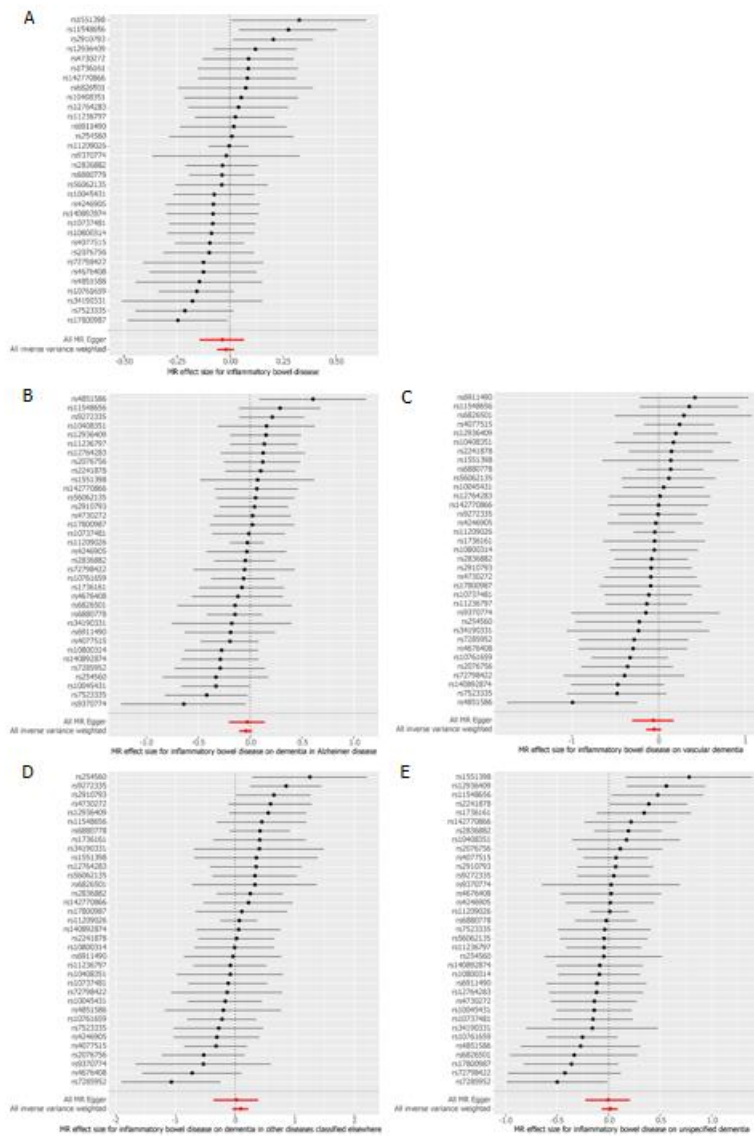


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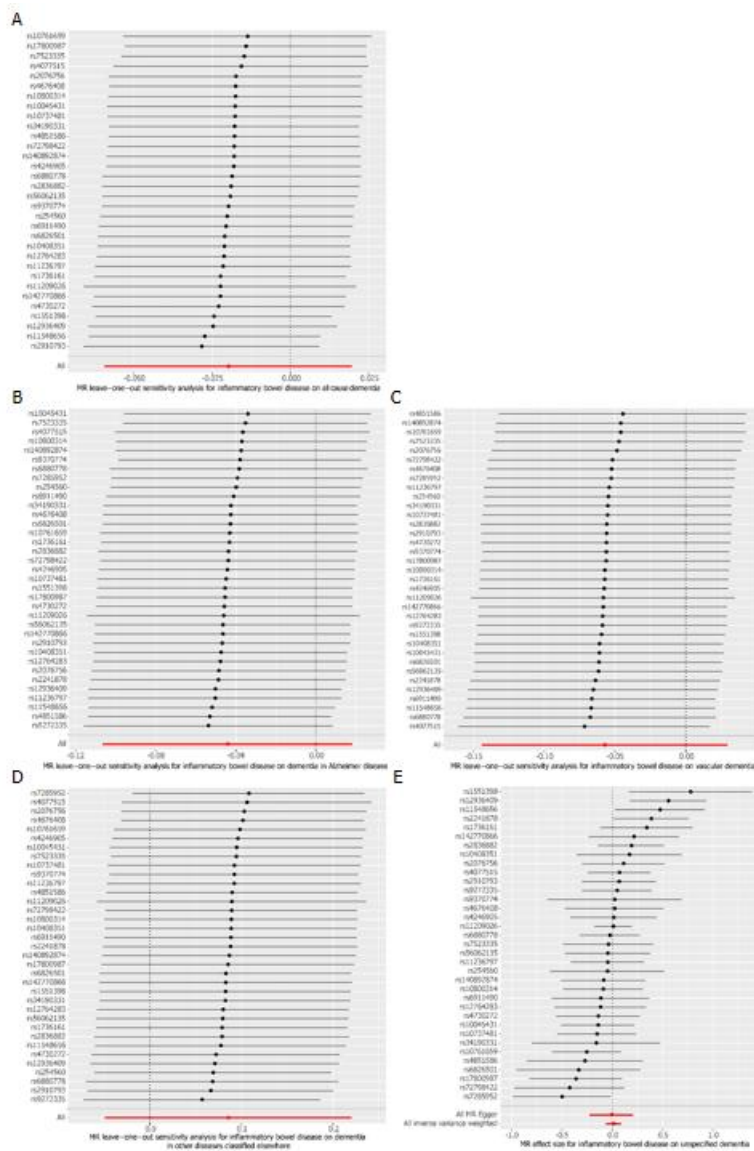
Supplementary Figure 1 Scatter plot to visualize causal effect of inflammatory bowel disease on dementia risk. The slope of the straight line indicates the magnitude of the causal association. The plot presents the effect sizes of the single nucleotide polymorphisms-inflammatory bowel disease association (X-axis, standard deviation units) and the single nucleotide polymorphisms-dementia [Y-axis, log (odds ratio)] with 95% confidence intervals. The regression slopes of the lines correspond to causal estimates using the three Mendelian Figure S1. Scatter plot to visualize causal effect of inflammatory Supplementary Figure 1 bowel disease on dementia risk. The slope of the straight line indicates the magnitude of the causal association.

The plot presents the effect sizes of the single nucleotide polymorphisms-inflammatory bowel disease association (X-axis, standard deviation units) and the single nucleotide polymorphisms-dementia association [Y-axis, log (odds ratio)] with 95% confidence intervals. The regression slopes of the lines correspond to causal estimates using the three Mendelian randomization methods. (A) Inflammatory bowel disease on all-cause dementia. (B) Inflammatory bowel disease on dementia in Alzheimer's disease. (C) Inflammatory bowel disease on vascular dementia. (D) Inflammatory bowel disease on dementia in other diseases classified elsewhere. (E) Inflammatory bowel disease on unspecified dementia. SNPs: Single nucleotide polymorphisms; MR: Mendelian randomization.



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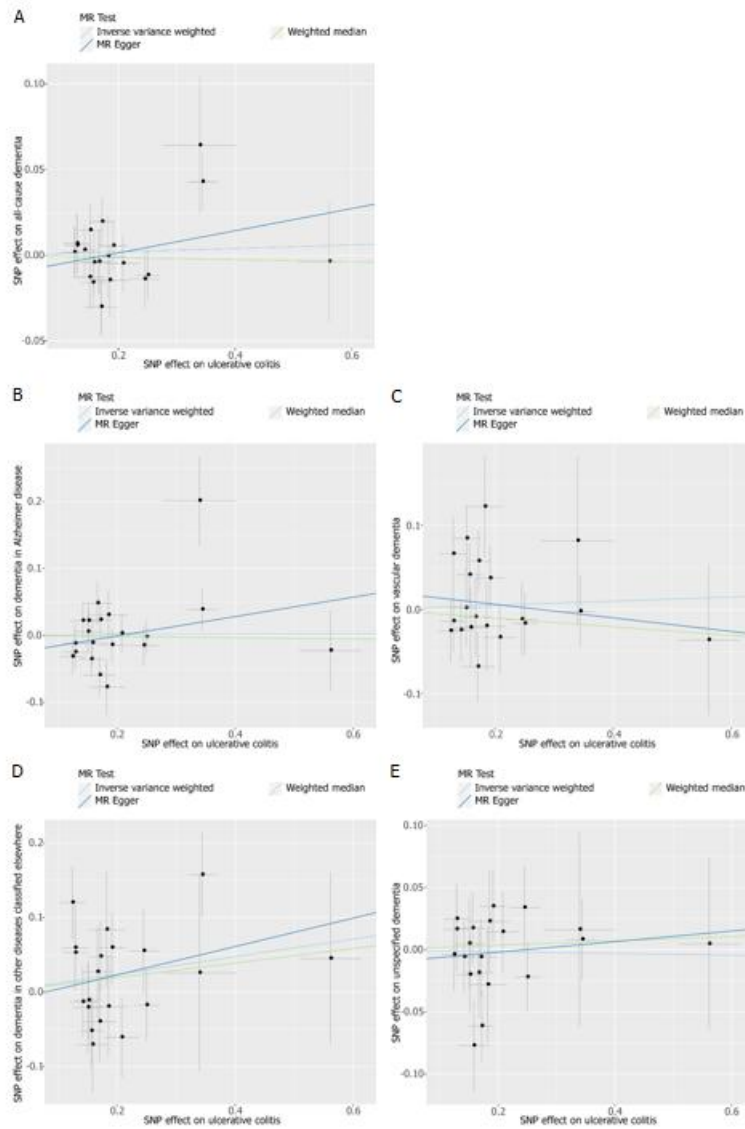
Supplementary Figure 2 Forest plot showing the association of each single nucleotide polymorphisms with dementia. Each black point represents result of the inverse variance weighted applied to estimate the causal effect of each single nucleotide polymorphism on dementia. Each red point depicts the inverse variance weighted and MR egger estimate using all single nucleotide polymorphisms. (A) Inflammatory bowel disease on all-cause dementia. (B) Inflammatory bowel disease on dementia in Alzheimer's disease. (C) Inflammatory bowel disease on vascular dementia. (D) Inflammatory bowel disease on dementia in other diseases classified elsewhere. (E) Inflammatory bowel disease on unspecified dementia. MR: Mendelian randomization.



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Supplementary Figure 3 Leave-one-out of each single nucleotide polymorphisms associated of inflammatory bowel disease with dementia risk. Each black point represents result of the inverse variance weighted applied to estimate the causal effect of inflammatory bowel disease on dementia excluding particular single nucleotide polymorphism from the analysis. Each red point depicts the inverse variance weighted estimate using all single nucleotide polymorphisms. (A) Inflammatory bowel disease on all-cause dementia. (B) Inflammatory bowel disease on dementia in Alzheimer's disease. (C) Inflammatory bowel disease on vascular dementia. (D) Inflammatory bowel disease on dementia in other diseases classified elsewhere.

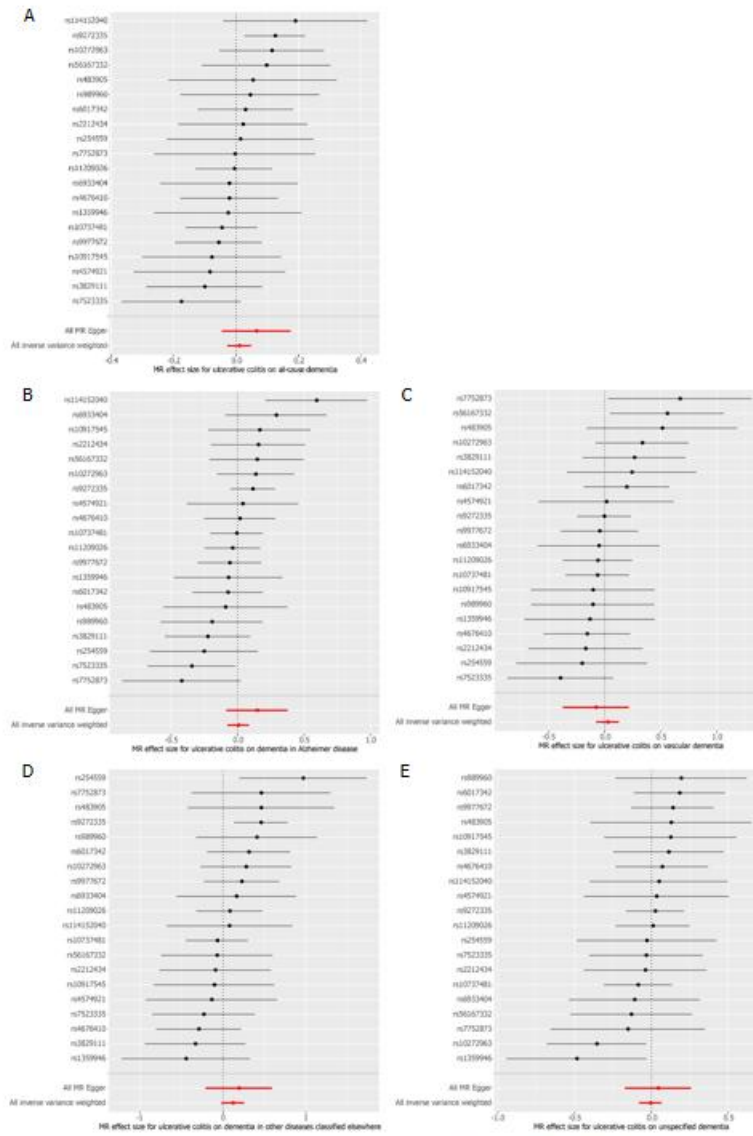
elsewhere. (E) Inflammatory bowel disease on unspecified dementia. MR:
Mendelian randomization.



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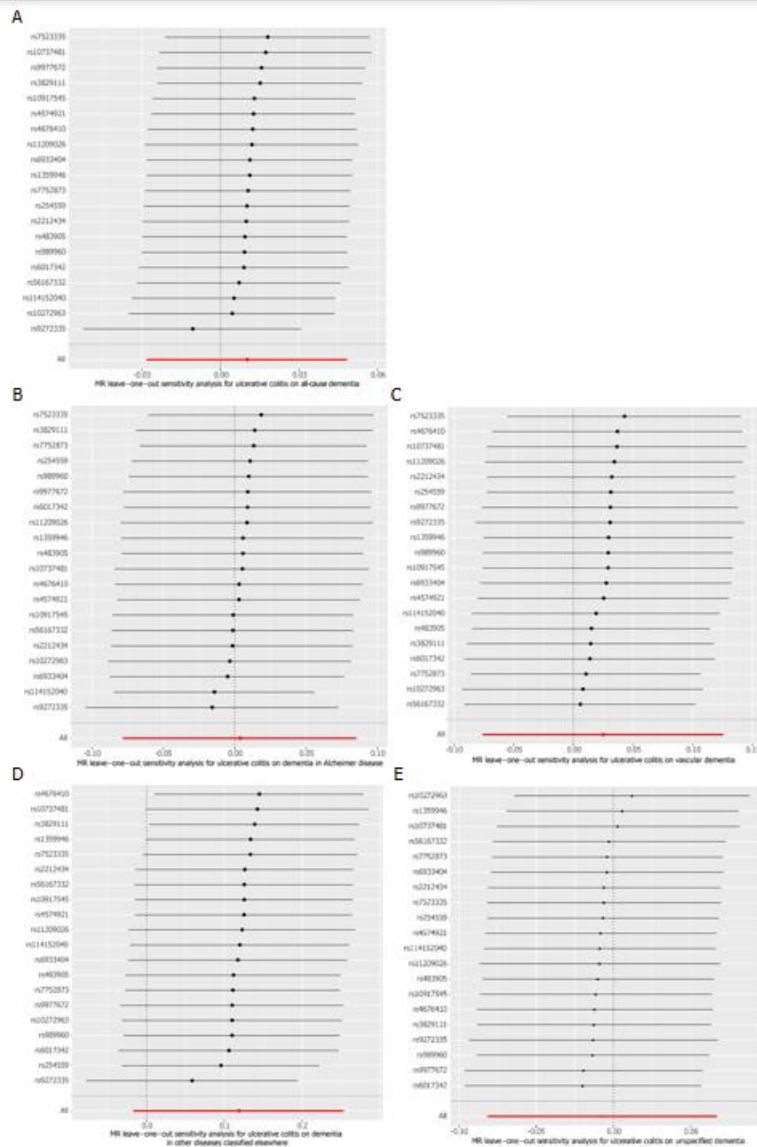
Supplementary Figure 4 Scatter plot to visualize causal effect of ulcerative colitis on dementia risk. The slope of the straight line indicates the magnitude of the causal association. The plot presents the effect sizes of the single nucleotide polymorphisms-ulcerative colitis association (X-axis, standard deviation units) and the single nucleotide polymorphisms-dementia association [Y-axis, log (odds ratio)] with 95% confidence intervals. The regression slopes of the lines correspond to causal estimates using the three Mendelian randomization methods. (A) Ulcerative colitis on all-cause dementia. (B) Ulcerative colitis on dementia in Alzheimer's disease. (C) Ulcerative colitis on vascular dementia. (D) Ulcerative colitis on dementia in

other diseases classified elsewhere. (E) Ulcerative colitis on unspecified dementia. SNPs: Single nucleotide polymorphisms; MR: Mendelian randomization.



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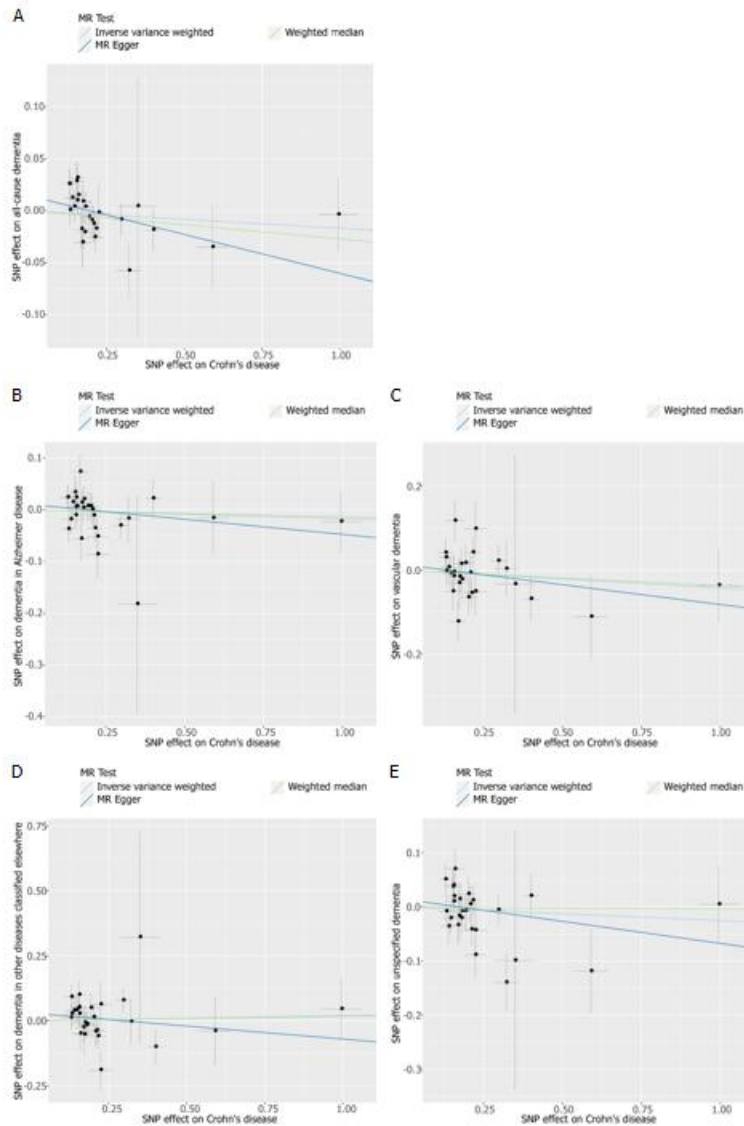
Supplementary Figure 5 Forest plot showing the association of each single nucleotide polymorphisms with dementia. Each black point represents result of the inverse variance weighted applied to estimate the causal effect of each single nucleotide polymorphism on dementia. Each red point depicts the inverse variance weighted and MR Egger estimate using all single nucleotide polymorphisms. (A) Ulcerative colitis on all-cause dementia. (B) Ulcerative colitis on dementia in Alzheimer's disease. (C) Ulcerative colitis on vascular dementia. (D) Ulcerative colitis on dementia in other diseases classified elsewhere. (E) Ulcerative colitis on unspecified dementia. MR: Mendelian randomization.



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Supplementary Figure 6 Leave-one-out of each single nucleotide polymorphisms associated of ulcerative colitis with dementia risk. Each black point represents result of the inverse variance weighted applied to estimate the causal effect of ulcerative colitis on dementia excluding particular single nucleotide polymorphism from the analysis. Each red point depicts the inverse variance weighted estimate using all single nucleotide polymorphisms. (A) Ulcerative colitis on all-cause dementia. (B) Ulcerative colitis on dementia in Alzheimer's disease. (C) Ulcerative colitis on vascular dementia. (D) Ulcerative colitis on dementia in other diseases classified elsewhere. (E) Ulcerative colitis on unspecified dementia. MR: Mendelian

randomization.

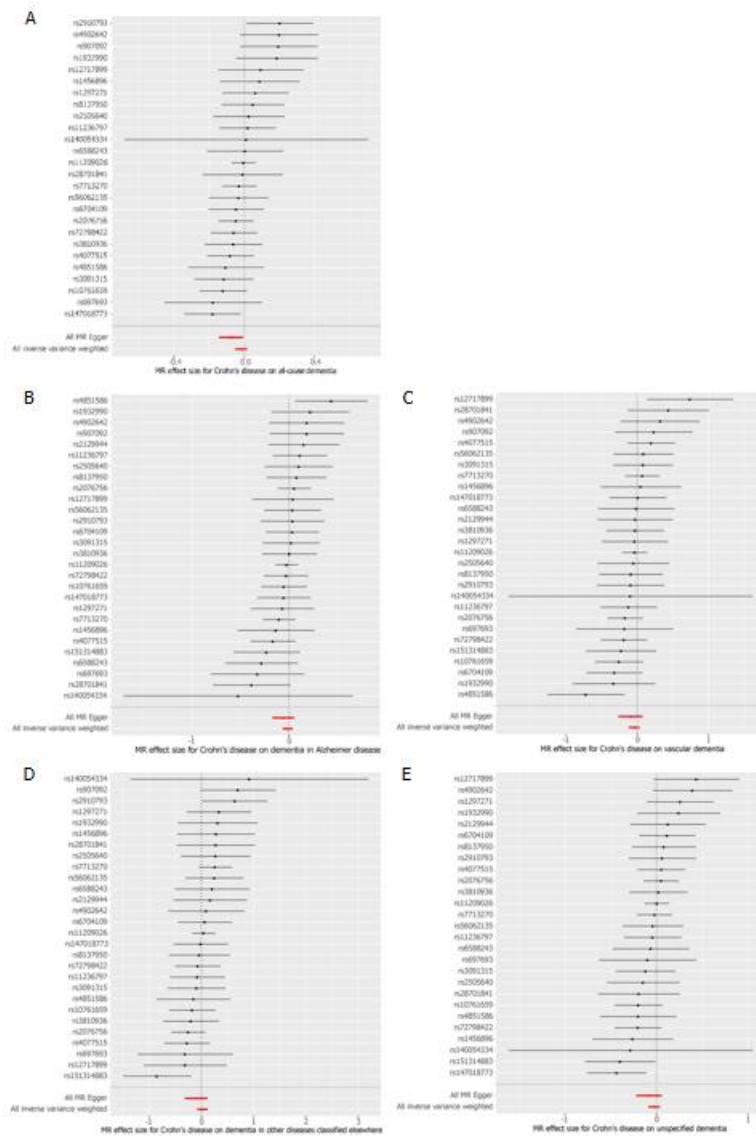


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Supplementary Figure 7 Scatter plot to visualize causal effect of Crohn's disease on dementia risk. The slope of the straight line indicates the magnitude of the causal association. The plot presents the effect sizes of the single nucleotide polymorphisms-Crohn's disease association (X-axis, standard deviation units) and the single nucleotide polymorphisms-dementia association [Y-axis, log (odds ratio)] with 95% confidence intervals. The regression slopes of the lines correspond to causal estimates using the three Mendelian randomization methods. (A) Crohn's disease on all-cause dementia. (B) Crohn's disease on dementia in Alzheimer's disease. (C) Crohn's disease on dementia in vascular dementia. (D) Crohn's disease on dementia in other

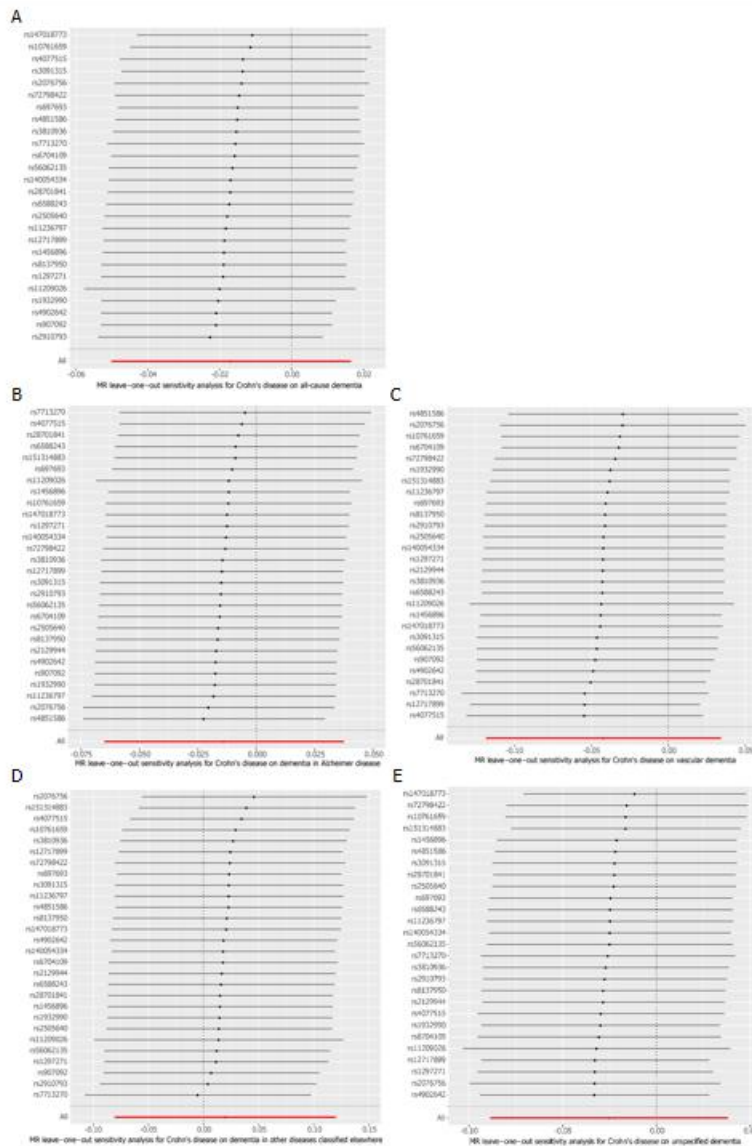
diseases classified elsewhere. (E) Crohn's disease on unspecified dementia.

SNPs: Single nucleotide polymorphisms; MR: Mendelian randomization.



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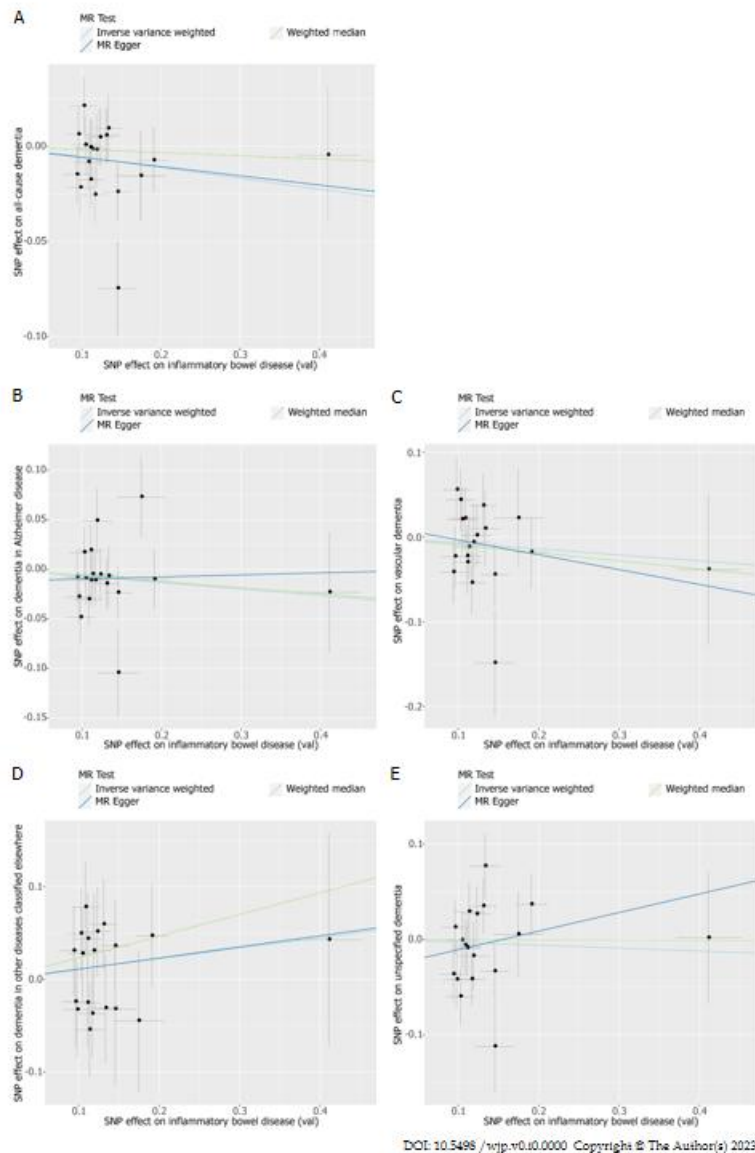
Supplementary Figure 8 Forest plot showing the association of each single nucleotide polymorphisms with dementia. Each black point represents result of the inverse variance weighted applied to estimate the causal effect of each single nucleotide polymorphism on dementia. Each red point depicts the inverse variance weighted and MR egger estimate using all single nucleotide polymorphisms. (A) Crohn's disease on all-cause dementia. (B) Crohn's disease on dementia in Alzheimer's disease. (C) Crohn's disease on vascular dementia. (D) Crohn's disease on dementia in other diseases classified elsewhere. (E) Crohn's disease on unspecified dementia. MR: Mendelian randomization.



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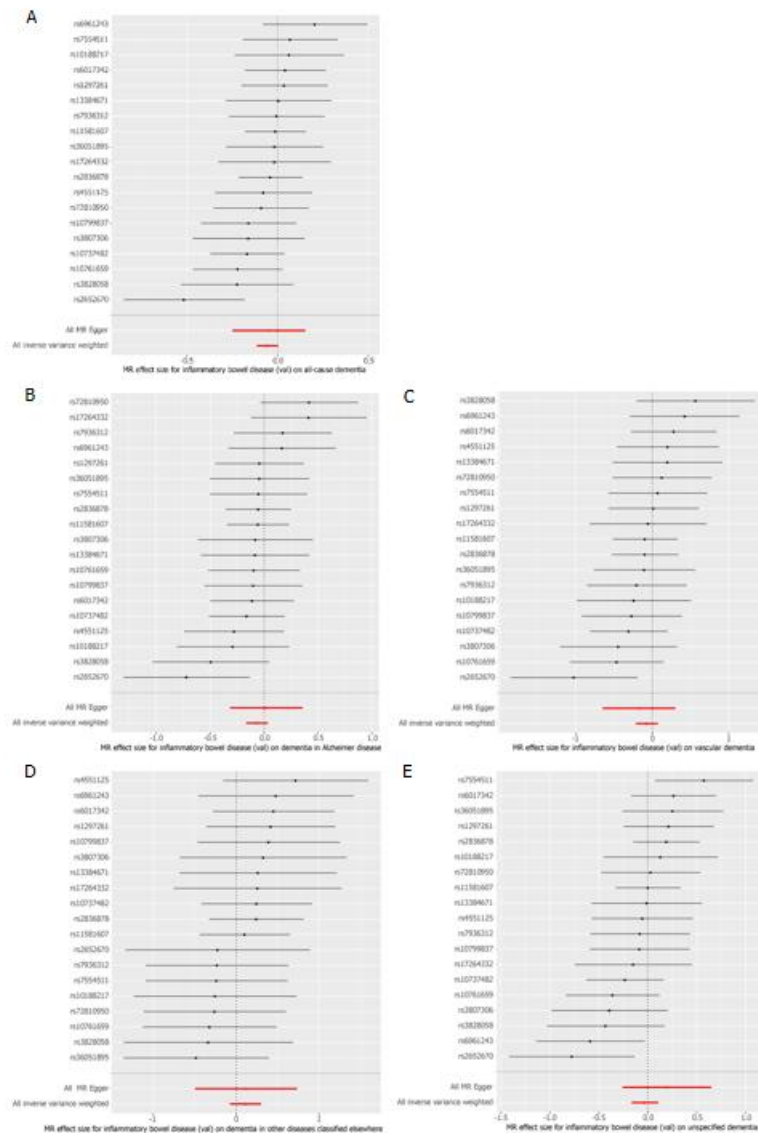
Supplementary Figure 9 Leave-one-out of each single nucleotide polymorphisms associated of Crohn's disease with dementia risk. Each black point represents result of the inverse variance weighted applied to estimate the causal effect of Crohn's disease on dementia excluding particular single nucleotide polymorphism from the analysis. Each red point depicts the inverse variance weighted estimate using all single nucleotide polymorphisms. (A) Crohn's disease on all-cause dementia. (B) Crohn's disease on dementia in Alzheimer's disease. (C) Crohn's disease on vascular dementia. (D) Crohn's disease on dementia in other diseases classified elsewhere. (E) Crohn's disease on unspecified dementia. MR: Mendelian

randomization.



Supplementary Figure 10 Scatter plot to visualize causal effect of inflammatory bowel disease (validation) on dementia risk. The slope of the straight line indicates the magnitude of the causal association. The plot presents the effect sizes of the single nucleotide polymorphisms-inflammatory bowel disease association (X-axis, standard deviation units) and the single nucleotide polymorphisms-dementia association [Y-axis, log (odds ratio)] with 95% confidence intervals. The regression slopes of the lines correspond to causal estimates using the three Mendelian randomization methods. (A) Inflammatory bowel disease (validation) on all-cause dementia. (B) Inflammatory bowel disease (validation) on dementia in Alzheimer's disease.

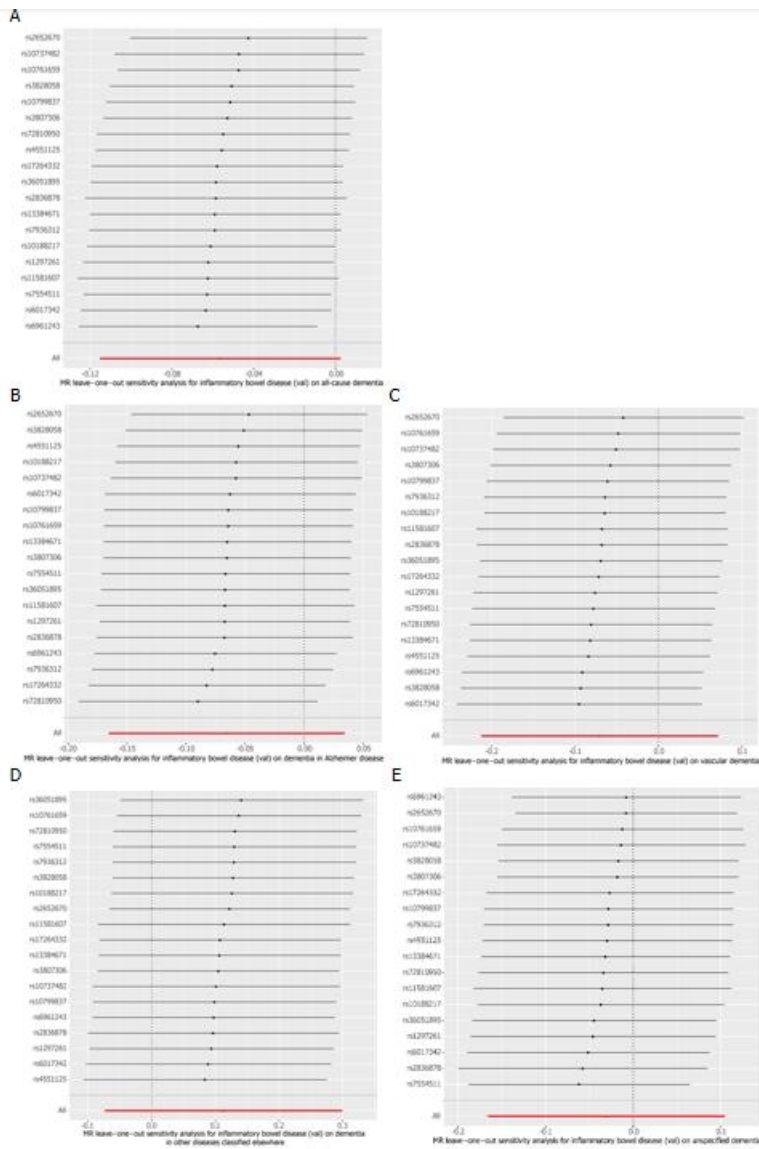
(C) Inflammatory bowel disease (validation) on vascular dementia. (D) Inflammatory bowel disease (validation) on dementia in other diseases classified elsewhere. (E) Inflammatory bowel disease (validation) on unspecified dementia. SNPs: Single nucleotide polymorphisms; MR: Mendelian randomization.



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Supplementary Figure 11 Forest plot showing the association of each single nucleotide polymorphisms with dementia. Each black point represents result of the inverse variance weighted applied to estimate the causal effect of each single nucleotide polymorphism on dementia. Each red point depicts the inverse variance weighted and MR egger estimate using all single nucleotide polymorphisms. (A) Inflammatory bowel disease (validation) on all-cause dementia. (B) Inflammatory bowel disease (validation) on dementia in Alzheimer's disease. (C) Inflammatory bowel disease (validation) on vascular dementia. (D) Inflammatory bowel disease (validation) on dementia in other diseases classified elsewhere. (E) Inflammatory bowel disease (validation) on

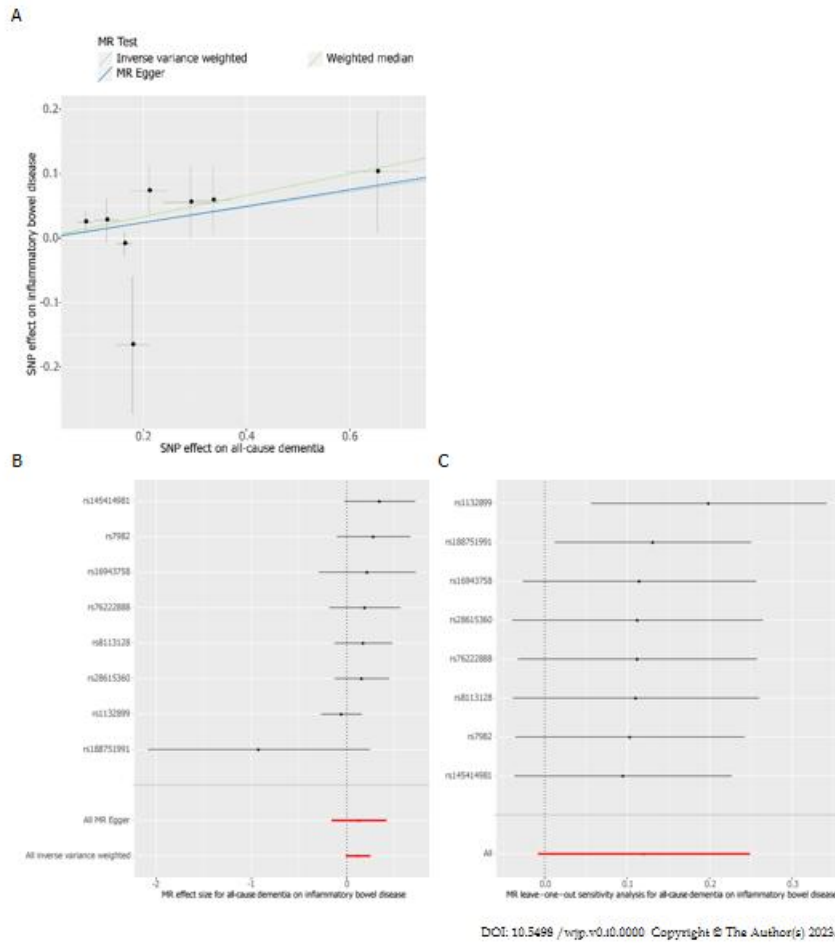
unspecified dementia. MR: Mendelian randomization.



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Supplementary Figure 12 Leave-one-out of each single nucleotide polymorphisms associated of inflammatory bowel disease (validation) with dementia risk. Each black point represents result of the inverse variance weighted applied to estimate the causal effect of inflammatory bowel disease (validation) on dementia excluding particular single nucleotide polymorphism from the analysis. Each red point depicts the inverse variance weighted estimate using all single nucleotide polymorphisms. (A) Inflammatory bowel disease (validation) on all-cause dementia. (B) Inflammatory bowel disease (validation) on dementia in Alzheimer's disease. (C) Inflammatory bowel disease (validation) on vascular dementia. (D)

Inflammatory bowel disease (validation) on dementia in other diseases classified elsewhere. (E) Inflammatory bowel disease (validation) on unspecified dementia. MR: Mendelian randomization.



Supplementary Figure 13 Mendelian randomization analyses of the causal effect of all-cause dementia on inflammatory bowel disease risk. (A) Scatter plot to visualize causal effect of all-cause dementia on inflammatory bowel disease. (B) Forest plot showing the association of each single nucleotide polymorphisms with inflammatory bowel disease. (C) Leave-one-out of each single nucleotide polymorphisms associated of all-cause dementia with inflammatory bowel disease risk. SNPs: Single nucleotide polymorphisms; MR: Mendelian randomization.

Supplementary Table 1 Descriptions of 15 genome-wide association study study cohorts in Liu's study

Study	Country	Cases	Controls
Crohn's disease			
BEL1	Belgium, France	513	884
BEL2	Belgium	153	94
CEDARS	USA	835	2881
CHOP	USA, Canada, Italy, Scotland	1495	6090
GERMAN	Germany	480	1114
NIDDK	USA, Canada	759	929
WTCCC	UK	1721	2935
Total		5956	14927
Ulcerative Colitis			
CEDARS	USA	836	2928
CHOP	USA, Canada, Italy, Scotland	664	6091
GERMANY	Germany	990	2915
NIDDK1	USA, Canada	498	1070
NIDDK2	USA, Canada	451	1428
NORWEGIAN	Norway	258	279
SWEDISH	Sweden	918	341
WTCCC	UK	2353	5412

Total		6968	20464
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Supplementary Table 2 Genetic variants selected as instrumental variables for inflammatory bowel disease

	SNP	Effect_allele	Other_allele	EAF	Beta	SE	Pval	Sample_size	R ² (%)	F statistics	Risk factors-related
1	rs1886731	C	T	0.481	-0.097	0.018	3.080E-08	34652	0.089	30.785	TRUE
2	rs10737481	G	T	0.555	0.141	0.017	1.190E-16	34652	0.198	68.889	FALSE
3	rs11209026	A	G	0.054	-0.726	0.042	1.760E-66	34652	0.848	296.190	FALSE
4	rs35730213	C	G	0.263	-0.151	0.019	6.910E-15	34652	0.175	60.904	FALSE
5	rs3024493	A	C	0.170	0.213	0.022	8.480E-22	34652	0.265	92.047	TRUE
6	rs7523335	A	G	0.173	-0.141	0.023	4.160E-10	34652	0.112	38.993	FALSE
7	rs10800314	A	C	0.649	-0.143	0.018	1.170E-15	34652	0.184	63.904	FALSE
8	rs112401990	A	G	0.375	0.142	0.017	2.840E-16	34652	0.192	66.786	TRUE
9	rs4851586	C	T	0.757	-0.122	0.019	2.320E-10	34652	0.116	40.220	FALSE
10	rs2241878	C	T	0.538	0.148	0.017	1.750E-18	34652	0.221	76.689	FALSE
11	rs4676408	A	G	0.515	0.118	0.018	6.620E-11	34652	0.123	42.574	FALSE
12	rs112694524	A	G	0.090	0.188	0.030	5.390E-10	34652	0.111	38.620	TRUE
13	rs11677953	A	G	0.415	0.098	0.017	1.050E-08	34652	0.094	32.574	TRUE
14	rs1873625	A	C	0.323	0.177	0.018	3.710E-23	34652	0.282	98.105	TRUE

4	rs6584283	C	T	0.511	-0.180	0.017	1.700E-26	34652	0.327	113.817	TRUE
2											
4	rs11236797	A	C	0.470	0.156	0.017	4.750E-20	34652	0.242	83.884	FALSE
3											
4	rs140892874	C	T	0.027	0.410	0.051	1.280E-15	34652	0.184	63.994	FALSE
4											
4	rs2193041	G	A	0.389	0.134	0.017	6.910E-15	34652	0.174	60.423	TRUE
5											
4	rs3850378	C	T	0.096	0.155	0.028	3.800E-08	34652	0.087	30.248	FALSE
6											
	no suitable proxy										
4	rs56062135	T	C	0.237	0.151	0.020	2.640E-14	34652	0.167	58.080	FALSE
7											
4	rs12446550	A	G	0.410	0.108	0.017	2.780E-10	34652	0.115	39.736	TRUE
8											
4	rs72798422	C	T	0.042	0.278	0.043	1.190E-10	34652	0.120	41.482	FALSE
9											
5	rs2076756	G	A	0.271	0.188	0.019	5.590E-24	34652	0.293	101.717	FALSE
0											
5	rs9934775	T	C	0.161	-0.140	0.023	1.710E-09	34652	0.104	36.203	TRUE
1											
5	rs11548656	G	A	0.034	-0.293	0.051	7.720E-09	34652	0.096	33.349	FALSE

6	rs131657	A	T	0.202	0.136	0.021	1.240E-10	34652	0.119	41.452	FALSE
3	no suitable proxy										
6	rs1003342	G	A	0.531	-0.095	0.017	1.670E-08	34652	0.092	31.975	TRUE
4											
6	rs7285952	G	T	0.157	-0.176	0.024	7.600E-14	34652	0.162	56.089	FALSE
5											

Note

1. SNPs related with potential risk factors: rs1886731, rs3024493, rs112401990, rs112694524, rs11677953, rs1873625, rs35260072, rs148844907, rs444210, rs1887428, rs1250573, rs6584283, rs2193041, rs12446550, rs9934775, rs744166, rs2542147, rs6062496, rs1003342
 2. SNPs fail to extract: rs45528737, rs6873866, rs9272514, rs28383456, rs113473719, rs1551399, rs3850378, rs8134436, rs131657
 3. Ambiguous or/and palindromic SNPs: rs35730213, rs13178036, rs4712528, rs6927172, rs113991740
-

Supplementary Table 3 Genetic variants selected as instrumental variables for ulcerative colitis

	SNP	Effect_allele	Other_allele	EAF	Beta	SE	Pval	Samplesize	R ² (%)	F statistics	Risk factors-related
1	rs11209026	A	G	0.059	-0.562	0.052	1.580E-27	27432	0.428	118.030	FALSE
2	rs7523335	A	G	0.177	-0.170	0.029	2.290E-09	27432	0.130	35.744	FALSE
3	rs3024493	A	C	0.168	0.236	0.028	1.090E-17	27432	0.266	73.294	TRUE
4	rs10917545	A	G	0.882	-0.185	0.034	3.290E-08	27432	0.111	30.528	FALSE
5	rs1886731	C	T	0.481	-0.141	0.022	2.250E-10	27432	0.147	40.415	TRUE
6	rs10737481	G	T	0.556	0.250	0.022	4.370E-31	27432	0.486	134.061	FALSE
7	rs1801274	G	A	0.483	-0.183	0.022	3.780E-17	27432	0.258	71.033	TRUE
8	rs35730213	C	G	0.267	-0.167	0.025	8.810E-12	27432	0.169	46.459	FALSE
9	rs10182512	A	G	0.350	0.161	0.022	5.190E-13	27432	0.189	51.991	TRUE
10	rs12612675	G	A	0.403	0.123	0.022	1.980E-08	27432	0.115	31.492	TRUE
11	rs4676410	A	G	0.197	0.208	0.028	2.460E-13	27432	0.195	53.534	FALSE
12	rs9823546	A	T	0.310	0.177	0.022	2.290E-15	27432	0.229	62.923	TRUE
13	rs114152040	A	G	0.032	0.340	0.062	4.950E-08	27432	0.108	29.712	FALSE
14	rs254559	A	C	0.404	0.124	0.022	7.630E-09	27432	0.122	33.424	FALSE

1	rs56167332	A	C	0.342	0.152	0.023	5.300E-11	27432	0.157	43.065	FALSE
5											
1	rs7752873	T	C	0.137	0.182	0.030	1.830E-09	27432	0.132	36.194	FALSE
6											
1	rs9272514	T	C	0.298	-0.402	0.027	4.000E-51	27432	0.818	226.219	FALSE
7											
	proxy		of								
	rs9272335										
	(r ² =0.83)										
1	rs28383456	T	C	0.335	-0.337	0.026	1.070E-39	27432	0.629	173.596	FALSE
8											
	no suitable proxy										
1	rs113473719	C	A	0.692	-0.259	0.027	1.110E-21	27432	0.333	91.686	FALSE
9											
	no suitable proxy										
2	rs6933404	C	T	0.216	0.167	0.025	3.680E-11	27432	0.159	43.808	FALSE
0											
2	rs148844907	A	T	0.010	1.341	0.109	7.170E-35	27432	0.550	151.693	TRUE
1											
2	rs10272963	T	C	0.426	-0.172	0.022	1.690E-15	27432	0.230	63.333	FALSE
2											
2	rs798502	C	A	0.283	-0.136	0.024	1.210E-08	27432	0.119	32.615	TRUE

3												
2	rs989960	T	C	0.425	-0.129	0.022	1.770E-09	27432	0.131	36.051	FALSE	
4												
2	rs1887428	C	G	0.623	-0.177	0.022	3.360E-15	27432	0.226	62.223	TRUE	
5												
2	rs4574921	T	C	0.741	0.151	0.026	4.240E-09	27432	0.126	34.605	FALSE	
6												
2	rs3829111	A	G	0.417	0.156	0.021	2.890E-13	27432	0.194	53.343	FALSE	
7												
2	rs7911680	C	A	0.490	-0.172	0.021	8.270E-16	27432	0.237	65.051	TRUE	
8												
2	rs483905	A	G	0.294	0.129	0.023	1.570E-08	27432	0.116	31.961	FALSE	
9												
3	rs484356	G	C	0.328	-0.134	0.023	3.950E-09	27432	0.126	34.642	FALSE	
0												
3	rs2212434	T	C	0.460	0.142	0.021	2.460E-11	27432	0.162	44.378	FALSE	
1												
3	rs12817473	G	A	0.382	0.191	0.022	1.710E-18	27432	0.281	77.224	TRUE	
2												
3	rs1359946	A	G	0.196	0.158	0.027	3.840E-09	27432	0.126	34.629	FALSE	
3												
3	rs9891174	A	T	0.470	0.145	0.021	7.170E-12	27432	0.171	46.906	FALSE	

4											
3	rs6017342	C	A	0.538	0.191	0.024	1.380E-15	27432	0.231	63.534	FALSE
5											
3	rs6062496	A	G	0.573	0.158	0.022	1.470E-12	27432	0.182	50.063	TRUE
6											
3	rs7282490	A	G	0.604	-0.140	0.021	7.080E-11	27432	0.155	42.612	FALSE
7											
	no suitable proxy										
3	rs9977672	A	G	0.251	-0.245	0.026	6.210E-21	27432	0.320	88.113	FALSE
8											
3	rs137845	G	A	0.515	0.118	0.021	2.380E-08	27432	0.113	31.083	TRUE

9

Note

1. SNPs related with potential risk factors: rs3024493, rs1886731, rs1801274, rs10182512, rs12612675, rs9823546, rs148844907, rs798502, rs1887428, rs7911680, rs12817473, rs6062496, rs137845

2. SNPs fail to extract: rs9272514, rs28383456, rs113473719, rs7282490

3. Ambiguous or/and palindromic SNPs: rs35730213, rs484356, rs9891174

(r ² =1)											
18	rs12717899	T	G	0.794	0.159	0.029	3.594E-08	20883	0.145	30.342	FALSE
19	rs12194825	A	T	0.186	-0.172	0.030	8.000E-09	20883	0.159	33.273	FALSE
20	rs148844907	A	T	0.008	0.958	0.142	1.471E-11	20883	0.218	45.575	TRUE
21	rs114607072	T	G	0.040	0.442	0.063	2.197E-12	20883	0.236	49.329	TRUE
22	rs28701841	A	G	0.117	0.224	0.037	1.851E-09	20883	0.173	36.159	FALSE
23	rs140054334	T	C	0.038	0.350	0.063	2.566E-08	20883	0.148	31.022	FALSE
24	rs444210	G	A	0.547	0.163	0.023	1.025E-12	20883	0.243	50.910	TRUE
25	rs1456896	T	C	0.698	0.139	0.025	2.897E-08	20883	0.147	30.798	FALSE
26	rs921720	G	A	0.619	0.163	0.024	6.396E-12	20883	0.226	47.236	TRUE
27	rs1887428	C	G	0.623	-0.168	0.024	4.224E-12	20883	0.229	47.849	TRUE
28	rs3810936	C	T	0.698	0.208	0.026	2.462E-15	20883	0.298	62.421	FALSE
29	rs4077515	T	C	0.420	0.216	0.024	4.370E-20	20883	0.403	84.398	FALSE
30	rs1250573	A	G	0.287	-0.171	0.026	9.005E-11	20883	0.200	41.900	TRUE
31	rs10761659	G	A	0.553	0.212	0.024	3.420E-19	20883	0.382	80.013	FALSE
32	rs2505640	G	A	0.644	-0.146	0.024	7.612E-10	20883	0.181	37.791	FALSE
33	rs1332099	C	T	0.515	-0.212	0.023	4.357E-20	20883	0.400	83.898	TRUE
34	rs11236797	A	C	0.473	0.181	0.023	4.854E-15	20883	0.293	61.460	FALSE
35	rs11564236	T	A	0.034	0.519	0.060	2.845E-18	20883	0.363	76.105	FALSE
36	rs1932990	T	C	0.254	0.153	0.026	6.021E-09	20883	0.162	33.796	FALSE
37	rs4902642	A	G	0.409	-0.129	0.024	4.339E-08	20883	0.143	29.967	FALSE
38	rs56062135	T	C	0.234	0.193	0.027	7.452E-13	20883	0.246	51.523	FALSE

39	rs147684209	C	T	0.369	0.155	0.024	2.336E-10	20883	0.193	40.298	TRUE
40	rs72798422	C	T	0.048	0.590	0.051	3.193E-31	20883	0.643	135.055	FALSE
41	rs2076756	G	A	0.284	0.400	0.024	3.245E-61	20883	1.290	272.914	FALSE
42	rs3091315	G	A	0.266	-0.180	0.026	9.521E-12	20883	0.223	46.578	FALSE
43	rs907092	A	G	0.471	0.130	0.023	1.011E-08	20883	0.156	32.705	FALSE
44	rs744166	G	A	0.408	-0.129	0.023	2.923E-08	20883	0.147	30.792	TRUE
45	rs80262450	A	G	0.113	0.283	0.035	1.082E-15	20883	0.307	64.312	TRUE
46	rs8178977	C	G	0.239	0.193	0.027	2.056E-12	20883	0.237	49.508	FALSE
47	rs2129944	G	T	0.291	-0.156	0.027	7.810E-09	20883	0.159	33.219	FALSE
48	rs281379	A	G	0.489	0.140	0.024	4.264E-09	20883	0.165	34.498	TRUE
49	rs1056441	C	T	0.698	0.167	0.026	5.441E-11	20883	0.205	42.886	TRUE
50	rs1297271	T	C	0.430	-0.155	0.024	6.278E-11	20883	0.204	42.714	FALSE
51	rs7276302	G	A	0.608	-0.172	0.023	1.226E-13	20883	0.264	55.177	FALSE
	no suitable proxy										
52	rs8137950	C	T	0.200	0.174	0.029	1.167E-09	20883	0.177	37.009	FALSE
53	rs151314883	A	G	0.158	-0.224	0.033	7.124E-12	20883	0.224	46.918	FALSE

Note

1. SNPs related with potential risk factors: rs7543234, rs3024505, rs78487399, rs112401990, rs1873625, rs13135092, rs2188962, rs148844907, rs114607072, rs444210, rs921720, rs1887428, rs1250573, rs1332099, rs147684209, rs744166, rs80262450, rs281379, rs1056441
2. SNPs fail to extract: rs6873866, rs7276302
3. Ambiguous or/and palindromic SNPs: rs12692254, rs4921497, rs12194825, rs11564236, rs8178977

Supplementary Table 5 Association of inflammatory bowel disease instrumental variants with outcome genome-wide association study

	SNP	Exposure (inflammatory disease)			Outcome (all-cause dementia)			Outcome (dementia in Alzheimer disease)			Outcome (vascular dementia)		
		Beta	SE	Pval	Beta	SE	Pval	Beta	SE	Pval	Beta	SE	Pval
1	rs10045431	0.177	0.019	6.590E-21	-0.013	0.017	0.439	-0.059	0.030	0.047	0.010	0.043	0.823
2	rs10408351	0.138	0.022	4.230E-10	0.007	0.019	0.706	0.021	0.033	0.518	0.023	0.047	0.628
3	rs10737481	0.141	0.017	1.190E-16	-0.012	0.015	0.427	-0.002	0.025	0.926	-0.017	0.036	0.645
4	rs10761659	0.162	0.017	4.070E-21	-0.026	0.015	0.082	-0.011	0.025	0.666	-0.054	0.036	0.137
5	rs10800314	-0.143	0.018	1.170E-15	0.013	0.015	0.398	0.040	0.026	0.123	0.008	0.037	0.833
6	rs11209026	-0.726	0.042	1.760E-66	0.004	0.035	0.916	0.023	0.060	0.706	0.036	0.089	0.683
7	rs11236797	0.156	0.017	4.750E-20	0.004	0.015	0.803	0.021	0.026	0.427	-0.022	0.037	0.551
8	rs11548656	-0.293	0.051	7.720E-09	-0.080	0.034	0.020	-0.083	0.059	0.158	-0.102	0.085	0.229
9	rs12764283	0.127	0.018	1.570E-12	0.005	0.015	0.746	0.015	0.026	0.560	0.001	0.038	0.969
10	rs12936409	0.146	0.017	3.870E-18	0.017	0.015	0.237	0.022	0.025	0.392	0.028	0.036	0.439
11	rs140892874	0.410	0.051	1.280E-15	-0.033	0.045	0.463	-0.120	0.078	0.125	-0.196	0.113	0.082
12	rs142770866	0.230	0.034	8.140E-12	0.019	0.027	0.490	0.014	0.047	0.766	-0.001	0.068	0.985
13	rs1736161	-0.123	0.017	1.340E-12	-0.010	0.015	0.483	0.010	0.026	0.691	0.006	0.037	0.864
14	rs17800987	0.202	0.031	3.710E-11	-0.050	0.024	0.040	0.004	0.042	0.931	-0.020	0.060	0.745
15	rs2076756	0.188	0.019	5.590E-24	-0.019	0.020	0.364	0.022	0.035	0.533	-0.068	0.051	0.177
16	rs2241878	0.148	0.017	1.750E-18	0.043	0.015	0.003	0.014	0.025	0.571	0.021	0.037	0.562
17	rs254560	0.100	0.017	6.160E-09	0.001	0.015	0.956	-0.033	0.026	0.197	-0.023	0.037	0.539

18	rs2836882	-0.196	0.020	1.490E-22	0.007	0.017	0.675	0.010	0.029	0.735	0.017	0.042	0.691
19	rs34190331	0.177	0.030	5.390E-09	-0.032	0.030	0.293	-0.032	0.052	0.537	-0.042	0.074	0.571
20	rs4077515	0.179	0.017	1.500E-25	-0.017	0.015	0.245	-0.036	0.026	0.165	0.042	0.037	0.249
21	rs4246905	0.163	0.020	1.420E-16	-0.013	0.018	0.480	-0.006	0.032	0.850	-0.006	0.046	0.894
22	rs4676408	0.118	0.018	6.620E-11	-0.015	0.015	0.327	-0.014	0.026	0.586	-0.035	0.038	0.351
23	rs4730272	-0.134	0.018	4.500E-14	-0.012	0.015	0.432	-0.003	0.025	0.917	0.013	0.036	0.726
24	rs4851586	-0.122	0.019	2.320E-10	0.018	0.019	0.341	-0.074	0.032	0.022	0.122	0.047	0.009
25	rs56062135	0.151	0.020	2.640E-14	-0.006	0.017	0.720	0.007	0.029	0.802	0.017	0.042	0.680
26	rs6826501	-0.093	0.017	4.120E-08	-0.007	0.015	0.653	0.014	0.026	0.595	-0.027	0.037	0.479
27	rs6880778	0.188	0.017	2.140E-27	-0.007	0.015	0.623	-0.028	0.026	0.270	0.025	0.037	0.493
28	rs6911490	-0.143	0.021	6.820E-12	-0.002	0.018	0.895	0.027	0.032	0.385	-0.059	0.046	0.196
29	rs72798422	0.278	0.043	1.190E-10	-0.035	0.040	0.382	-0.016	0.069	0.815	-0.111	0.099	0.262
30	rs7285952	-0.176	0.024	7.600E-14	0.058	0.023	0.010	0.051	0.039	0.189	0.051	0.057	0.370
31	rs7523335	-0.141	0.023	4.160E-10	0.030	0.017	0.069	0.059	0.029	0.038	0.068	0.041	0.099
32	rs9370774	-0.131	0.022	2.540E-09	0.002	0.023	0.918	0.084	0.040	0.036	0.020	0.057	0.729
33	rs1551398	-0.101	0.017	5.580E-09	-0.033	0.016	0.044	-0.007	0.028	0.808	-0.014	0.041	0.737
34	rs2910793	0.155	0.023	1.490E-11	0.032	0.015	0.036	0.006	0.026	0.824	-0.014	0.037	0.705
35	rs9272335	0.186	0.020	1.930E-21	0.043	0.017	0.012	0.039	0.030	0.194	-0.002	0.043	0.958

Supplementary Table 5 Association of inflammatory bowel disease instrumental variants with outcome genome-wide association study

SNP	Exposure (inflammatory bowel disease)			Outcome (dementia in other diseases classified elsewhere)			Outcome (unspecified dementia)		
	Beta	SE	Pval	Beta	SE	Pval	Beta	SE	Pval
1 rs10045431	0.177	0.019	6.590E-21	-0.031	0.057	0.586	-0.026	0.033	0.439
2 rs10408351	0.138	0.022	4.230E-10	-0.013	0.063	0.841	0.023	0.037	0.530
3 rs10737481	0.141	0.017	1.190E-16	-0.018	0.048	0.710	-0.022	0.028	0.435
4 rs10761659	0.162	0.017	4.070E-21	-0.037	0.048	0.439	-0.042	0.028	0.141
5 rs10800314	-0.143	0.018	1.170E-15	0.002	0.049	0.960	0.014	0.029	0.641
6 rs11209026	-0.726	0.042	1.760E-66	-0.045	0.114	0.695	-0.005	0.069	0.947
7 rs11236797	0.156	0.017	4.750E-20	-0.014	0.049	0.774	-0.008	0.029	0.789
8 rs11548656	-0.293	0.051	7.720E-09	-0.129	0.112	0.252	-0.138	0.067	0.038
9 rs12764283	0.127	0.018	1.570E-12	0.043	0.050	0.383	-0.015	0.029	0.602
10 rs12936409	0.146	0.017	3.870E-18	0.080	0.048	0.097	0.081	0.028	0.004
11 rs140892874	0.410	0.051	1.280E-15	0.021	0.147	0.888	-0.037	0.088	0.674
12 rs142770866	0.230	0.034	8.140E-12	0.049	0.088	0.575	0.049	0.053	0.355
13 rs1736161	-0.123	0.017	1.340E-12	-0.050	0.049	0.308	-0.042	0.029	0.147
14 rs17800987	0.202	0.031	3.710E-11	0.021	0.079	0.791	-0.074	0.047	0.119
15 rs2076756	0.188	0.019	5.590E-24	-0.101	0.067	0.130	0.020	0.040	0.609
16 rs2241878	0.148	0.017	1.750E-18	0.002	0.048	0.959	0.057	0.029	0.046
17 rs254560	0.100	0.017	6.160E-09	0.124	0.049	0.011	-0.005	0.029	0.858

18	rs2836882	-0.196	0.020	1.490E-22	-0.048	0.056	0.385	-0.037	0.033	0.265
19	rs34190331	0.177	0.030	5.390E-09	0.070	0.099	0.477	-0.029	0.058	0.617
20	rs4077515	0.179	0.017	1.500E-25	-0.059	0.048	0.221	0.012	0.029	0.678
21	rs4246905	0.163	0.020	1.420E-16	-0.051	0.060	0.390	0.002	0.036	0.964
22	rs4676408	0.118	0.018	6.620E-11	-0.086	0.050	0.084	0.002	0.030	0.938
23	rs4730272	-0.134	0.018	4.500E-14	-0.079	0.048	0.102	0.019	0.028	0.499
24	rs4851586	-0.122	0.019	2.320E-10	0.025	0.061	0.678	0.034	0.036	0.349
25	rs56062135	0.151	0.020	2.640E-14	0.049	0.055	0.371	-0.007	0.033	0.820
26	rs6826501	-0.093	0.017	4.120E-08	-0.030	0.049	0.543	0.031	0.029	0.282
27	rs6880778	0.188	0.017	2.140E-27	0.077	0.048	0.113	-0.005	0.029	0.854
28	rs6911490	-0.143	0.021	6.820E-12	0.006	0.060	0.914	0.017	0.035	0.632
29	rs72798422	0.278	0.043	1.190E-10	-0.040	0.132	0.764	-0.119	0.078	0.125
30	rs7285952	-0.176	0.024	7.600E-14	0.190	0.075	0.011	0.089	0.044	0.043
31	rs7523335	-0.141	0.023	4.160E-10	0.040	0.054	0.461	0.006	0.032	0.852
32	rs9370774	-0.131	0.022	2.540E-09	0.071	0.076	0.350	-0.003	0.045	0.954
33	rs1551398	-0.101	0.017	5.580E-09	-0.035	0.053	0.513	-0.078	0.032	0.013
34	rs2910793	0.155	0.023	1.490E-11	0.100	0.049	0.043	0.010	0.029	0.734
35	rs9272335	0.186	0.020	1.930E-21	0.157	0.057	0.005	0.008	0.033	0.804

Supplementary Table 6 Association of ulcerative colitis instrumental variants with outcome genome-wide association study

	SNP	Exposure (inflammatory bowel disease)			Outcome (all-cause dementia)			Outcome (dementia in Alzheimer disease)			Outcome (vascular dementia)		
		Beta	SE	Pval	Beta	SE	Pval	Beta	SE	Pval	Beta	SE	Pval
1	rs10272963	-0.172	0.022	1.690E-15	-0.020	0.015	0.183	-0.023	0.025	0.365	-0.057	0.037	0.116
2	rs10737481	0.250	0.022	4.370E-31	-0.012	0.015	0.427	-0.002	0.025	0.926	-0.017	0.036	0.645
3	rs10917545	-0.185	0.034	3.290E-08	0.015	0.021	0.488	-0.030	0.036	0.404	0.020	0.052	0.705
4	rs11209026	-0.562	0.052	1.580E-27	0.004	0.035	0.916	0.023	0.060	0.706	0.036	0.089	0.683
5	rs114152040	0.340	0.062	4.950E-08	0.064	0.040	0.109	0.201	0.066	0.002	0.081	0.100	0.416
6	rs1359946	0.158	0.027	3.840E-09	-0.004	0.019	0.826	-0.011	0.033	0.731	-0.021	0.047	0.649
7	rs2212434	0.142	0.021	2.460E-11	0.003	0.015	0.840	0.022	0.026	0.398	-0.025	0.037	0.506
8	rs254559	0.124	0.022	7.630E-09	0.002	0.015	0.913	-0.032	0.026	0.218	-0.026	0.037	0.491
9	rs3829111	0.156	0.021	2.890E-13	-0.016	0.015	0.284	-0.036	0.026	0.166	0.041	0.037	0.265
10	rs4574921	0.151	0.026	4.240E-09	-0.013	0.019	0.492	0.005	0.032	0.866	0.002	0.046	0.967
11	rs4676410	0.208	0.028	2.460E-13	-0.005	0.017	0.776	0.003	0.029	0.916	-0.033	0.041	0.418
12	rs483905	0.129	0.023	1.570E-08	0.007	0.018	0.701	-0.012	0.031	0.692	0.066	0.044	0.136
13	rs56167332	0.152	0.023	5.300E-11	0.015	0.016	0.357	0.022	0.027	0.427	0.084	0.039	0.032
14	rs6017342	0.191	0.024	1.380E-15	0.006	0.015	0.709	-0.014	0.026	0.577	0.037	0.037	0.320
15	rs6933404	0.167	0.025	3.680E-11	-0.004	0.019	0.841	0.048	0.032	0.138	-0.009	0.046	0.845
16	rs7523335	-0.170	0.029	2.290E-09	0.030	0.017	0.069	0.059	0.029	0.038	0.068	0.041	0.099
17	rs7752873	0.182	0.030	1.830E-09	-0.001	0.024	0.972	-0.077	0.042	0.062	0.122	0.060	0.041

18	rs989960	-0.129	0.022	1.770E-09	-0.006	0.015	0.696	0.025	0.025	0.318	0.014	0.036	0.699
19	rs9977672	-0.245	0.026	6.210E-21	0.014	0.017	0.425	0.015	0.030	0.614	0.012	0.043	0.783
20	rs9272335	0.344	0.025	1.930E-43	0.043	0.017	0.012	0.039	0.030	0.194	-0.002	0.043	0.958

Supplementary Table 6 Association of ulcerative colitis instrumental variants with outcome genome-wide association study

	SNP	Exposure (inflammatory bowel disease)			Outcome (dementia in other diseases classified elsewhere)			Outcome (unspecified dementia)		
		Beta	SE	Pval	Beta	SE	Pval	Beta	SE	Pval
1	rs10272963	-0.172	0.022	1.690E-15	-0.048	0.048	0.322	0.061	0.028	0.030
2	rs10737481	0.250	0.022	4.370E-31	-0.018	0.048	0.710	-0.022	0.028	0.435
3	rs10917545	-0.185	0.034	3.290E-08	0.020	0.069	0.774	-0.023	0.041	0.575
4	rs11209026	-0.562	0.052	1.580E-27	-0.045	0.114	0.695	-0.005	0.069	0.947
5	rs114152040	0.340	0.062	4.950E-08	0.026	0.132	0.846	0.016	0.078	0.835
6	rs1359946	0.158	0.027	3.840E-09	-0.071	0.063	0.259	-0.077	0.037	0.036
7	rs2212434	0.142	0.021	2.460E-11	-0.013	0.049	0.784	-0.006	0.029	0.842
8	rs254559	0.124	0.022	7.630E-09	0.120	0.049	0.014	-0.004	0.029	0.892
9	rs3829111	0.156	0.021	2.890E-13	-0.052	0.048	0.279	0.017	0.029	0.545
10	rs4574921	0.151	0.026	4.240E-09	-0.021	0.061	0.731	0.005	0.036	0.894
11	rs4676410	0.208	0.028	2.460E-13	-0.061	0.054	0.260	0.014	0.032	0.655
12	rs483905	0.129	0.023	1.570E-08	0.059	0.058	0.310	0.016	0.035	0.634
13	rs56167332	0.152	0.023	5.300E-11	-0.011	0.052	0.828	-0.020	0.031	0.513
14	rs6017342	0.191	0.024	1.380E-15	0.059	0.049	0.224	0.035	0.029	0.229
15	rs6933404	0.167	0.025	3.680E-11	0.027	0.061	0.662	-0.019	0.036	0.609
16	rs7523335	-0.170	0.029	2.290E-09	0.040	0.054	0.461	0.006	0.032	0.852
17	rs7752873	0.182	0.030	1.830E-09	0.084	0.078	0.283	-0.028	0.047	0.547

18	rs989960	-0.129	0.022	1.770E-09	-0.052	0.048	0.274	-0.025	0.028	0.380
19	rs9977672	-0.245	0.026	6.210E-21	-0.055	0.057	0.333	-0.034	0.034	0.313
20	rs9272335	0.344	0.025	1.930E-43	0.157	0.057	0.005	0.008	0.033	0.804

Supplementary Table 7 Association of Crohn's disease instrumental variants with outcome genome-wide association study

	SNP	Exposure			Outcome			Outcome			Outcome		
		(inflammatory disease)	bowel	(all-cause dementia)	(dementia disease)	in Alzheimer	(vascular dementia)	Beta	SE	Pval	Beta	SE	Pval
1	rs10761659	0.212	0.024	3.420E-19	-0.026	0.015	0.082	-0.011	0.025	0.666	-0.054	0.036	0.137
2	rs11209026	-0.995	0.064	1.050E-54	0.004	0.035	0.916	0.023	0.060	0.706	0.036	0.089	0.683
3	rs11236797	0.181	0.023	4.850E-15	0.004	0.015	0.803	0.021	0.026	0.427	-0.022	0.037	0.551
4	rs12717899	0.159	0.029	3.590E-08	0.015	0.020	0.443	0.007	0.034	0.848	0.118	0.049	0.016
5	rs1297271	-0.155	0.024	6.280E-11	-0.010	0.015	0.505	0.010	0.026	0.685	0.006	0.037	0.880
6	rs140054334	0.350	0.063	2.570E-08	0.004	0.124	0.972	-0.182	0.211	0.387	-0.033	0.307	0.914
7	rs1456896	0.139	0.025	2.900E-08	0.012	0.016	0.449	-0.019	0.028	0.506	0.007	0.040	0.867
8	rs147018773	0.322	0.038	8.890E-18	-0.058	0.027	0.029	-0.017	0.046	0.710	0.003	0.066	0.962
9	rs151314883	-0.224	0.033	7.120E-12	0.058	0.023	0.010	0.052	0.039	0.187	0.051	0.057	0.370
10	rs1932990	0.153	0.026	6.020E-09	0.029	0.018	0.118	0.034	0.032	0.285	-0.051	0.046	0.266
11	rs2076756	0.400	0.024	3.240E-61	-0.019	0.020	0.364	0.022	0.035	0.533	-0.068	0.051	0.177
12	rs2129944	-0.156	0.027	7.810E-09	-0.040	0.017	0.019	-0.024	0.029	0.415	0.004	0.042	0.920
13	rs2505640	-0.146	0.024	7.610E-10	-0.004	0.015	0.800	-0.015	0.026	0.571	0.008	0.038	0.839
14	rs28701841	0.224	0.037	1.850E-09	-0.002	0.026	0.942	-0.086	0.046	0.059	0.098	0.066	0.134
15	rs3091315	-0.180	0.026	9.520E-12	0.021	0.015	0.180	-0.004	0.027	0.884	-0.015	0.038	0.699
16	rs3810936	0.208	0.026	2.460E-15	-0.013	0.017	0.466	0.001	0.030	0.977	-0.006	0.043	0.891
17	rs4077515	0.216	0.024	4.370E-20	-0.017	0.015	0.245	-0.036	0.026	0.165	0.042	0.037	0.249

18	rs4851586	-0.169	0.026	9.940E-11	0.018	0.019	0.341	-0.074	0.032	0.022	0.122	0.047	0.009
19	rs4902642	-0.129	0.024	4.340E-08	-0.026	0.015	0.080	-0.024	0.026	0.351	-0.042	0.037	0.256
20	rs56062135	0.193	0.027	7.450E-13	-0.006	0.017	0.720	0.007	0.029	0.802	0.017	0.042	0.680
21	rs6588243	0.132	0.023	1.780E-08	0.001	0.015	0.970	-0.037	0.025	0.141	-0.002	0.036	0.960
22	rs6704109	0.202	0.026	2.770E-15	-0.009	0.016	0.574	0.007	0.028	0.804	-0.064	0.041	0.112
23	rs697693	0.172	0.028	8.360E-10	-0.031	0.025	0.212	-0.056	0.042	0.186	-0.031	0.060	0.610
24	rs72798422	0.590	0.051	3.190E-31	-0.035	0.040	0.382	-0.016	0.069	0.815	-0.111	0.099	0.262
25	rs7713270	0.297	0.024	6.970E-35	-0.009	0.015	0.563	-0.031	0.026	0.233	0.022	0.037	0.547
26	rs8137950	0.174	0.029	1.170E-09	0.009	0.016	0.580	0.014	0.027	0.618	-0.015	0.040	0.703
27	rs907092	0.130	0.023	1.010E-08	0.026	0.015	0.082	0.024	0.025	0.346	0.030	0.036	0.404
28	rs2910793	0.155	0.023	1.490E-11	0.032	0.015	0.036	0.006	0.026	0.824	-0.014	0.037	0.705

Supplementary Table 7 Association of Crohn's disease instrumental variants with outcome GWAS

	SNP	Exposure (inflammatory bowel disease)			Outcome (dementia in other diseases classified elsewhere)			Outcome (unspecified dementia)		
		Beta	SE	Pval	Beta	SE	Pval	Beta	SE	Pval
1	rs10761659	0.212	0.024	3.420E-19	-0.037	0.048	0.439	-0.042	0.028	0.141
2	rs11209026	-0.995	0.064	1.050E-54	-0.045	0.114	0.695	-0.005	0.069	0.947
3	rs11236797	0.181	0.023	4.850E-15	-0.014	0.049	0.774	-0.008	0.029	0.789
4	rs12717899	0.159	0.029	3.590E-08	-0.049	0.064	0.443	0.070	0.038	0.065
5	rs1297271	-0.155	0.024	6.280E-11	-0.053	0.049	0.281	-0.040	0.029	0.164

6	rs140054334	0.350	0.063	2.570E-08	0.321	0.407	0.430	-0.099	0.239	0.677
7	rs1456896	0.139	0.025	2.900E-08	0.039	0.053	0.455	-0.036	0.031	0.248
8	rs147018773	0.322	0.038	8.890E-18	-0.004	0.086	0.965	-0.140	0.053	0.009
9	rs151314883	-0.224	0.033	7.120E-12	0.190	0.075	0.011	0.089	0.044	0.042
10	rs1932990	0.153	0.026	6.020E-09	0.048	0.060	0.420	0.037	0.036	0.294
11	rs2076756	0.400	0.024	3.240E-61	-0.101	0.067	0.130	0.020	0.040	0.609
12	rs2129944	-0.156	0.027	7.810E-09	-0.026	0.056	0.636	-0.020	0.033	0.554
13	rs2505640	-0.146	0.024	7.610E-10	-0.040	0.050	0.422	0.021	0.029	0.471
14	rs28701841	0.224	0.037	1.850E-09	0.063	0.085	0.463	-0.043	0.051	0.398
15	rs3091315	-0.180	0.026	9.520E-12	0.016	0.051	0.748	0.021	0.030	0.483
16	rs3810936	0.208	0.026	2.460E-15	-0.041	0.057	0.466	0.005	0.034	0.885
17	rs4077515	0.216	0.024	4.370E-20	-0.059	0.048	0.221	0.012	0.029	0.678
18	rs4851586	-0.169	0.026	9.940E-11	0.025	0.061	0.678	0.034	0.036	0.349
19	rs4902642	-0.129	0.024	4.340E-08	-0.012	0.048	0.800	-0.051	0.029	0.076
20	rs56062135	0.193	0.027	7.450E-13	0.049	0.055	0.371	-0.007	0.033	0.820
21	rs6588243	0.132	0.023	1.780E-08	0.028	0.048	0.566	-0.008	0.028	0.773
22	rs6704109	0.202	0.026	2.770E-15	0.013	0.053	0.801	0.024	0.032	0.457
23	rs697693	0.172	0.028	8.360E-10	-0.053	0.080	0.507	-0.017	0.047	0.718
24	rs72798422	0.590	0.051	3.190E-31	-0.040	0.132	0.764	-0.119	0.078	0.125
25	rs7713270	0.297	0.024	6.970E-35	0.078	0.048	0.106	-0.006	0.029	0.839
26	rs8137950	0.174	0.029	1.170E-09	-0.007	0.052	0.890	0.014	0.031	0.650
27	rs907092	0.130	0.023	1.010E-08	0.091	0.048	0.058	0.091	0.028	0.001

28	rs2910793	0.155	0.023	1.490E-11	0.100	0.049	0.043	0.010	0.029	0.734
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Note

After MR-PRESSO testing, two SNPs (rs151314883, rs2129944) were deleted in MR estimates for effects on all-cause dementia, and one SNP (rs907092) were deleted in MR estimates for effects on unspecified dementia.

Supplementary Table 8 Genetic variants selected as instrumental variables for inflammatory bowel disease (validation)

	SNP	Effect_allele	Other_allele	EAF	Beta	SE	Pval	Samplesize	R ² (%)	F	Risk
										statistics	factors-related
1	rs10799837	G	A	0.432	0.111	0.017	1.600E-10	456327	0.009	40.905	FALSE
2	rs10737482	T	C	0.386	-0.145	0.018	3.400E-16	456327	0.015	66.571	FALSE
3	rs11581607	G	A	0.933	0.411	0.040	2.200E-24	456327	0.023	103.854	FALSE
4	rs3828058	G	A	0.629	-0.098	0.018	3.200E-08	456327	0.007	30.583	FALSE
5	rs6671847	G	A	0.490	0.121	0.017	1.600E-12	456327	0.011	49.944	TRUE
6	rs7554511	C	A	0.706	0.133	0.019	2.900E-12	456327	0.011	48.728	FALSE
7	rs3024505	G	A	0.846	-0.172	0.022	8.700E-15	456327	0.013	60.165	TRUE
8	rs10188217	T	C	0.483	-0.096	0.017	4.300E-08	456327	0.007	30.011	FALSE
9	rs13384671	A	G	0.692	-0.104	0.018	9.000E-09	456327	0.007	33.039	FALSE
10	rs2652670	G	A	0.852	0.145	0.025	1.100E-08	456327	0.007	32.656	FALSE
11	rs4551125	G	A	0.393	-0.108	0.018	7.500E-10	456327	0.008	37.889	FALSE
12	rs55722650	C	T	0.579	-0.100	0.017	4.500E-09	456327	0.008	34.411	TRUE
13	rs148844907	T	A	0.989	-0.757	0.057	9.700E-41	456327	0.039	178.619	TRUE
14	rs4713572	T	C	0.603	0.157	0.018	1.900E-18	456327	0.017	76.811	TRUE
15	rs17264332	A	G	0.780	-0.119	0.020	2.500E-09	456327	0.008	35.561	FALSE
16	rs6961243	G	A	0.590	0.102	0.018	5.000E-09	456327	0.007	34.188	FALSE
17	rs3807306	G	T	0.507	-0.094	0.017	3.700E-08	456327	0.007	30.277	FALSE
18	rs36051895	G	T	0.714	-0.113	0.018	8.500E-10	456327	0.008	37.645	FALSE
19	rs10761659	A	G	0.460	-0.117	0.017	9.700E-12	456327	0.010	46.387	FALSE

20	rs72810950	T	C	0.903	0.174	0.031	1.500E-08	456327	0.007	32.021	FALSE
21	rs4129133	T	C	0.485	0.112	0.017	3.400E-11	456327	0.010	43.913	TRUE
22	rs7936312	G	T	0.522	-0.111	0.017	6.700E-11	456327	0.009	42.607	FALSE
23	rs35788599	G	C	0.615	-0.116	0.017	3.200E-11	456327	0.010	44.060	TRUE
24	rs12720356	A	C	0.903	-0.151	0.027	2.300E-08	456327	0.007	31.252	TRUE
25	rs6017342	A	C	0.483	-0.131	0.017	1.600E-14	456327	0.013	58.937	FALSE
26	rs1297261	T	C	0.573	0.123	0.017	1.600E-12	456327	0.011	49.980	FALSE
27	rs2836878	G	A	0.733	0.191	0.020	2.100E-21	456327	0.020	90.264	FALSE
28	rs59998884	T	C	0.396	0.107	0.017	1.000E-09	456327	0.008	37.236	FALSE

no suitable

proxy

Note

1. SNPs related with potential risk factors: rs6671847, rs3024505, rs55722650, rs148844907, rs4713572, rs4129133, rs35788599, rs12720356

2. SNPs fail to extract: rs59998884

3. ambiguous or/and palindromic SNPs: none

Supplementary Table 9 Association of inflammatory bowel disease instrumental variants (validation) with outcome genome-wide association study

	SNP	Exposure (inflammatory bowel disease)			Outcome (all-cause dementia)			Outcome (dementia in Alzheimer disease)			Outcome (vascular dementia)		
		Beta	SE	Pval	Beta	SE	Pval	Beta	SE	Pval	Beta	SE	Pval
1	rs10188217	-0.096	0.017	4.30E-08	-0.006	0.015	0.674	0.028	0.025	0.276	0.023	0.037	0.528
2	rs10737482	-0.145	0.018	3.40E-16	0.024	0.015	0.110	0.023	0.026	0.368	0.044	0.038	0.236
3	rs10761659	-0.117	0.017	9.70E-12	0.026	0.015	0.082	0.011	0.025	0.666	0.054	0.036	0.137
4	rs10799837	0.111	0.017	1.60E-10	-0.018	0.015	0.236	-0.011	0.026	0.670	-0.030	0.037	0.422
5	rs11581607	0.411	0.040	2.20E-24	-0.005	0.035	0.894	-0.023	0.060	0.703	-0.039	0.089	0.664
6	rs1297261	0.123	0.017	1.60E-12	0.005	0.015	0.760	-0.005	0.026	0.842	0.002	0.037	0.959
7	rs13384671	-0.104	0.018	9.00E-09	-0.001	0.016	0.972	0.009	0.027	0.748	-0.021	0.038	0.588
8	rs17264332	-0.119	0.020	2.50E-09	0.002	0.019	0.914	-0.049	0.032	0.130	0.006	0.046	0.892
9	rs2652670	0.145	0.025	1.10E-08	-0.075	0.025	0.002	-0.104	0.043	0.016	-0.149	0.062	0.016
10	rs2836878	0.191	0.020	2.10E-21	-0.008	0.017	0.660	-0.010	0.029	0.735	-0.018	0.042	0.669
11	rs36051895	-0.113	0.018	8.50E-10	0.002	0.015	0.905	0.005	0.027	0.857	0.012	0.038	0.760
12	rs3807306	-0.094	0.017	3.70E-08	0.015	0.015	0.310	0.007	0.025	0.770	0.041	0.037	0.257
13	rs3828058	-0.098	0.018	3.20E-08	0.022	0.016	0.161	0.048	0.027	0.073	-0.056	0.039	0.150
14	rs4551125	-0.108	0.018	7.50E-10	0.008	0.015	0.571	0.030	0.026	0.239	-0.022	0.037	0.551
15	rs6017342	-0.131	0.017	1.60E-14	-0.006	0.015	0.709	0.014	0.026	0.577	-0.037	0.037	0.320
16	rs6961243	0.102	0.018	5.00E-09	0.021	0.015	0.160	0.017	0.026	0.510	0.044	0.037	0.241
17	rs72810950	0.174	0.031	1.50E-08	-0.016	0.023	0.503	0.073	0.040	0.070	0.022	0.058	0.700

18	rs7554511	0.133	0.019	2.90E-12	0.009	0.018	0.603	-0.007	0.031	0.825	0.010	0.044	0.822
19	rs7936312	-0.111	0.017	6.70E-11	0.001	0.015	0.964	-0.019	0.026	0.453	0.023	0.037	0.540

Supplementary Table 9 Association of inflammatory bowel disease instrumental variants (validation) with outcome genome-wide association study

	SNP	Exposure (inflammatory bowel disease)			Outcome (dementia in other diseases classified elsewhere)			Outcome (unspecified dementia)		
		Beta	SE	Pval	Beta	SE	Pval	Beta	SE	Pval
1	rs10188217	-0.096	0.017	4.30E-08	0.024	0.048	0.614	-0.013	0.029	0.658
2	rs10737482	-0.145	0.018	3.40E-16	-0.036	0.049	0.465	0.034	0.029	0.251
3	rs10761659	-0.117	0.017	9.70E-12	0.037	0.048	0.439	0.042	0.028	0.141
4	rs10799837	0.111	0.017	1.60E-10	0.044	0.049	0.368	-0.009	0.029	0.751
5	rs11581607	0.411	0.040	2.20E-24	0.043	0.115	0.709	0.001	0.070	0.983
6	rs1297261	0.123	0.017	1.60E-12	0.051	0.049	0.291	0.026	0.029	0.361
7	rs13384671	-0.104	0.018	9.00E-09	-0.028	0.051	0.584	0.001	0.030	0.975
8	rs17264332	-0.119	0.020	2.50E-09	-0.031	0.061	0.614	0.018	0.036	0.629
9	rs2652670	0.145	0.025	1.10E-08	-0.032	0.082	0.697	-0.113	0.048	0.018
10	rs2836878	0.191	0.020	2.10E-21	0.047	0.056	0.399	0.037	0.033	0.265
11	rs36051895	-0.113	0.018	8.50E-10	0.054	0.051	0.282	-0.029	0.030	0.332
12	rs3807306	-0.094	0.017	3.70E-08	-0.031	0.048	0.520	0.037	0.028	0.199
13	rs3828058	-0.098	0.018	3.20E-08	0.033	0.051	0.522	0.042	0.030	0.160
14	rs4551125	-0.108	0.018	7.50E-10	-0.078	0.048	0.107	0.006	0.029	0.840
15	rs6017342	-0.131	0.017	1.60E-14	-0.059	0.049	0.224	-0.035	0.029	0.229
16	rs6961243	0.102	0.018	5.00E-09	0.049	0.049	0.314	-0.060	0.029	0.038

17	rs72810950	0.174	0.031	1.50E-08	-0.045	0.076	0.557	0.005	0.045	0.907
18	rs7554511	0.133	0.019	2.90E-12	-0.031	0.058	0.592	0.077	0.034	0.024
19	rs7936312	-0.111	0.017	6.70E-11	0.025	0.049	0.602	0.009	0.029	0.763

Supplementary Table 10 Reverse MR analysis: Genetic variants selected as instrumental variables for all-cause dementia

	SNP	Effect_allele	Other_allele	EAF	Beta	SE	Pval	Samplesize	R ² (%)	F	Risk
										statistics	factors-related
1	rs7982	G	A	0.586	0.088	0.015	4.372E-09	306102	0.011	34.450	FALSE
2	rs76222888	C	T	0.019	0.292	0.053	3.156E-08	306102	0.010	30.609	FALSE
3	rs7232	A	T	0.303	-0.098	0.016	1.259E-09	306102	0.012	36.876	TRUE
4	rs16943758	G	A	0.114	-0.129	0.024	4.889E-08	306102	0.010	29.760	FALSE
5	rs5848	T	C	0.343	0.093	0.015	1.805E-09	306102	0.012	36.173	TRUE
6	rs145414981	C	T	0.051	-0.211	0.035	2.478E-09	306102	0.012	35.556	FALSE
7	rs138573164	T	A	0.036	0.662	0.036	3.037E-76	306102	0.111	341.479	FALSE
8	rs28615360	A	G	0.012	0.653	0.062	6.266E-26	306102	0.036	110.886	FALSE
9	rs12972156	G	C	0.172	0.575	0.018	1.000E-200	306102	0.330	1013.637	TRUE
10	rs1132899	C	T	0.555	0.164	0.015	3.051E-28	306102	0.040	121.447	FALSE
11	rs8113128	C	A	0.043	0.335	0.035	5.304E-22	306102	0.030	92.971	FALSE
12	rs188751991	T	C	0.056	0.179	0.032	1.281E-08	306102	0.011	32.360	FALSE

Note

1. SNPs related with potential risk factors: rs7232, rs5848, rs12972156

2. SNPs fail to extract: none

3. ambiguous or/and palindromic SNPs: rs138573164

Supplementary Table 11 Association of all-cause dementia instrumental variants with outcome genome-wide association study

SNP	Exposure (all-cause dementia)			Outcome (inflammatory bowel disease)		
	Beta	SE	Pval	Beta	SE	Pval
1 rs1132899	0.164	0.015	3.050E-28	-0.009	0.018	0.617
2 rs145414981	-0.211	0.035	2.480E-09	-0.073	0.040	0.070
3 rs16943758	-0.129	0.024	4.890E-08	-0.028	0.034	0.406
4 rs188751991	0.179	0.032	1.280E-08	-0.166	0.106	0.119
5 rs28615360	0.653	0.062	6.270E-26	0.103	0.095	0.278
6 rs76222888	0.292	0.053	3.160E-08	0.055	0.055	0.317
7 rs7982	0.088	0.015	4.370E-09	0.025	0.017	0.153
8 rs8113128	0.335	0.035	5.300E-22	0.058	0.052	0.258

Supplementary Table 12 Pleiotropy and heterogeneity test of genetic instrumental variants (IVs) in outcome genome-wide association study

Effect	Pleiotropy test			Heterogeneity test				
	MR Egger			PRESSO	MR Egger		IVW	
	Intercept	SE	Pval	Pval	Q	Pval	Q	Pval
Primary analysis								
IBD on all-cause dementia	0.003	0.009	0.727	0.249	36.096	0.205	36.246	0.237
IBD on dementia in Alzheimer disease	-0.002	0.015	0.883	0.372	36.328	0.316	36.352	0.360
IBD on vascular dementia	0.002	0.020	0.936	0.814	26.893	0.764	26.899	0.802
IBD on dementia in other diseases classified elsewhere	0.014	0.032	0.672	0.070	47.178	0.052	47.439	0.063
IBD on unspecified dementia	0.004	0.018	0.829	0.134	43.738	0.100	43.801	0.121
UC on all-cause dementia	-0.012	0.011	0.316	0.431	17.445	0.493	18.507	0.489
UC on dementia in Alzheimer disease	-0.030	0.023	0.218	0.075	26.768	0.083	29.192	0.063
UC on vascular dementia	0.022	0.030	0.469	0.351	20.743	0.293	21.373	0.317
UC on dementia in other diseases classified elsewhere	-0.015	0.040	0.710	0.259	22.051	0.230	22.226	0.273
UC on unspecified dementia	-0.010	0.022	0.634	0.709	15.031	0.660	15.265	0.706
CD on all-cause dementia	0.015	0.008	0.072	0.253	26.226	0.342	30.089	0.221
CD on dementia in Alzheimer disease	0.011	0.013	0.385	0.613	24.018	0.575	24.800	0.586
CD on vascular dementia	0.013	0.019	0.503	0.398	28.141	0.352	28.640	0.379
CD on dementia in other diseases classified elsewhere	0.030	0.024	0.236	0.374	27.279	0.395	28.825	0.369

CD on unspecified dementia	0.014	0.016	0.387	0.271	29.667	0.237	30.588	0.244
Validation analysis								
IBD on all-cause dementia	-0.001	0.013	0.935	0.429	19.092	0.323	19.099	0.386
IBD on dementia in Alzheimer disease	-0.012	0.022	0.606	0.465	18.213	0.376	18.509	0.423
IBD on vascular dementia	0.014	0.031	0.656	0.556	16.762	0.471	16.967	0.525
IBD on dementia in other diseases classified elsewhere	-0.001	0.040	0.981	0.889	11.444	0.833	11.445	0.875
IBD on unspecified dementia	-0.030	0.030	0.320	0.088	25.355	0.087	26.922	0.080
Reverse MR analysis								
all-cause dementia on IBD	-0.001	0.026	0.956	0.331	8.203	0.224	8.208	0.315

Supplementary Table 13 Mendelian randomization estimates for causal effects of inflammatory bowel disease on dementia

Effect	MR Methods	Beta	SE	OR (95% CI)	Pval
Primary analysis					
IBD on all-cause dementia	Inverse variance weighted	-0.020	0.020	0.980 (0.942-1.020)	0.325
	Weighted median	-0.036	0.027	0.964 (0.914-1.017)	0.180
	MR Egger	-0.037	0.054	0.963 (0.867-1.070)	0.492
IBD on dementia in Alzheimer disease	Inverse variance weighted	-0.044	0.032	0.957 (0.899-1.018)	0.165
	Weighted median	-0.033	0.048	0.968 (0.881-1.064)	0.497
	MR Egger	-0.032	0.088	0.968 (0.815-1.151)	0.718
IBD on vascular dementia	Inverse variance weighted	-0.057	0.044	0.944 (0.866-1.030)	0.195

	Weighted median	-0.050	0.061	0.951 (0.844-1.071)	0.407
	MR Egger	-0.067	0.122	0.935 (0.736-1.189)	0.590
IBD on dementia in other diseases classified elsewhere	Inverse variance weighted	0.085	0.069	1.089 (0.952-1.246)	0.214
	Weighted median	0.058	0.090	1.059 (0.888-1.264)	0.522
	MR Egger	0.010	0.190	1.010 (0.696-1.465)	0.959
IBD on unspecified dementia	Inverse variance weighted	0.011	0.039	1.011 (0.936-1.092)	0.776
	Weighted median	-0.007	0.054	0.993 (0.894-1.103)	0.897
	MR Egger	-0.011	0.110	0.989 (0.797-1.227)	0.920
UC on all-cause dementia	Inverse variance weighted	0.010	0.020	1.010 (0.972-1.050)	0.605
	Weighted median	-0.006	0.028	0.994 (0.941-1.050)	0.823
	MR Egger	0.065	0.056	1.067 (0.955-1.191)	0.267
UC on dementia in Alzheimer disease	Inverse variance weighted	0.004	0.042	1.004 (0.925-1.090)	0.932
	Weighted median	-0.009	0.050	0.991 (0.898-1.094)	0.858
	MR Egger	0.145	0.118	1.156 (0.917-1.458)	0.236
UC on vascular dementia	Inverse variance weighted	0.025	0.052	1.025 (0.927-1.134)	0.632
	Weighted median	-0.051	0.069	0.950 (0.830-1.087)	0.454
	MR Egger	-0.080	0.151	0.923 (0.686-1.241)	0.602
UC on dementia in other diseases classified elsewhere	Inverse variance weighted	0.118	0.069	1.126 (0.983-1.289)	0.087
	Weighted median	0.097	0.097	1.102 (0.912-1.332)	0.315
	MR Egger	0.191	0.204	1.210 (0.811-1.805)	0.362
UC on unspecified dementia	Inverse variance weighted	-0.007	0.038	0.993 (0.922-1.069)	0.848
	Weighted median	0.018	0.053	1.018 (0.918-1.129)	0.734

	MR Egger	0.043	0.110	1.044 (0.841-1.294)	0.703
	Inverse variance weighted	-0.017	0.017	0.983 (0.951-1.017)	0.323
CD on all-cause dementia	Weighted median	-0.027	0.022	0.973 (0.932-1.016)	0.220
	MR Egger	-0.075	0.035	0.928 (0.867-0.994)	0.042
CD on dementia in Alzheimer disease	Inverse variance weighted	-0.014	0.026	0.986 (0.937-1.038)	0.600
	Weighted median	-0.017	0.038	0.983 (0.912-1.059)	0.651
	MR Egger	-0.059	0.057	0.943 (0.843-1.055)	0.314
	Inverse variance weighted	-0.042	0.039	0.959 (0.888-1.035)	0.280
CD on vascular dementia	Weighted median	-0.036	0.056	0.964 (0.863-1.077)	0.519
	MR Egger	-0.094	0.087	0.910 (0.768-1.078)	0.285
CD on dementia in other diseases classified elsewhere	Inverse variance weighted	0.020	0.051	1.020 (0.923-1.127)	0.700
	Weighted median	0.017	0.078	1.017 (0.873-1.184)	0.831
	MR Egger	-0.100	0.111	0.905 (0.728-1.124)	0.376
	Inverse variance weighted	-0.025	0.032	0.975 (0.915-1.039)	0.434
CD on unspecified dementia	Weighted median	-0.004	0.043	0.996 (0.915-1.085)	0.933
	MR Egger	-0.082	0.072	0.922 (0.801-1.061)	0.266
Validation analysis					
	Inverse variance weighted	-0.056	0.030	0.945 (0.891-1.002)	0.060
IBD on all-cause dementia	Weighted median	-0.017	0.039	0.983 (0.910-1.062)	0.670
	MR Egger	-0.048	0.102	0.953 (0.780-1.165)	0.643
IBD on dementia in Alzheimer disease	Inverse variance weighted	-0.066	0.051	0.937 (0.847-1.035)	0.199
	Weighted median	-0.061	0.067	0.941 (0.826-1.072)	0.360

	MR Egger	0.021	0.172	1.021 (0.729-1.430)	0.906
	Inverse variance weighted	-0.070	0.072	0.932 (0.809-1.074)	0.331
IBD on vascular dementia	Weighted median	-0.094	0.100	0.910 (0.748-1.107)	0.346
	MR Egger	-0.175	0.243	0.839 (0.522-1.350)	0.480
IBD on dementia in other diseases classified elsewhere	Inverse variance weighted	0.113	0.095	1.119 (0.929-1.349)	0.235
	Weighted median	0.233	0.130	1.263 (0.979-1.629)	0.072
	MR Egger	0.120	0.315	1.128 (0.609-2.089)	0.707
IBD on unspecified dementia	Inverse variance weighted	-0.031	0.069	0.970 (0.847-1.110)	0.656
	Weighted median	-0.002	0.083	0.998 (0.849-1.174)	0.981
	MR Egger	0.195	0.231	1.216 (0.773-1.911)	0.410

Supplementary Table 14 Mendelian randomization estimates for causal effects of all-cause dementia on inflammatory bowel disease

MR Methods	Beta	SE	OR (95% CI)	Pval
Inverse variance weighted	0.120	0.066	1.128 (0.992-1.282)	0.066
Weighted median	0.166	0.086	1.181 (0.998-1.397)	0.053
MR Egger	0.128	0.147	1.136 (0.852-1.515)	0.417

The R-code Statement

PART ONE: MR analysis

```
1. library(TwoSampleMR) # Load "TwoSampleMR" R package
2. library(data.table) # Load "data.table" R package
3. exp_dat <-extract_instruments(outcomes='ieu-a-31',access_token = NULL) # Extract IVs from the
IBD GWAS available on the ieu open gwas project (default parameters: P=5×10-8, R2=0.001,
kb=10000)
4. setwd("~/~/") # Set work path: storage location of GWAS data
5. dat1 <-fread("finngen_R7_F5_DEMENTIA.gz") # Read dementia GWAS (download at
https://storage.googleapis.com/finngen-public-data-r7/summary\_stats/finngen\_R7\_F5\_DEMENTIA
A.gz) with "fread" function
6. out_dat <- format_data(
  dat = dat1,
  type = "outcome",
  snps = exp_dat$SNP,
  header = TRUE,
  snp_col = "rsids",
  beta_col = "beta",
  se_col = "sebeta",
  effect_allele_col = "alt",
  other_allele_col = "ref",
  eaf_col = "af_alt",
  pval_col = "pval",
  samplesize_col = "N",
  chr_col = "#chrom",
  pos_col = "pos"
) # Convert "out_dat" to the TwoSampleMR format
7. har_dat<- harmonise_data(
  exposure_dat = exp_dat, outcome_dat = out_dat, action = 2
) # Harmonise exposure and outcome datasets
8. write.csv(har_dat, file="harmonise_data.csv") # Save the harmonized data in .csv format
```

```

9. har_dat<-read.csv("~/harmonise_data.csv")    # Read the harmonized data
10. mr_pleiotropy_test(har_dat)                # Perform MR_Egger intercept analysis
11. run_mr_presso(har_dat, NbDistribution = 10000) # Perform MR-PRESSO test
12. mr_heterogeneity(har_dat)                 # Perform heterogeneity test
13. mr(har_dat)                               # Perform MR analysis
14. generate_odds_ratios(mr_res = mr(har_dat)) # Convert beta to OR
mr_scatter_plot(
  mr_results = mr(har_dat,method_list =
c("mr_ivw_mre","mr_weighted_median","mr_egger_regression")),
har_dat
) # Scatter plot visualization of IVW, weighted median, and MR Egger estimates
15. mr_forest_plot(singlesnp_results = mr_singlesnp(har_dat)) #Forest plot visualization of IVW
estimates
16. mr_leaveoneout_plot(leaveoneout_results = mr_leaveoneout(har_dat)) #Perform "leave one
out" analysis
17. Repeat steps 4 to 16 four times: read four subtypes of all-cause dementia GWAS sequentially
(download https://storage.googleapis.com/finngen-public-data-r7/summary\_stats/finngen\_R7\_F5\_ALZHDEMENT.gz,
https://storage.googleapis.com/finngen-public-data-r7/summary\_stats/finngen\_R7\_F5\_VASCDEM.gz,
https://storage.googleapis.com/finngen-public-data-r7/summary\_stats/finngen\_R7\_F5\_DEMINOTH.gz,
and
https://storage.googleapis.com/finngen-public-data-r7/summary\_stats/finngen\_R7\_F5\_DEMNAS.gz,
respectively)
18. Repeat steps 3 to 17 two times: extract IVs from the UC (ID: ieu-a-32) and CD (ID: ieu-a-30)
GWAS available on the ieu open gwas project

```

PART TWO: Reverse MR analysis

```
library(TwoSampleMR) # Load "TwoSampleMR" R package
library(data.table) # Load "data.table" R package
setwd("~/~/") # Set work path: storage location of GWAS data
dat2<-fread("finngen_R7_F5_DEMENTIA.gz") # Read dementia GWAS
exp_dat2 <- format_data(
  dat = dat2,
  type = "exposure",
  header = TRUE,
  snp_col = "rsids",
  beta_col = "beta",
  se_col = "sebeta",
  effect_allele_col = "alt",
  other_allele_col = "ref",
  eaf_col = "af_alt",
  pval_col = "pval",
  samplesize_col = "N",
  chr_col = "#chrom",
  pos_col = "pos"
) # Convert "exp_dat" to the TwoSampleMR format
exp_dat<-subset(exp_dat2, pval.exposure<5e-08) # Extract SNPs strongly associated with the
exposure
exp_dat_clumped<-clump_data(
  exp_dat,
  clump_kb = 10000,
  clump_r2 = 0.001
) # Remove IVs with linkage disequilibrium
out_dat <- extract_outcome_data(
  snps= exp_dat_clumped$SNP,
  outcomes="ieu-a-31",
  proxies = FALSE,
  maf_threshold = 0.01,
```

```

access_token = NULL
) # Get IBD GWAS available on the ieu open gwas project
har_dat<- harmonise_data(
exposure_dat = exp_dat_clumped,
outcome_dat = out_dat,
action = 2
) # Harmonise exposure and outcome datasets
write.csv(har_dat, file="harmonise_data.csv") # Save the harmonized data in .csv format
har_dat<-read.csv("~/harmonise_data.csv") # Read the harmonized data
mr_pleiotropy_test(har_dat) # Perform MR_Egger intercept analysis
run_mr_presso(har_dat, NbDistribution = 10000) # Perform MR-PRESSO test
mr_heterogeneity(har_dat) # Perform heterogeneity test
mr(har_dat) # Perform MR analysis
generate_odds_ratios(mr_res = mr(har_dat)) # Convert beta to OR
mr_scatter_plot(
mr_results = mr(har_dat,method_list =
c("mr_ivw_mre","mr_weighted_median","mr_egger_regression")),
har_dat
) # Scatter plot visualization of IVW, weighted median, and MR Egger estimates
mr_forest_plot(singlesnp_results = mr_singlesnp(har_dat)) #Forest plot visualization of IVW
estimates
mr_leaveoneout_plot(leaveoneout_results = mr_leaveoneout(har_dat)) #Perform "leave one out"
analysis

```