7. Life expectancy and years of life gained according to epilepsy status at baseline. Life expectancy according to epilepsy status at baseline (A). Years of life gained in participants without epilepsy compared with those with epilepsy (B). Model was adjusted for age at recruitment, sex, ethnicity, BMI, education level, employment status, smoking status, drinking status, MET, and healthy diet score.