

Table S1 The result of heterogeneity test and horizontal pleiotropic test

Outcomes	Exposures	Heterogeneity test				Horizontal pleiotropic test			Global_test
		Method	Q	Q_df	Q_pval	Egger_intercept	SE	P-value	global_test_p
Barrett's esophagus(Finngen)	full_SurfArea	MR Egger	52.739	44	0.172	-0.010	0.026	0.687	0.206
		Inverse variance weighted	52.936	45	0.195				
	full_Thickness	MR Egger	41.222	34	0.184	0.010	0.036	0.782	0.218
	full_Thickness	Inverse variance weighted	41.316	35	0.214				
	bankssts_thick	MR Egger	4.790	6	0.571	0.053	0.075	0.506	0.638
	bankssts_thick	Inverse variance weighted	5.290	7	0.625				
	parahippocampal_thick	MR Egger	21.831	19	0.293	0.016	0.044	0.718	0.375
	parahippocampal_thick	Inverse variance weighted	21.985	20	0.341				
	precentral_surf	MR Egger	13.550	20	0.853	0.000	0.016	0.981	0.906
	precentral_surf	Inverse variance weighted	13.550	21	0.888				
	superiortemporal_surf	MR Egger	31.279	24	0.146	-0.055	0.047	0.259	0.156
	superiortemporal_surf	Inverse variance weighted	33.020	25	0.131				

Table S2 The result of heterogeneity test and horizontal pleiotropic test

Outcomes	Exposures	Heterogeneity test				Horizontal pleiotropic test			Global_test
		Method	Q	Q_df	Q_pval	Egger_intercept	SE	P-value	global_test_p
Barrett's esophagus(IEU)	full_SurfArea	MR Egger	23.495	12	0.024	0.117	0.048	0.030	0.003
		Inverse variance weighted	35.335	13	0.001				
	full_Thickness	MR Egger	7.592	11	0.749	0.018	0.023	0.452	0.782
	full_Thickness id:enigma3-global-full-th	Inverse variance weighted	8.201	12	0.769				
	bankssts_surf	MR Egger	0.954	3	0.812	0.037	0.037	0.392	0.777
	wSA_Mean_bankssts_surfavg	Inverse variance weighted	1.949	4	0.745				
	middletemporal_surf	MR Egger	7.459	10	0.681	-0.042	0.023	0.098	0.484
	wSA_Mean_middletemporal_surfavg	Inverse variance weighted	10.791	11	0.461				
	medialorbitofrontal_surf	MR Egger	0.758	3	0.860	-0.039	0.094	0.707	0.927
	wSA_Mean_medialorbitofrontal_surfavg	Inverse variance weighted	0.929	4	0.920				
	supramarginal_thick	MR Egger	1.045	4	0.903	-0.071	0.042	0.168	0.607
	wTHICK_Mean_supramarginal_thickavg	Inverse variance weighted	3.871	5	0.568				
	precuneus_surf	MR Egger	6.144	7	0.523	0.020	0.041	0.649	0.627
	wSA_Mean_precuneus_surfavg	Inverse variance weighted	6.371	8	0.606				
	parsorbitalis_thick	MR Egger	1.195	2	0.550	-0.050	0.107	0.687	0.713
	wTHICK_Mean_parsorbitalis_thickavg	Inverse variance weighted	1.412	3	0.703				

Table S3 The MR Steiger Tests of Directionality

id/exposure	id/outcome	steiger_test_pval	steiger_test_direction
enigma3-global-full-sa	Barrett's Esophagu(Finngen)	5.27E-279	TRUE
enigma3-global-full-th	Barrett's Esophagu(Finngen)	2.39E-163	TRUE
enigma3-withglobal-bankssts-surfavg	Barrett's Esophagu(Finngen)	2.32E-84	TRUE
enigma3-withglobal-bankssts-thickavg	Barrett's Esophagu(Finngen)	5.52E-43	TRUE
enigma3-withglobal-caudalanteriorcingulate-surfavg	Barrett's Esophagu(Finngen)	4.56E-89	TRUE
enigma3-withglobal-caudalanteriorcingulate-thickavg	Barrett's Esophagu(Finngen)	8.48E-57	TRUE
enigma3-withglobal-caudalmiddlefrontal-surfavg	Barrett's Esophagu(Finngen)	3.53E-97	TRUE
enigma3-withglobal-caudalmiddlefrontal-thickavg	Barrett's Esophagu(Finngen)	8.31E-95	TRUE
enigma3-withglobal-cuneus-surfavg	Barrett's Esophagu(Finngen)	1.26E-157	TRUE
enigma3-withglobal-cuneus-thickavg	Barrett's Esophagu(Finngen)	1.97E-46	TRUE
enigma3-withglobal-entorhinal-surfavg	Barrett's Esophagu(Finngen)	1.20E-109	TRUE
enigma3-withglobal-entorhinal-thickavg	Barrett's Esophagu(Finngen)	7.36E-55	TRUE
enigma3-withglobal-frontalpole-surfavg	Barrett's Esophagu(Finngen)	5.12E-63	TRUE
enigma3-withglobal-frontalpole-thickavg	Barrett's Esophagu(Finngen)	8.41E-71	TRUE
enigma3-withglobal-fusiform-surfavg	Barrett's Esophagu(Finngen)	1.09E-104	TRUE
enigma3-withglobal-fusiform-thickavg	Barrett's Esophagu(Finngen)	5.29E-46	TRUE
enigma3-withglobal-inferiorparietal-surfavg	Barrett's Esophagu(Finngen)	1.72E-171	TRUE
enigma3-withglobal-inferiorparietal-thickavg	Barrett's Esophagu(Finngen)	2.42E-60	TRUE
enigma3-withglobal-inferiortemporal-surfavg	Barrett's Esophagu(Finngen)	3.52E-117	TRUE
enigma3-withglobal-inferiortemporal-thickavg	Barrett's Esophagu(Finngen)	1.09E-54	TRUE
enigma3-withglobal-insula-surfavg	Barrett's Esophagu(Finngen)	1.62E-154	TRUE
enigma3-withglobal-insula-thickavg	Barrett's Esophagu(Finngen)	1.86E-103	TRUE
enigma3-withglobal-isthmuscingulate-surfavg	Barrett's Esophagu(Finngen)	8.64E-66	TRUE
enigma3-withglobal-isthmuscingulate-thickavg	Barrett's Esophagu(Finngen)	1.06E-98	TRUE
enigma3-withglobal-lateraloccipital-surfavg	Barrett's Esophagu(Finngen)	3.59E-161	TRUE
enigma3-withglobal-lateraloccipital-thickavg	Barrett's Esophagu(Finngen)	4.95E-79	TRUE
enigma3-withglobal-lateralorbitofrontal-surfavg	Barrett's Esophagu(Finngen)	3.29E-191	TRUE
enigma3-withglobal-lateralorbitofrontal-thickavg	Barrett's Esophagu(Finngen)	4.79E-31	TRUE
enigma3-withglobal-lingual-surfavg	Barrett's Esophagu(Finngen)	1.20E-217	TRUE
enigma3-withglobal-lingual-thickavg	Barrett's Esophagu(Finngen)	1.48E-103	TRUE
enigma3-withglobal-medialorbitofrontal-surfavg	Barrett's Esophagu(Finngen)	2.07E-52	TRUE
enigma3-withglobal-medialorbitofrontal-thickavg	Barrett's Esophagu(Finngen)	2.31E-52	TRUE
enigma3-withglobal-middletemporal-surfavg	Barrett's Esophagu(Finngen)	1.93E-138	TRUE
enigma3-withglobal-middletemporal-thickavg	Barrett's Esophagu(Finngen)	1.91E-64	TRUE
enigma3-withglobal-paracentral-surfavg	Barrett's Esophagu(Finngen)	8.87E-94	TRUE
enigma3-withglobal-paracentral-thickavg	Barrett's Esophagu(Finngen)	5.17E-71	TRUE
enigma3-withglobal-parahippocampal-surfavg	Barrett's Esophagu(Finngen)	3.87E-78	TRUE
enigma3-withglobal-parahippocampal-thickavg	Barrett's Esophagu(Finngen)	1.84E-99	TRUE
enigma3-withglobal-parsopercularis-surfavg	Barrett's Esophagu(Finngen)	5.45E-104	TRUE
enigma3-withglobal-parsopercularis-thickavg	Barrett's Esophagu(Finngen)	2.86E-88	TRUE
enigma3-withglobal-parsorbitalis-surfavg	Barrett's Esophagu(Finngen)	4.46E-118	TRUE
enigma3-withglobal-parsorbitalis-thickavg	Barrett's Esophagu(Finngen)	2.78E-62	TRUE
enigma3-withglobal-parstriangularis-surfavg	Barrett's Esophagu(Finngen)	1.09E-200	TRUE
enigma3-withglobal-parstriangularis-thickavg	Barrett's Esophagu(Finngen)	5.00E-83	TRUE
enigma3-withglobal-pericalcarine-surfavg	Barrett's Esophagu(Finngen)	0	TRUE
enigma3-withglobal-pericalcarine-thickavg	Barrett's Esophagu(Finngen)	5.10E-59	TRUE
enigma3-withglobal-postcentral-surfavg	Barrett's Esophagu(Finngen)	2.92E-167	TRUE
enigma3-withglobal-postcentral-thickavg	Barrett's Esophagu(Finngen)	8.70E-198	TRUE
enigma3-withglobal-posteriorcingulate-surfavg	Barrett's Esophagu(Finngen)	5.49E-95	TRUE
enigma3-withglobal-posteriorcingulate-thickavg	Barrett's Esophagu(Finngen)	4.83E-94	TRUE

Table S3 (continued)

Table S3 (continued)

id/exposure	id/outcome	steiger_test_pval	steiger_test_direction
enigma3-withglobal-precentral-surfavg	Barrett's Esophagu(Finngen)	1.86E-228	TRUE
enigma3-withglobal-precentral-thickavg	Barrett's Esophagu(Finngen)	8.00E-94	TRUE
enigma3-withglobal-precuneus-surfavg	Barrett's Esophagu(Finngen)	5.23E-192	TRUE
enigma3-withglobal-precuneus-thickavg	Barrett's Esophagu(Finngen)	1.35E-108	TRUE
enigma3-withglobal-rostralanteriorcingulate-surfavg	Barrett's Esophagu(Finngen)	4.06E-83	TRUE
enigma3-withglobal-rostralanteriorcingulate-thickavg	Barrett's Esophagu(Finngen)	2.84E-70	TRUE
enigma3-withglobal-rostralmiddlefrontal-surfavg	Barrett's Esophagu(Finngen)	7.78E-163	TRUE
enigma3-withglobal-rostralmiddlefrontal-thickavg	Barrett's Esophagu(Finngen)	2.13E-70	TRUE
enigma3-withglobal-superiorfrontal-surfavg	Barrett's Esophagu(Finngen)	1.07E-98	TRUE
enigma3-withglobal-superiorfrontal-thickavg	Barrett's Esophagu(Finngen)	7.26E-74	TRUE
enigma3-withglobal-superiorparietal-surfavg	Barrett's Esophagu(Finngen)	2.51E-200	TRUE
enigma3-withglobal-superiorparietal-thickavg	Barrett's Esophagu(Finngen)	6.91E-111	TRUE
enigma3-withglobal-superiortemporal-surfavg	Barrett's Esophagu(Finngen)	5.80E-124	TRUE
enigma3-withglobal-superiortemporal-thickavg	Barrett's Esophagu(Finngen)	7.62E-97	TRUE
enigma3-withglobal-supramarginal-surfavg	Barrett's Esophagu(Finngen)	6.20E-146	TRUE
enigma3-withglobal-supramarginal-thickavg	Barrett's Esophagu(Finngen)	8.49E-54	TRUE
enigma3-withglobal-temporalpole-surfavg	Barrett's Esophagu(Finngen)	6.79E-54	TRUE
enigma3-withglobal-temporalpole-thickavg	Barrett's Esophagu(Finngen)	1.50E-67	TRUE
enigma3-withglobal-transversetemporal-surfavg	Barrett's Esophagu(Finngen)	1.11E-121	TRUE
enigma3-withglobal-transversetemporal-thickavg	Barrett's Esophagu(Finngen)	8.15E-57	TRUE
enigma3-global-full-sa	Barrett's Esophagu(IEU)	2.17E-29	TRUE
enigma3-global-full-th	Barrett's Esophagu(IEU)	1.09E-40	TRUE
enigma3-withglobal-bankssts-surfavg	Barrett's Esophagu(IEU)	2.00E-13	TRUE
enigma3-withglobal-bankssts-thickavg	Barrett's Esophagu(IEU)	2.54E-20	TRUE
enigma3-withglobal-caudalanteriorcingulate-surfavg	Barrett's Esophagu(IEU)	1.53E-13	TRUE
enigma3-withglobal-caudalanteriorcingulate-thickavg	Barrett's Esophagu(IEU)	6.60E-06	TRUE
enigma3-withglobal-caudalmiddlefrontal-surfavg	Barrett's Esophagu(IEU)	3.48E-28	TRUE
enigma3-withglobal-caudalmiddlefrontal-thickavg	Barrett's Esophagu(IEU)	9.55E-16	TRUE
enigma3-withglobal-cuneus-surfavg	Barrett's Esophagu(IEU)	2.21E-33	TRUE
enigma3-withglobal-cuneus-thickavg	Barrett's Esophagu(IEU)	2.31E-09	TRUE
enigma3-withglobal-entorhinal-surfavg	Barrett's Esophagu(IEU)	5.34E-37	TRUE
enigma3-withglobal-entorhinal-thickavg	Barrett's Esophagu(IEU)	3.29E-15	TRUE
enigma3-withglobal-frontalpole-surfavg	Barrett's Esophagu(IEU)	4.71E-14	TRUE
enigma3-withglobal-frontalpole-thickavg	Barrett's Esophagu(IEU)	1.30E-07	TRUE
enigma3-withglobal-fusiform-surfavg	Barrett's Esophagu(IEU)	3.01E-11	TRUE
enigma3-withglobal-fusiform-thickavg	Barrett's Esophagu(IEU)	0.000393866	TRUE
enigma3-withglobal-inferiorparietal-surfavg	Barrett's Esophagu(IEU)	6.32E-38	TRUE
enigma3-withglobal-inferiorparietal-thickavg	Barrett's Esophagu(IEU)	6.14E-06	TRUE
enigma3-withglobal-inferiortemporal-surfavg	Barrett's Esophagu(IEU)	1.36E-22	TRUE
enigma3-withglobal-inferiortemporal-thickavg	Barrett's Esophagu(IEU)	1.16E-05	TRUE
enigma3-withglobal-insula-surfavg	Barrett's Esophagu(IEU)	4.91E-27	TRUE
enigma3-withglobal-insula-thickavg	Barrett's Esophagu(IEU)	1.24E-15	TRUE
enigma3-withglobal-isthmuscingulate-surfavg	Barrett's Esophagu(IEU)	2.73E-07	TRUE
enigma3-withglobal-isthmuscingulate-thickavg	Barrett's Esophagu(IEU)	1.18E-20	TRUE
enigma3-withglobal-lateraloccipital-surfavg	Barrett's Esophagu(IEU)	1.51E-25	TRUE
enigma3-withglobal-lateraloccipital-thickavg	Barrett's Esophagu(IEU)	2.32E-20	TRUE
enigma3-withglobal-lateralorbitofrontal-surfavg	Barrett's Esophagu(IEU)	4.60E-38	TRUE
enigma3-withglobal-lateralorbitofrontal-thickavg	Barrett's Esophagu(IEU)	7.27E-08	TRUE
enigma3-withglobal-lingual-surfavg	Barrett's Esophagu(IEU)	1.05E-42	TRUE

Table S3 (continued)

Table S3 (continued)

id/exposure	id/outcome	steiger_test_pval	steiger_test_direction
enigma3-withglobal-lingual-thickavg	Barrett's Esophagu(IEU)	3.04E-24	TRUE
enigma3-withglobal-medialorbitofrontal-surfavg	Barrett's Esophagu(IEU)	8.92E-14	TRUE
enigma3-withglobal-medialorbitofrontal-thickavg	Barrett's Esophagu(IEU)	3.17E-06	TRUE
enigma3-withglobal-middletemporal-surfavg	Barrett's Esophagu(IEU)	2.15E-31	TRUE
enigma3-withglobal-middletemporal-thickavg	Barrett's Esophagu(IEU)	1.81E-19	TRUE
enigma3-withglobal-paracentral-surfavg	Barrett's Esophagu(IEU)	6.85E-22	TRUE
enigma3-withglobal-paracentral-thickavg	Barrett's Esophagu(IEU)	3.37E-13	TRUE
enigma3-withglobal-parahippocampal-surfavg	Barrett's Esophagu(IEU)	1.70E-10	TRUE
enigma3-withglobal-parahippocampal-thickavg	Barrett's Esophagu(IEU)	4.07E-25	TRUE
enigma3-withglobal-parsopercularis-surfavg	Barrett's Esophagu(IEU)	2.34E-31	TRUE
enigma3-withglobal-parsopercularis-thickavg	Barrett's Esophagu(IEU)	4.18E-29	TRUE
enigma3-withglobal-parsorbitalis-surfavg	Barrett's Esophagu(IEU)	3.76E-31	TRUE
enigma3-withglobal-parsorbitalis-thickavg	Barrett's Esophagu(IEU)	1.00E-09	TRUE
enigma3-withglobal-parstriangularis-surfavg	Barrett's Esophagu(IEU)	1.48E-58	TRUE
enigma3-withglobal-parstriangularis-thickavg	Barrett's Esophagu(IEU)	1.06E-09	TRUE
enigma3-withglobal-pericalcarine-surfavg	Barrett's Esophagu(IEU)	9.10E-76	TRUE
enigma3-withglobal-pericalcarine-thickavg	Barrett's Esophagu(IEU)	8.46E-06	TRUE
enigma3-withglobal-postcentral-surfavg	Barrett's Esophagu(IEU)	1.28E-70	TRUE
enigma3-withglobal-postcentral-thickavg	Barrett's Esophagu(IEU)	1.92E-72	TRUE
enigma3-withglobal-posteriorcingulate-surfavg	Barrett's Esophagu(IEU)	7.89E-12	TRUE
enigma3-withglobal-posteriorcingulate-thickavg	Barrett's Esophagu(IEU)	5.26E-24	TRUE
enigma3-withglobal-precentral-surfavg	Barrett's Esophagu(IEU)	1.18E-102	TRUE
enigma3-withglobal-precentral-thickavg	Barrett's Esophagu(IEU)	7.42E-20	TRUE
enigma3-withglobal-precuneus-surfavg	Barrett's Esophagu(IEU)	8.40E-23	TRUE
enigma3-withglobal-precuneus-thickavg	Barrett's Esophagu(IEU)	2.91E-20	TRUE
enigma3-withglobal-rostralanteriorcingulate-surfavg	Barrett's Esophagu(IEU)	2.35E-24	TRUE
enigma3-withglobal-rostralanteriorcingulate-thickavg	Barrett's Esophagu(IEU)	0.000392211	TRUE
enigma3-withglobal-rostralmiddlefrontal-surfavg	Barrett's Esophagu(IEU)	1.63E-43	TRUE
enigma3-withglobal-rostralmiddlefrontal-thickavg	Barrett's Esophagu(IEU)	3.12E-10	TRUE
enigma3-withglobal-superiorfrontal-surfavg	Barrett's Esophagu(IEU)	4.56E-19	TRUE
enigma3-withglobal-superiorfrontal-thickavg	Barrett's Esophagu(IEU)	1.75E-13	TRUE
enigma3-withglobal-superiorparietal-surfavg	Barrett's Esophagu(IEU)	5.07E-19	TRUE
enigma3-withglobal-superiorparietal-thickavg	Barrett's Esophagu(IEU)	3.37E-13	TRUE
enigma3-withglobal-superiortemporal-surfavg	Barrett's Esophagu(IEU)	6.77E-29	TRUE
enigma3-withglobal-superiortemporal-thickavg	Barrett's Esophagu(IEU)	2.77E-25	TRUE
enigma3-withglobal-supramarginal-surfavg	Barrett's Esophagu(IEU)	6.31E-38	TRUE
enigma3-withglobal-supramarginal-thickavg	Barrett's Esophagu(IEU)	1.45E-13	TRUE
enigma3-withglobal-temporalpole-surfavg	Barrett's Esophagu(IEU)	3.69E-09	TRUE
enigma3-withglobal-temporalpole-thickavg	Barrett's Esophagu(IEU)	6.47E-17	TRUE
enigma3-withglobal-transversetemporal-surfavg	Barrett's Esophagu(IEU)	4.01E-26	TRUE
enigma3-withglobal-transversetemporal-thickavg	Barrett's Esophagu(IEU)	5.54E-07	TRUE