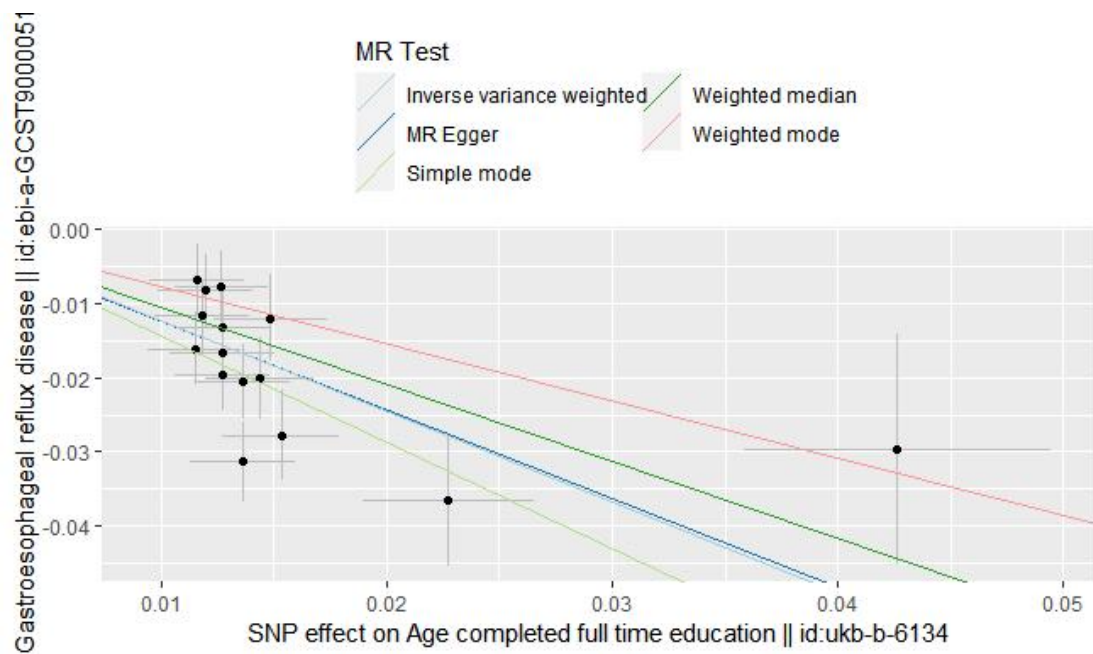
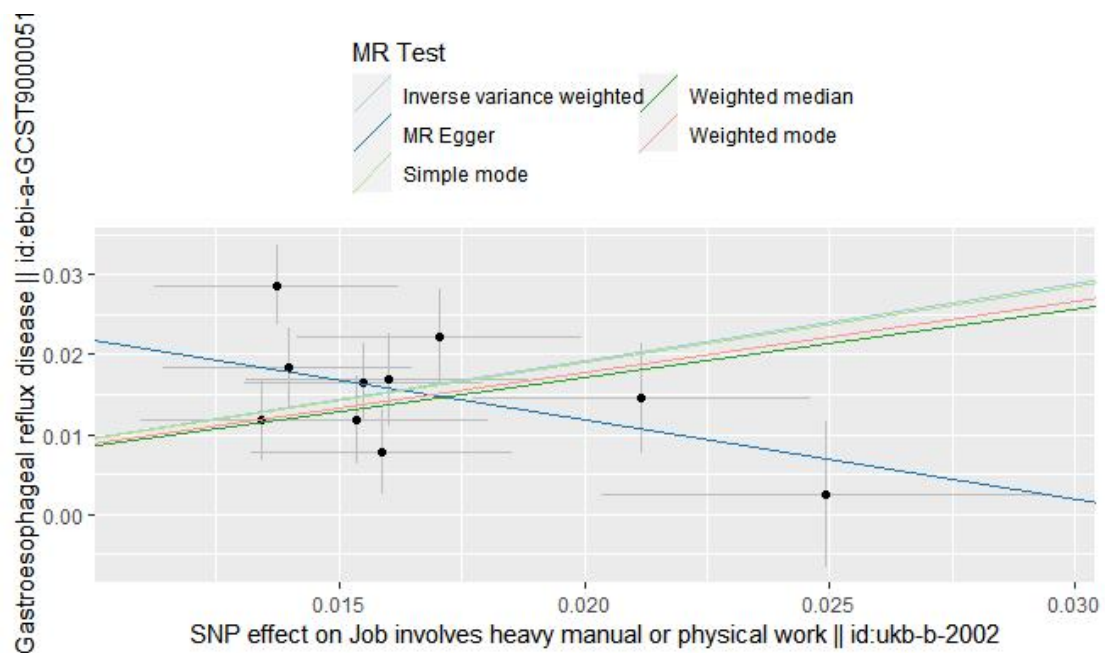


- **Supplementary Figures**

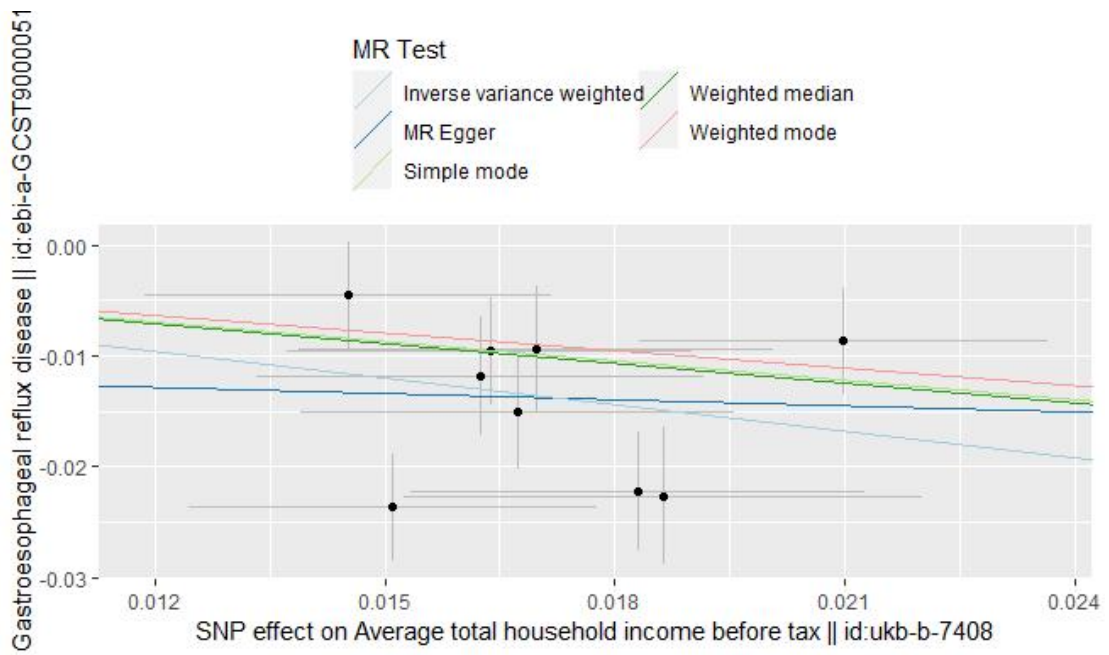
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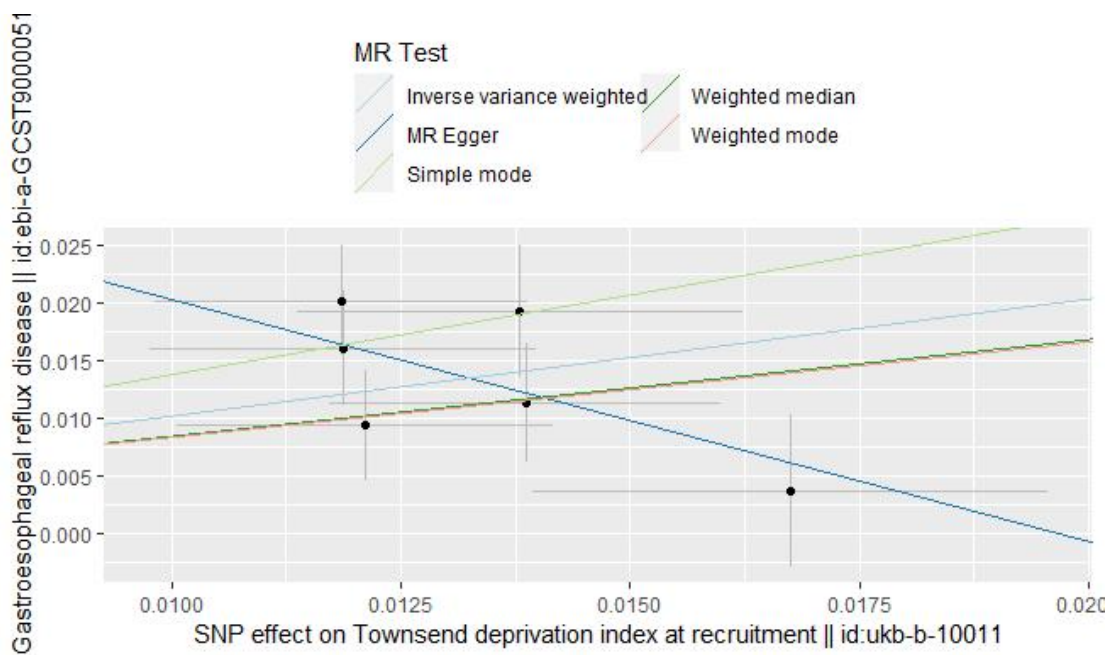
Supplementary Figure 1. SNP, single-nucleotide polymorphism; MR, Mendelian Randomization.



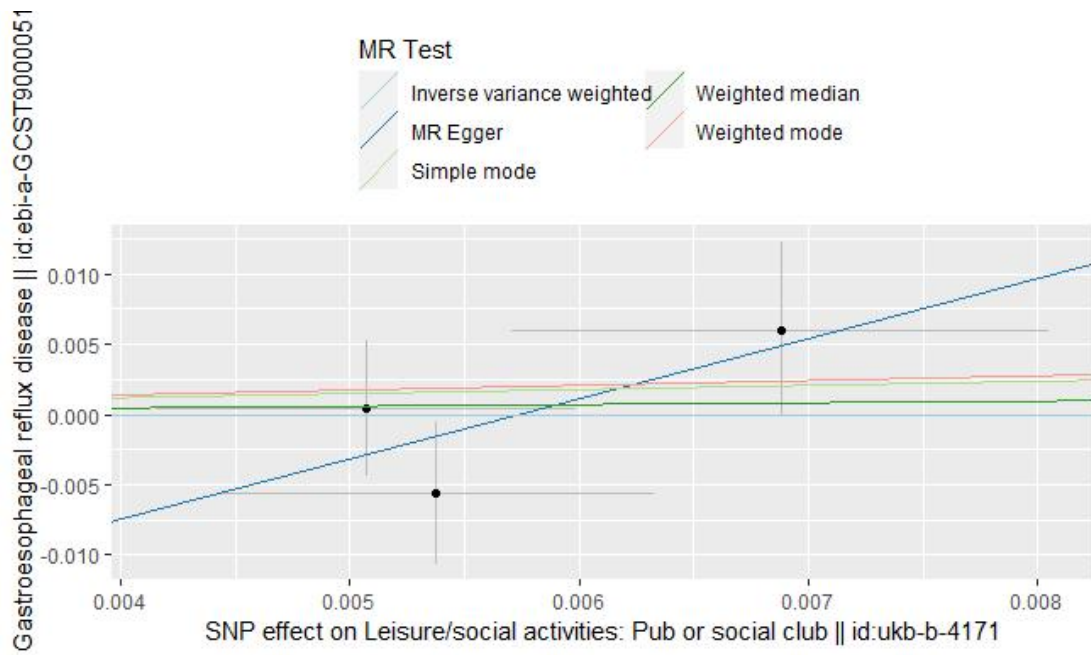
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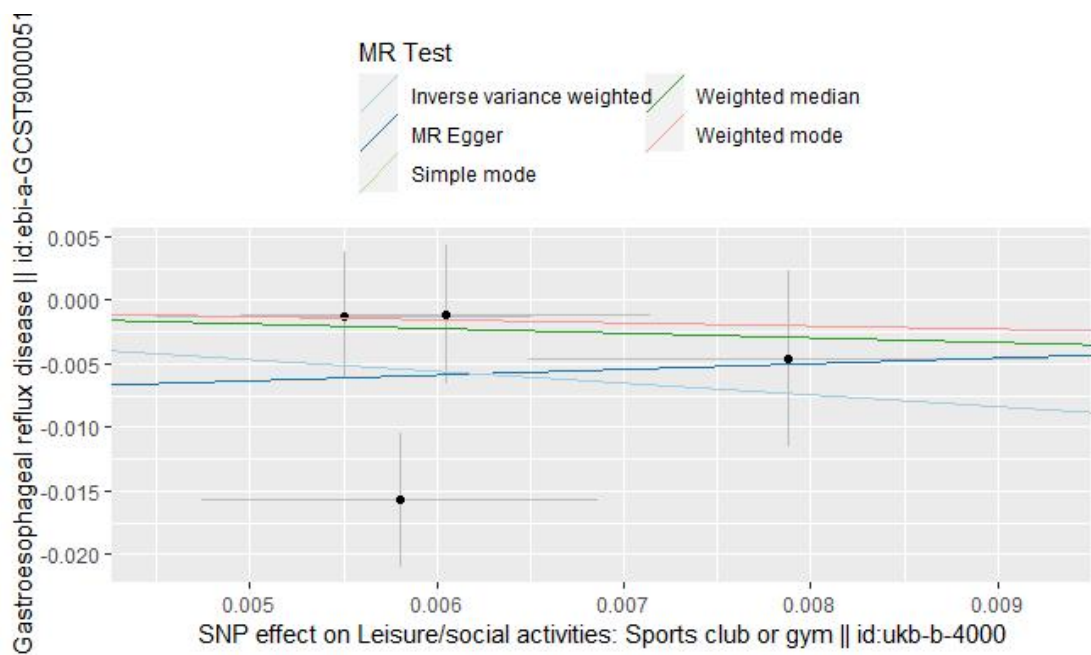
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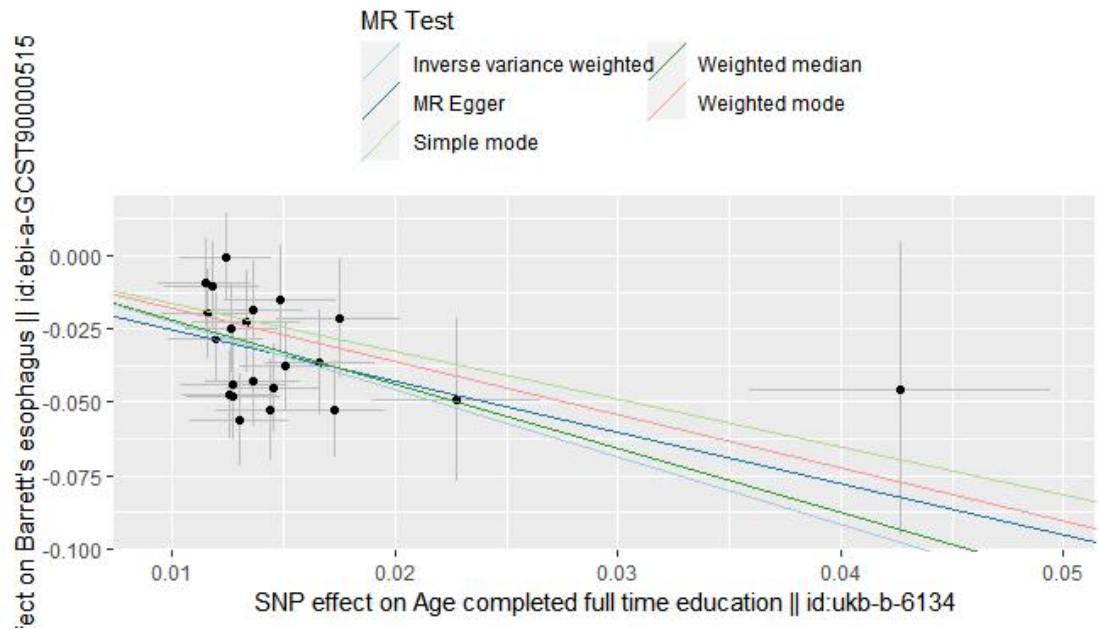
Supplementary Figure 4. SNP, single-nucleotide polymorphism; MR, Mendelian Randomization.



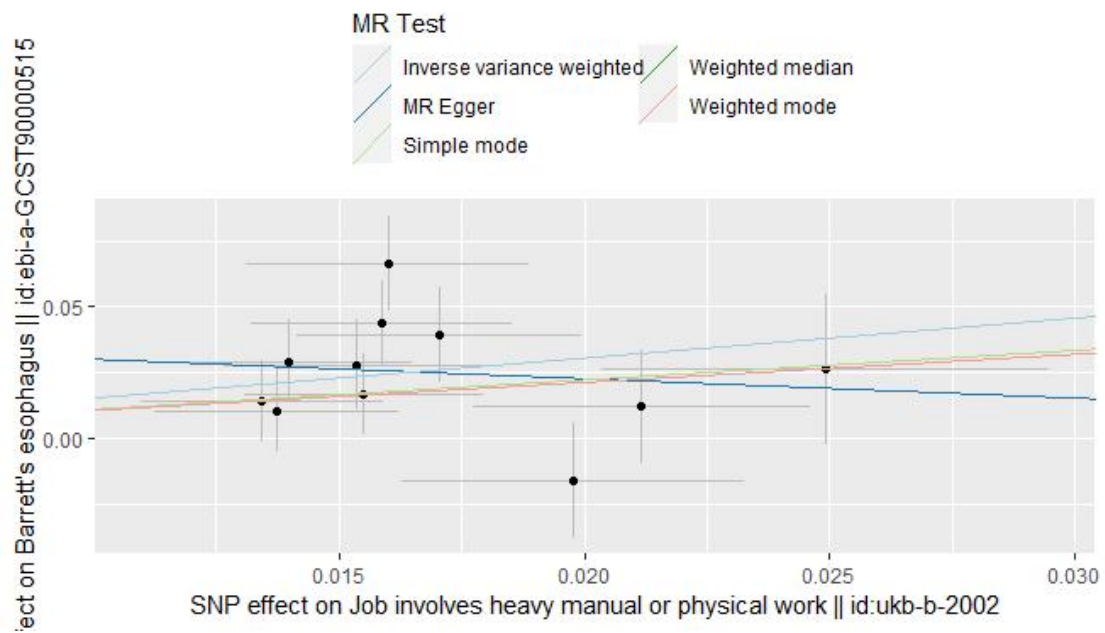
Supplementary Figure 5. SNP, single-nucleotide polymorphism; MR, Mendelian Randomization.



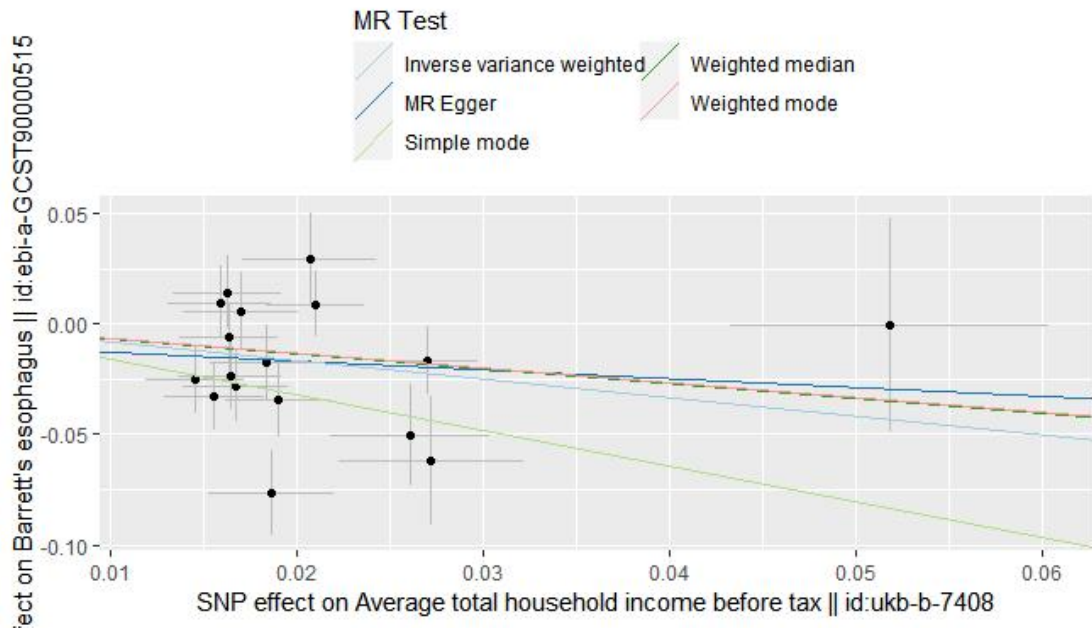
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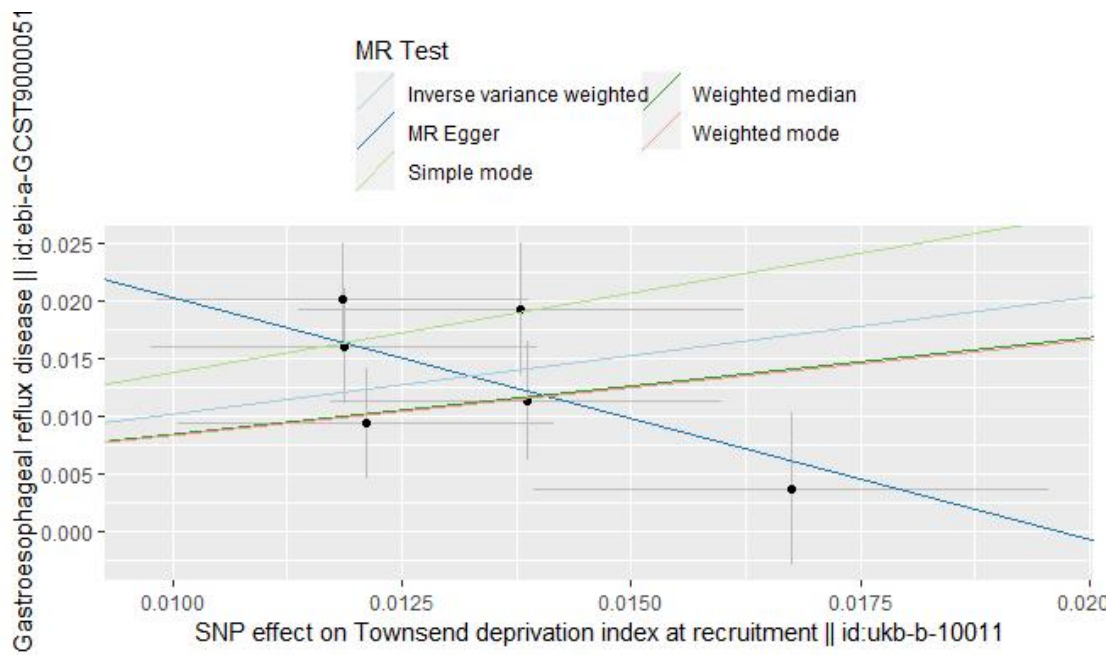
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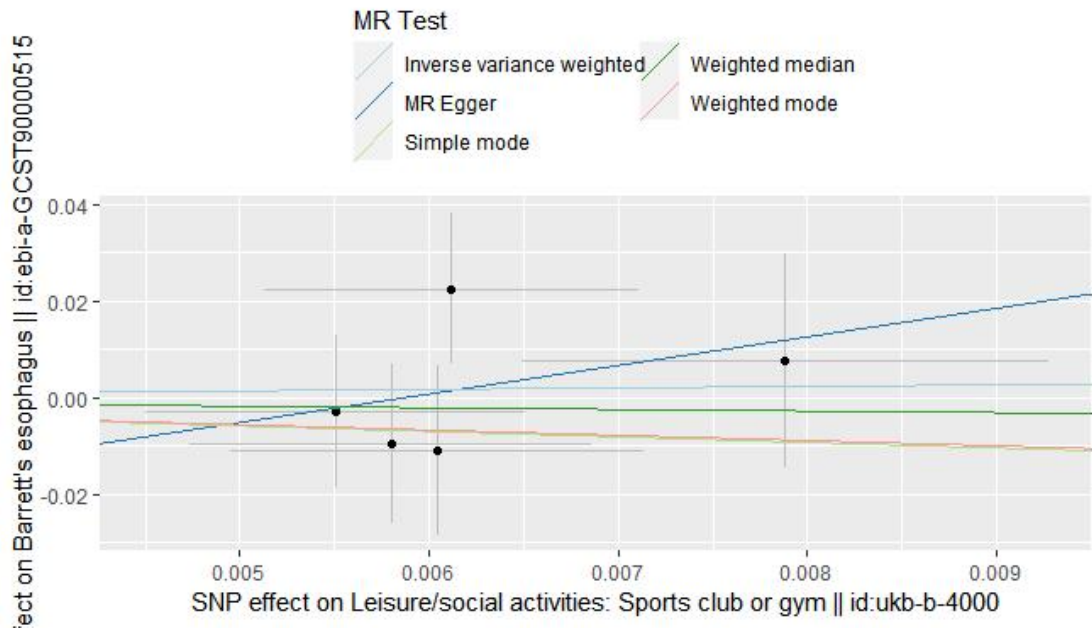
Supplementary Figure 8. SNP, single-nucleotide polymorphism; MR, Mendelian Randomization.



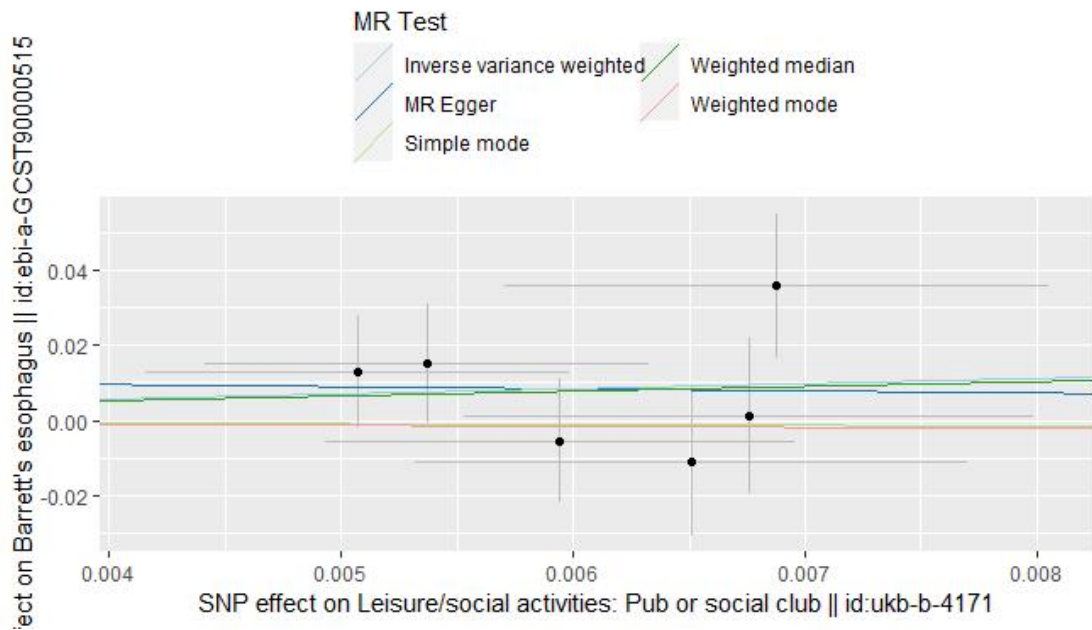
Supplementary Figure 9. SNP, single-nucleotide polymorphism; MR, Mendelian Randomization.



Supplementary Figure 10. SNP, single-nucleotide polymorphism; MR, Mendelian Randomization.

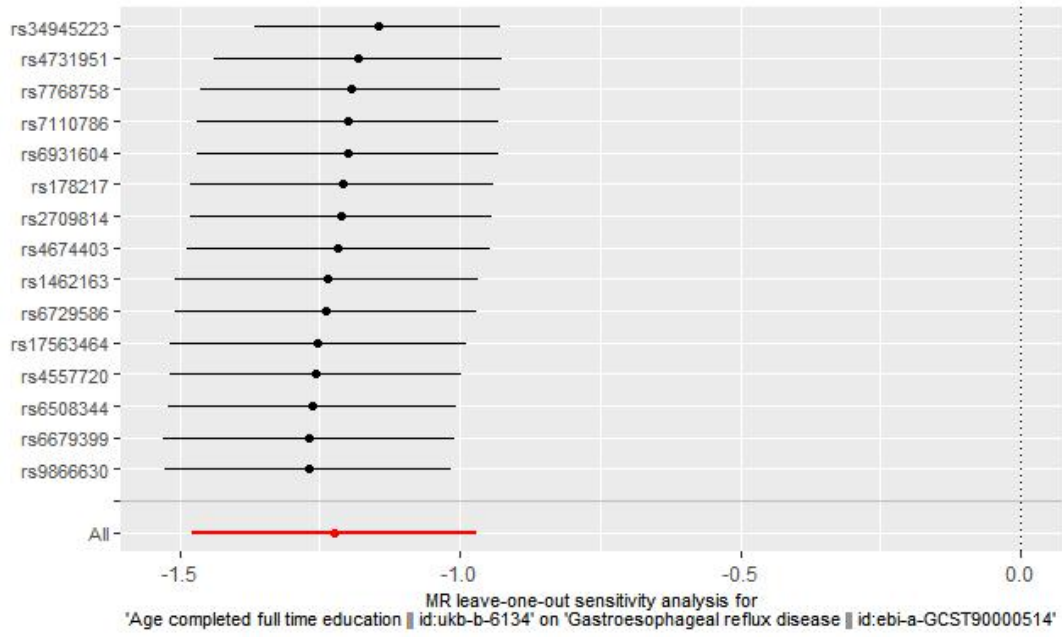


Supplementary Figure 11. SNP, single-nucleotide polymorphism; MR, Mendelian Randomization.

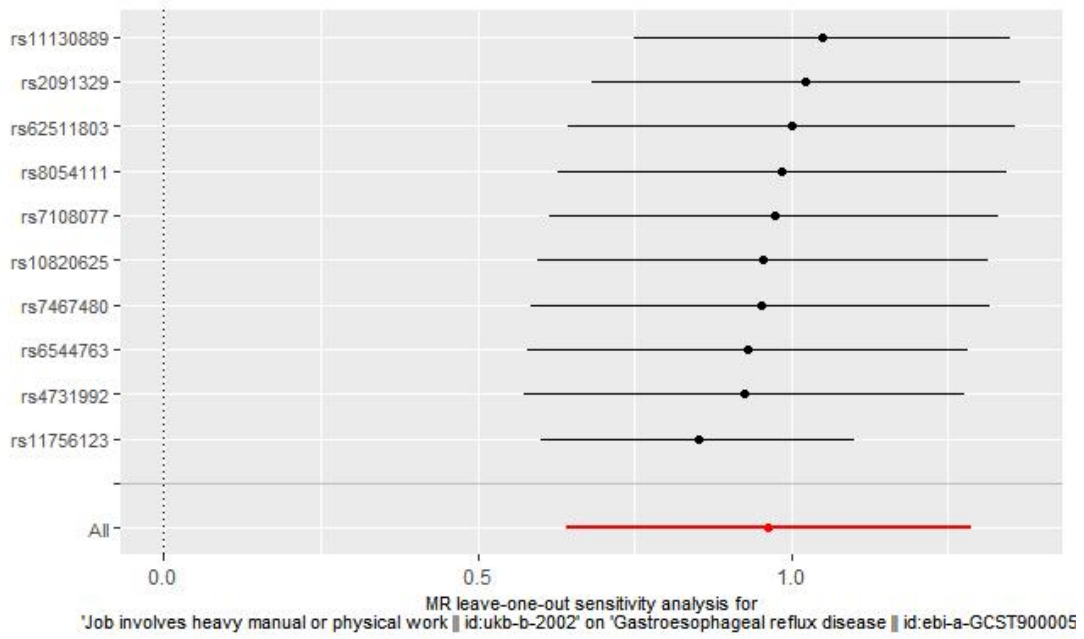


Supplementary Figure 12. SNP, single-nucleotide polymorphism; MR, Mendelian Randomization.

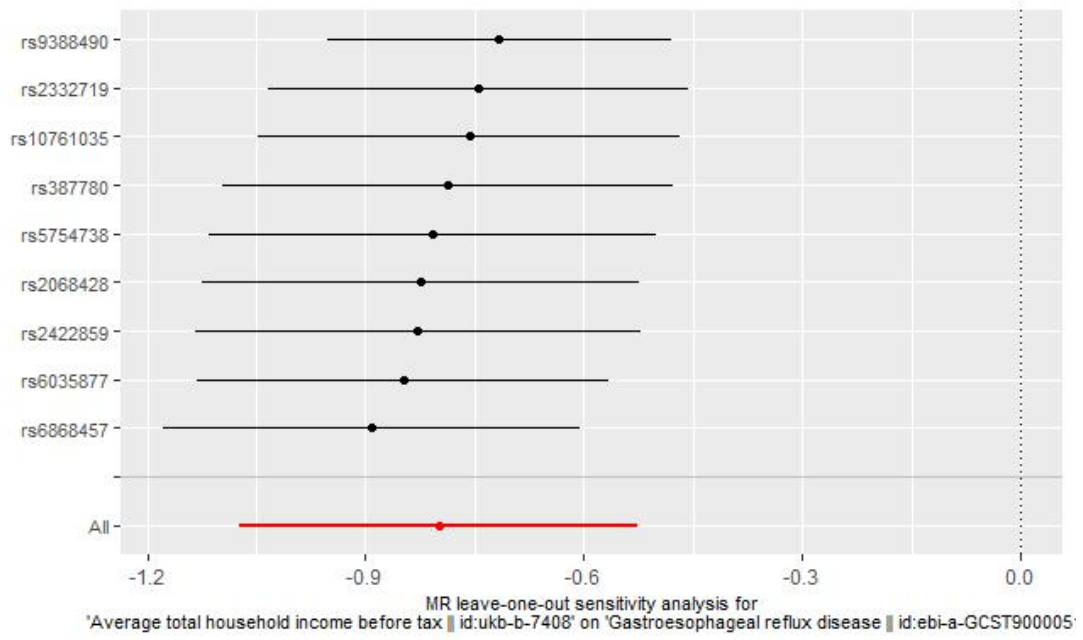
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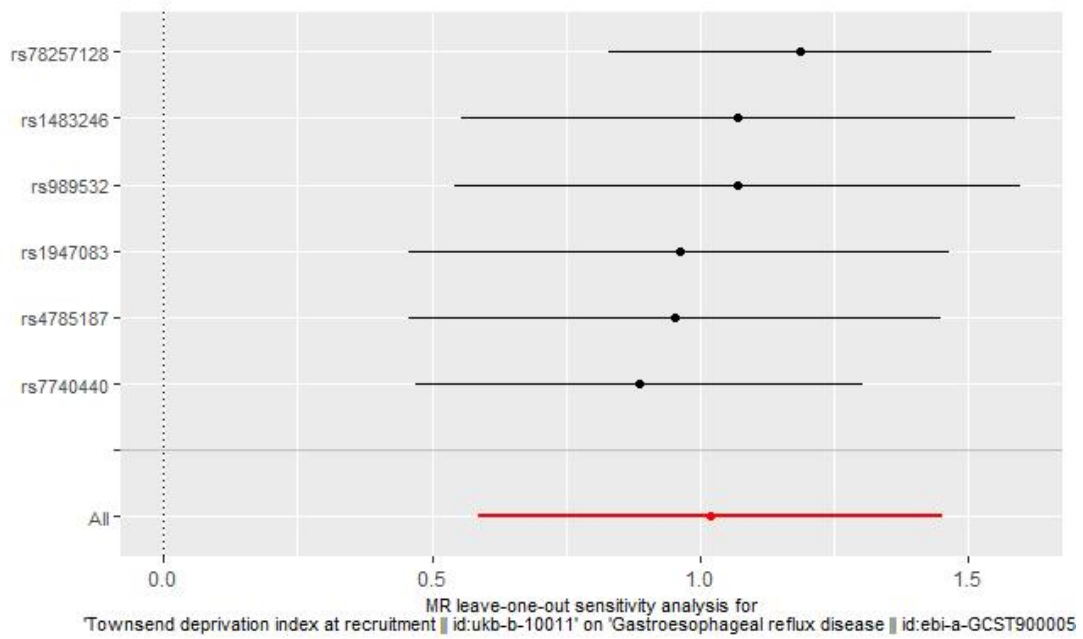
Supplementary Figure 13; MR, Mendelian Randomization.



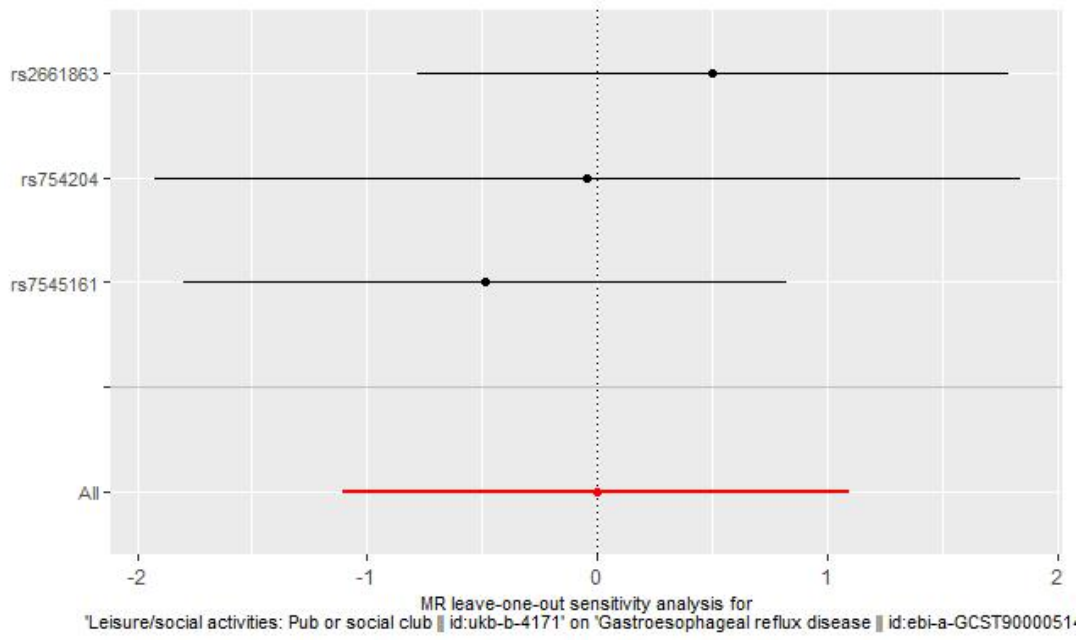
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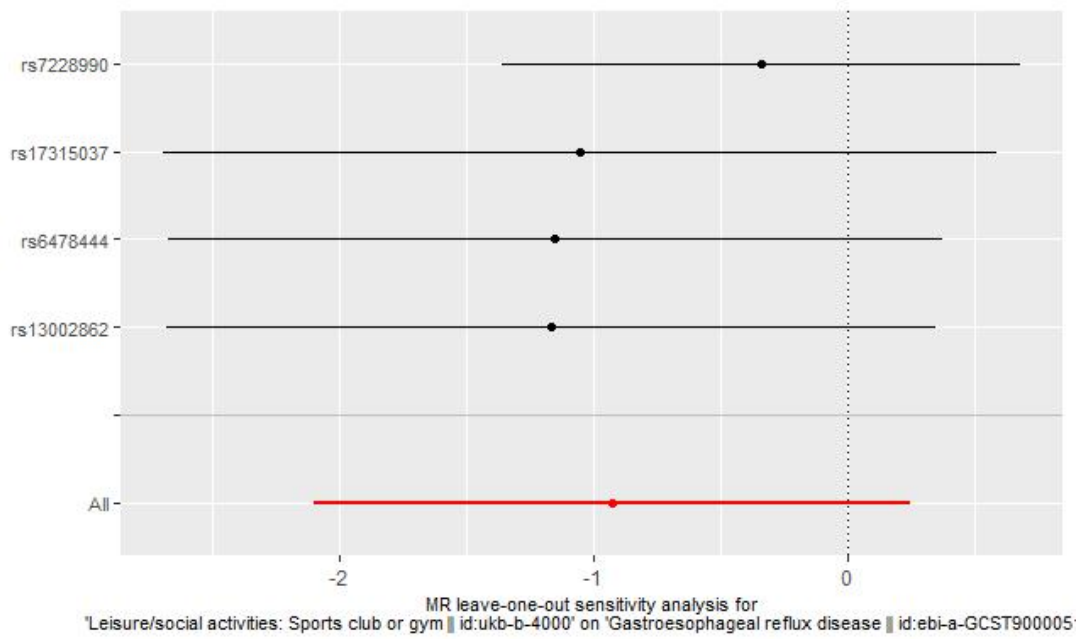
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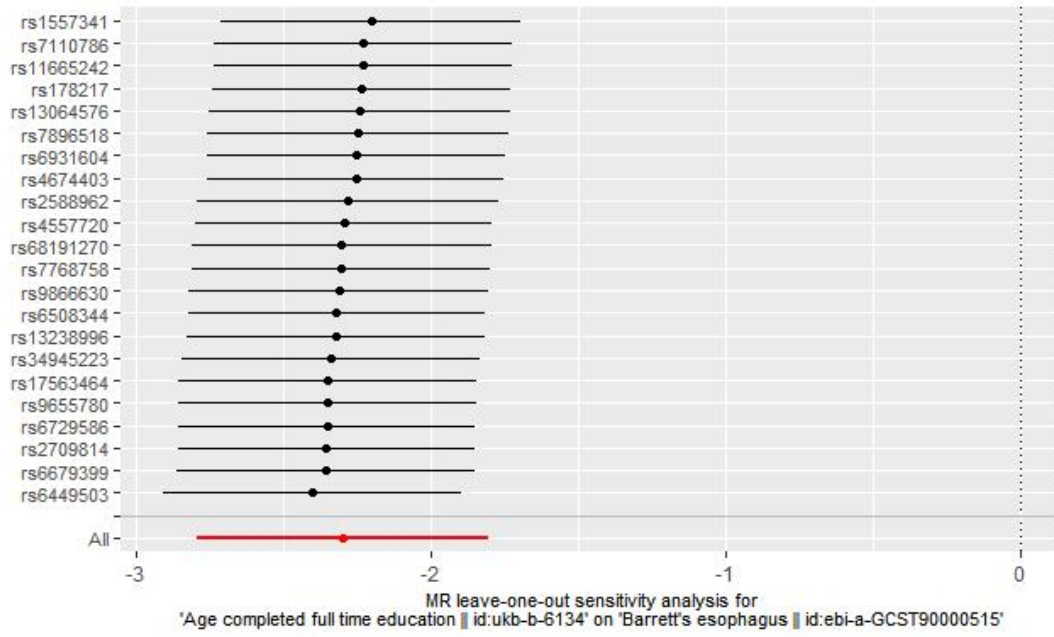
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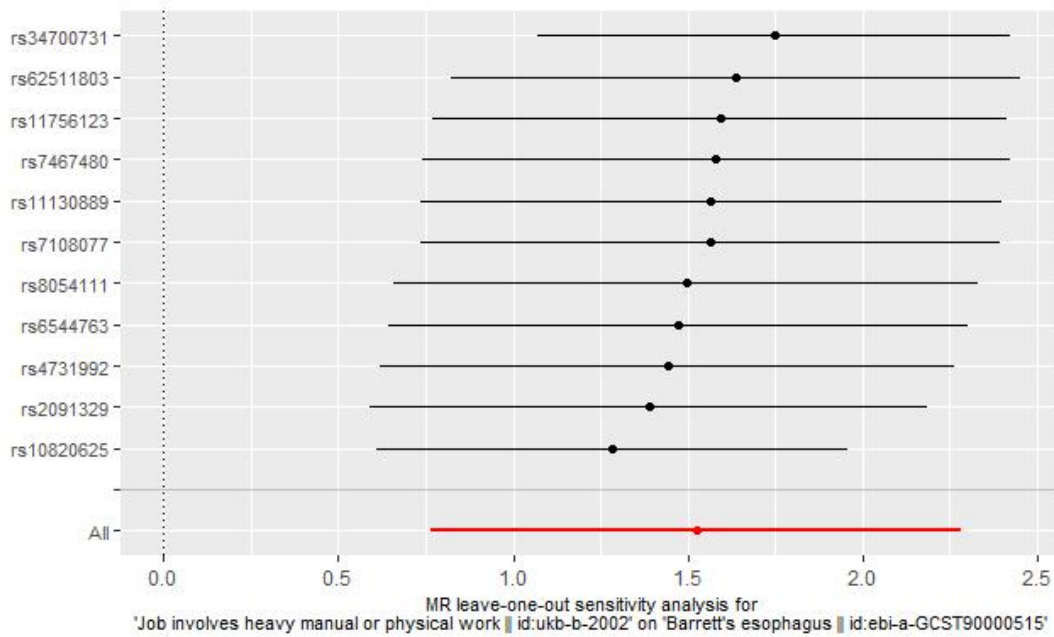
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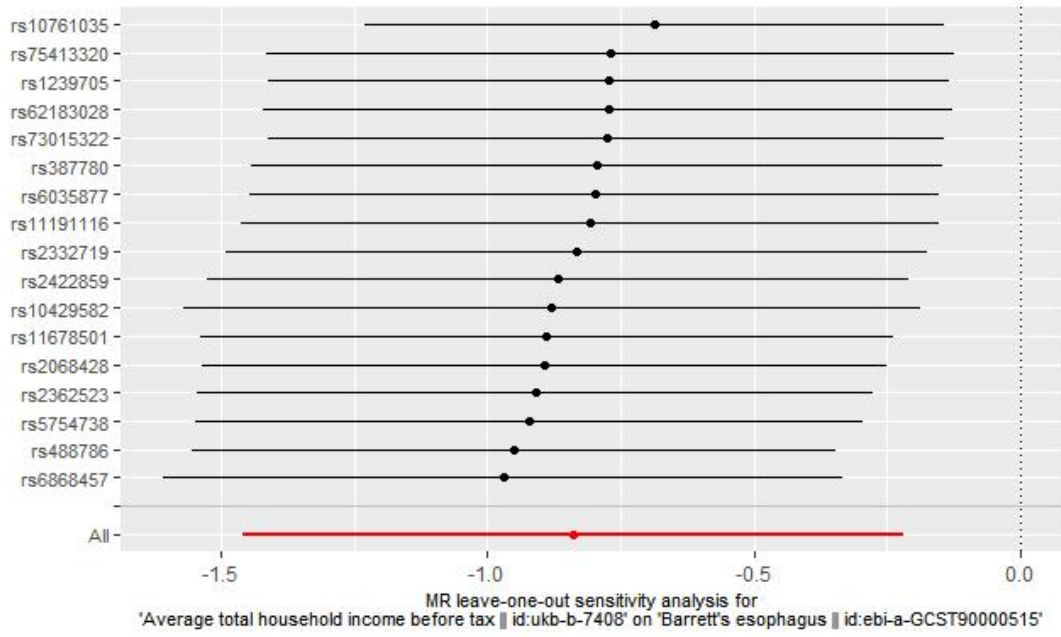
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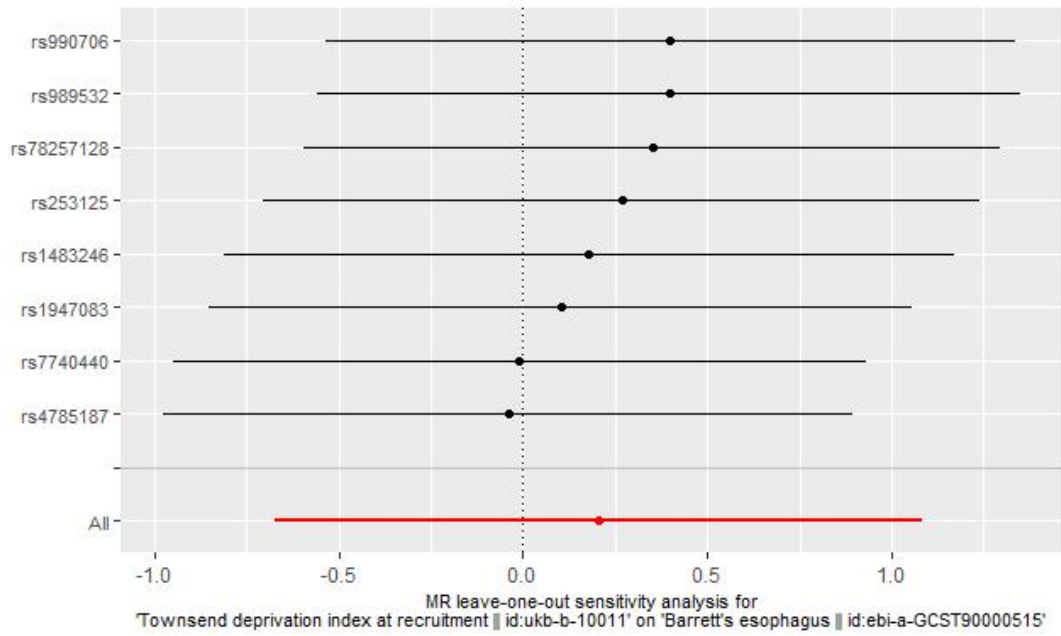
Supplementary Figure 19; MR, Mendelian Randomization.



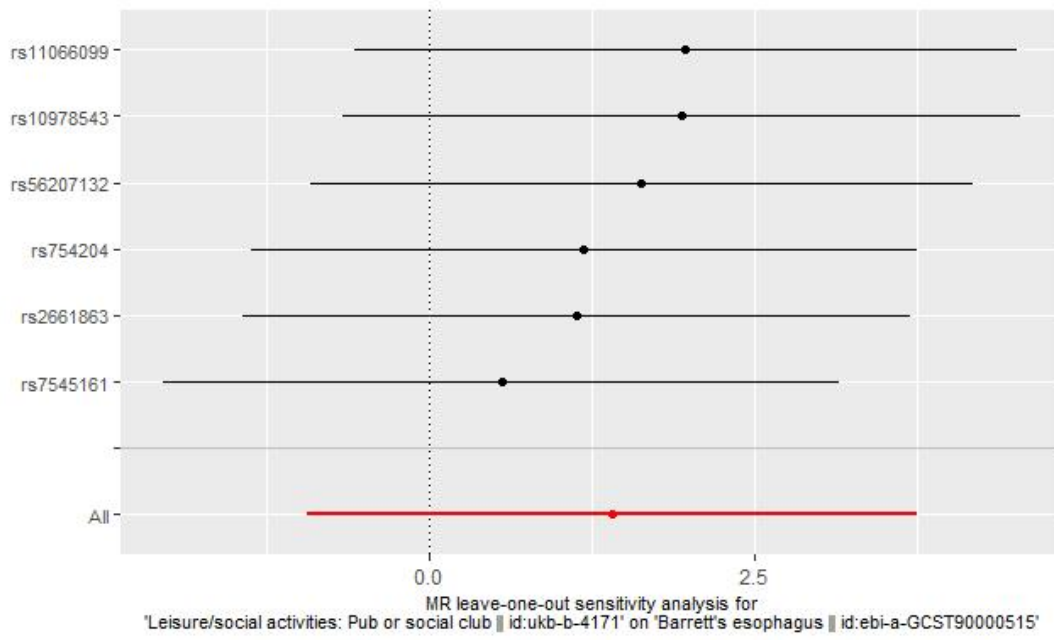
Supplementary Figure 20; MR, Mendelian Randomization.



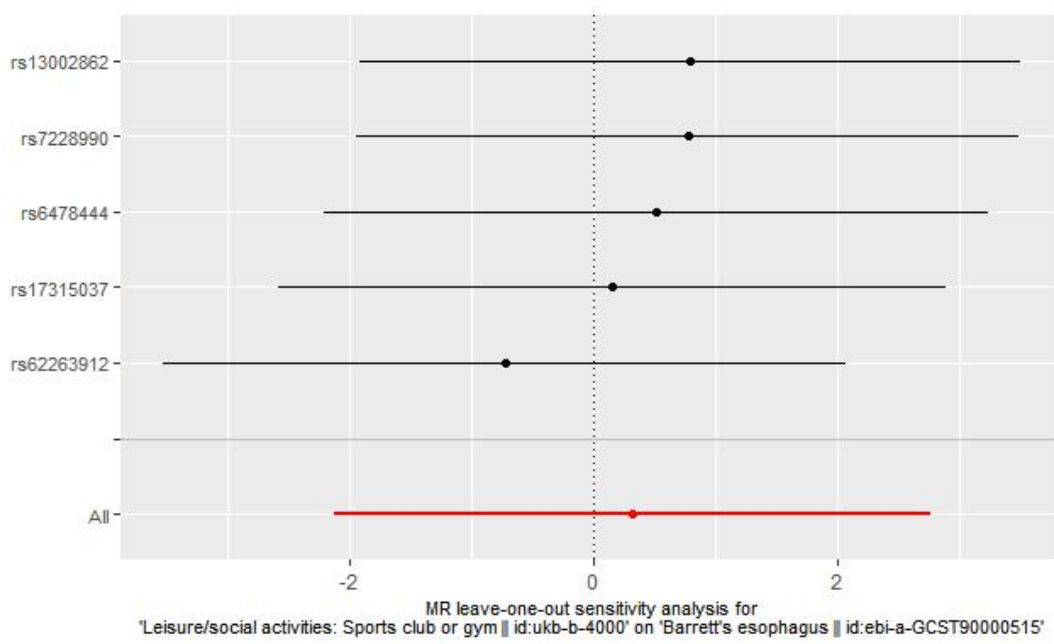
Supplementary Figure 21; MR, Mendelian Randomization.



Supplementary Figure 22; MR, Mendelian Randomization.

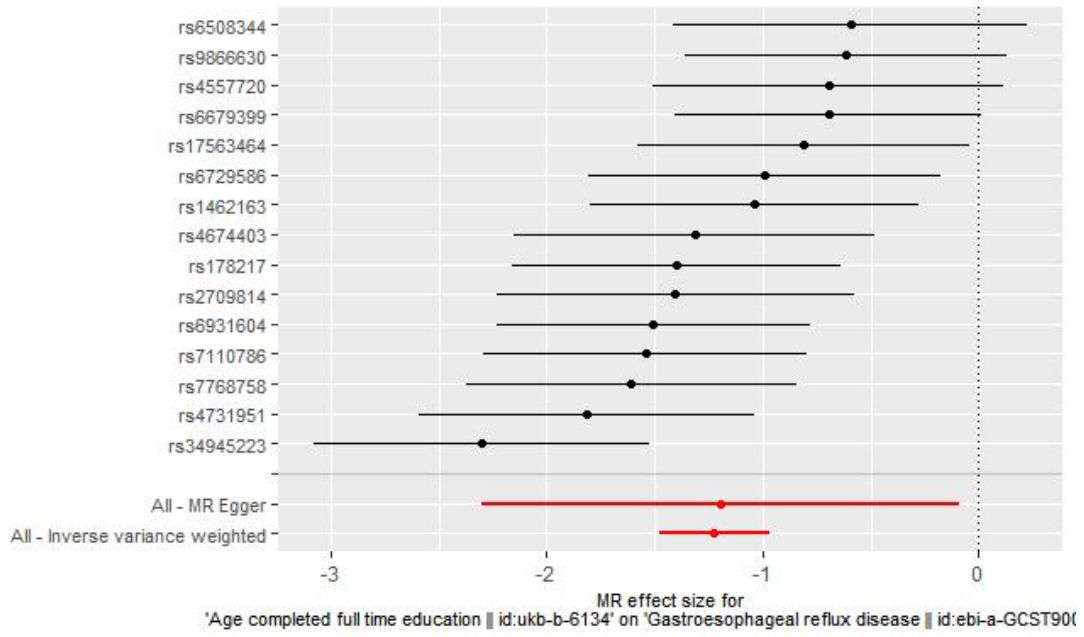


Supplementary Figure 23; MR, Mendelian Randomization.

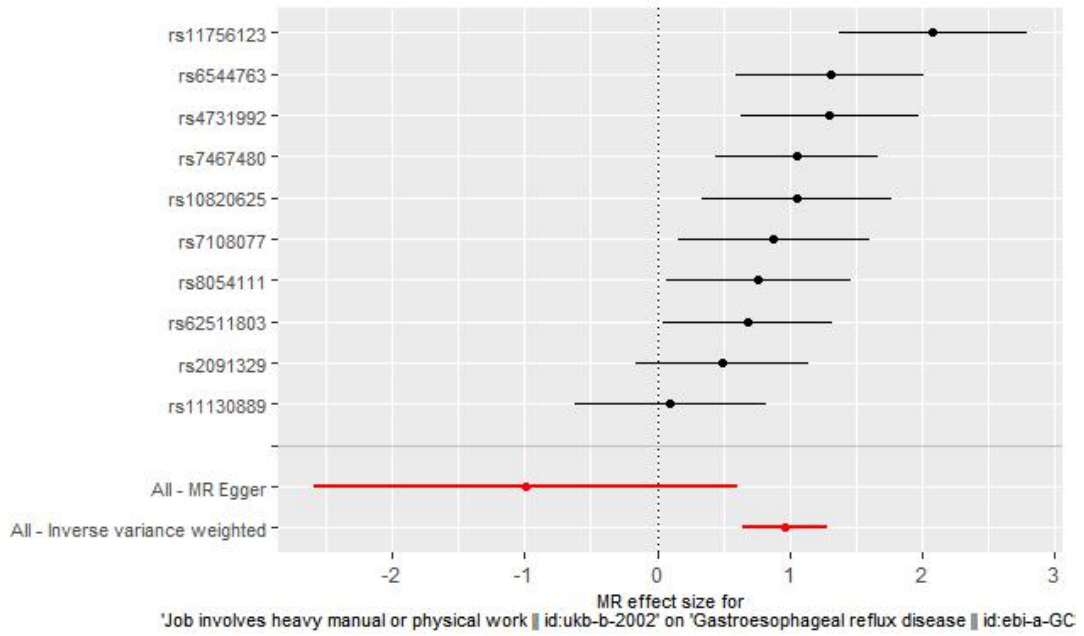


Supplementary Figure 24; MR, Mendelian Randomization.

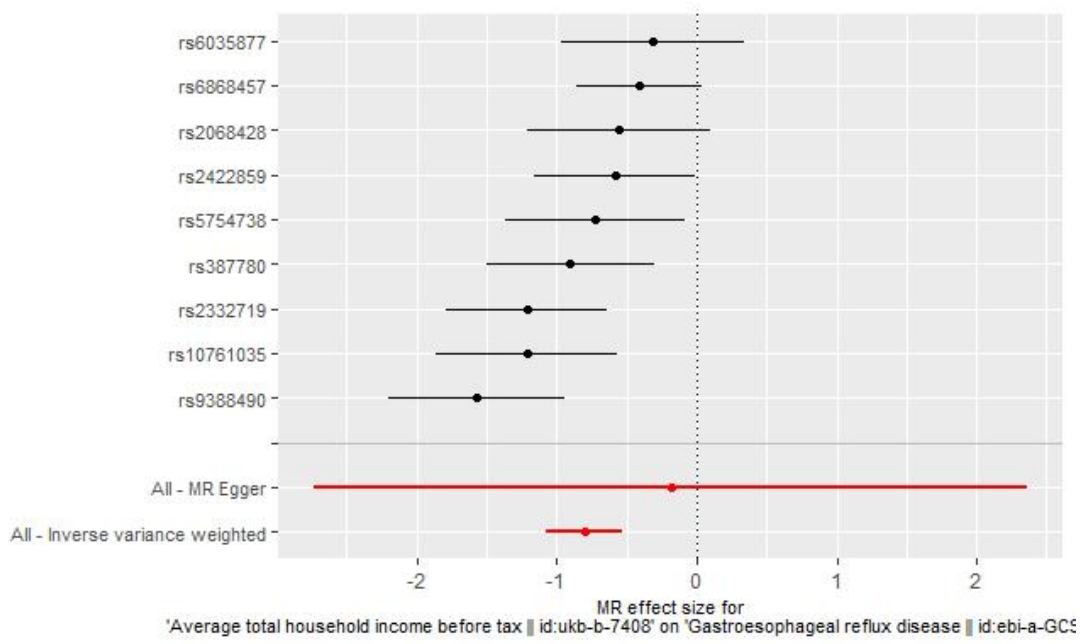
Supplementary Figure 25-36 Forest plot figure



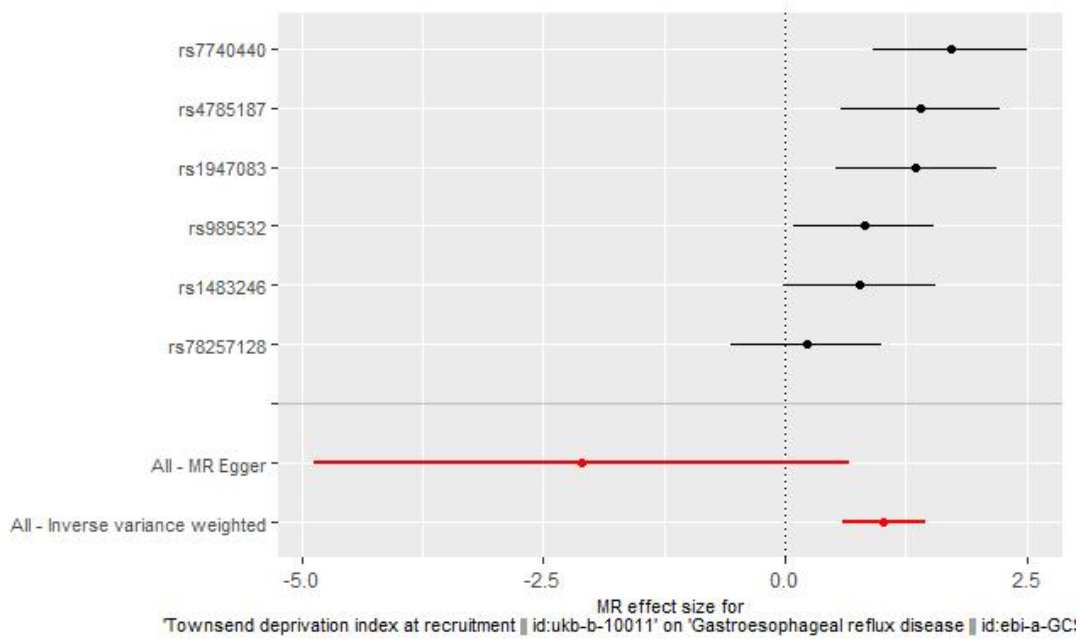
Supplementary Figure 25. MR, Mendelian Randomization.



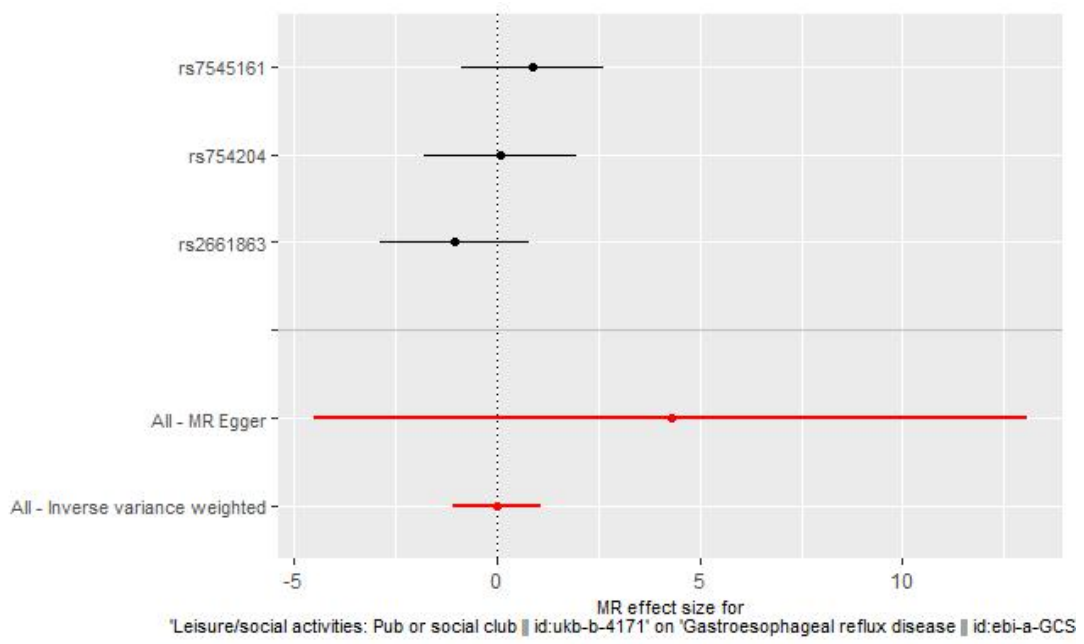
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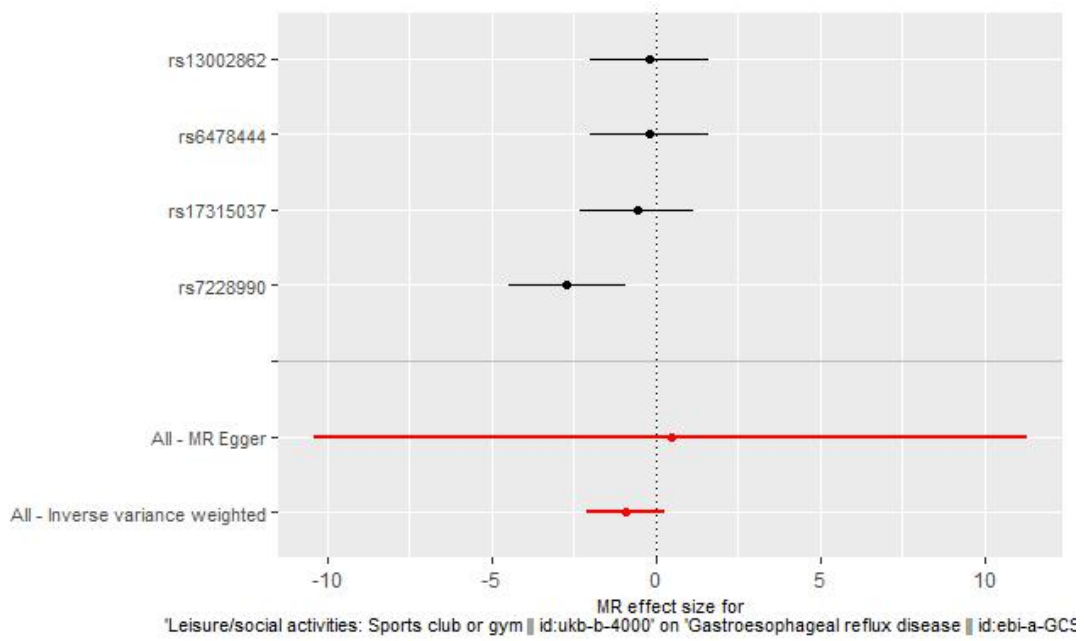
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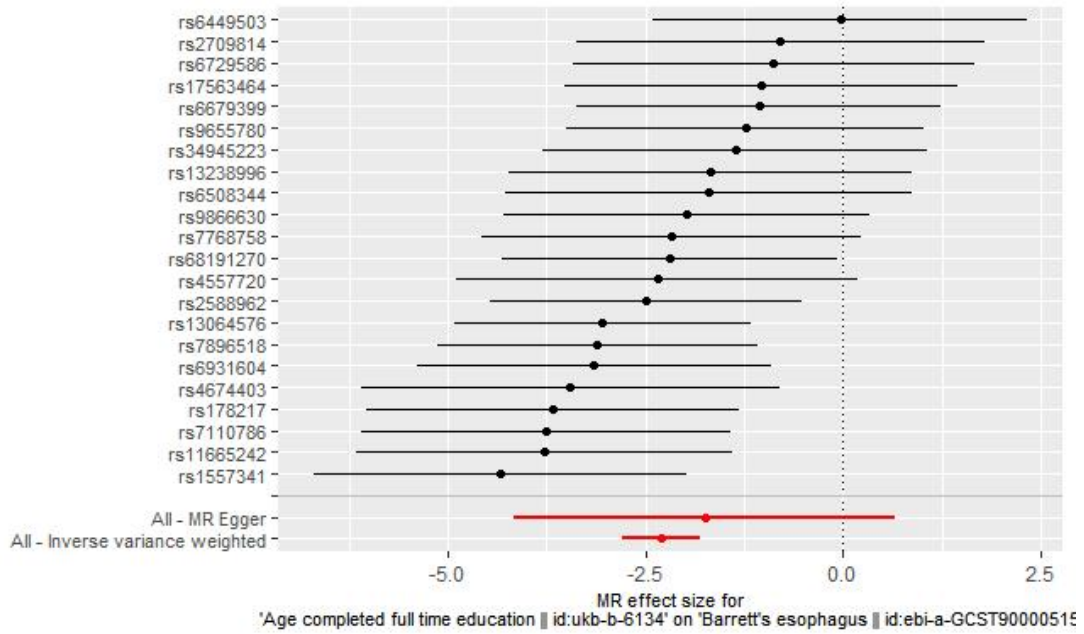
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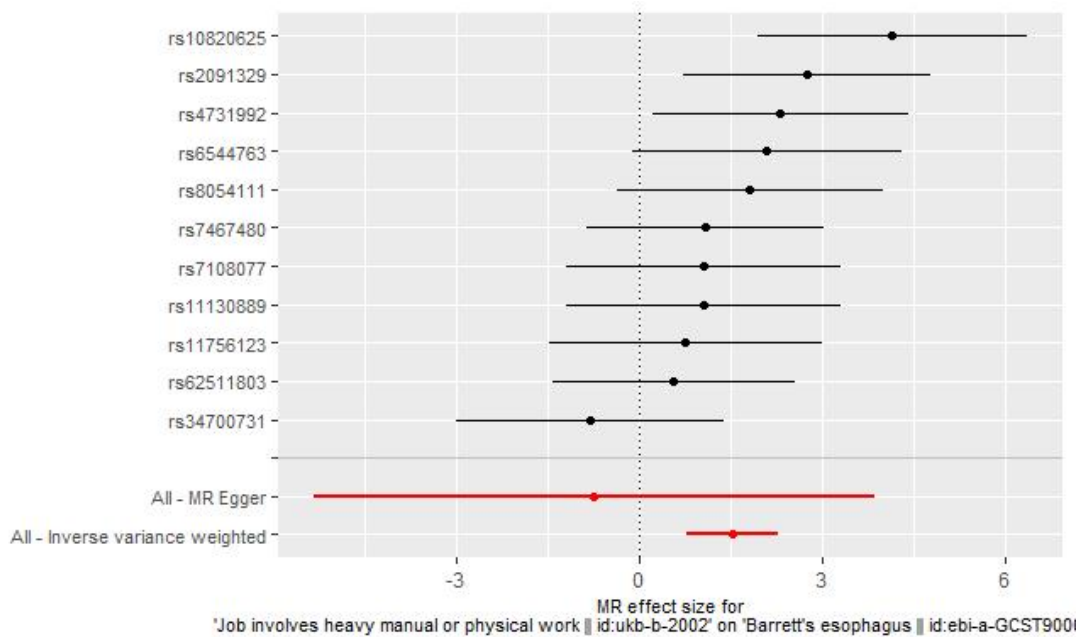
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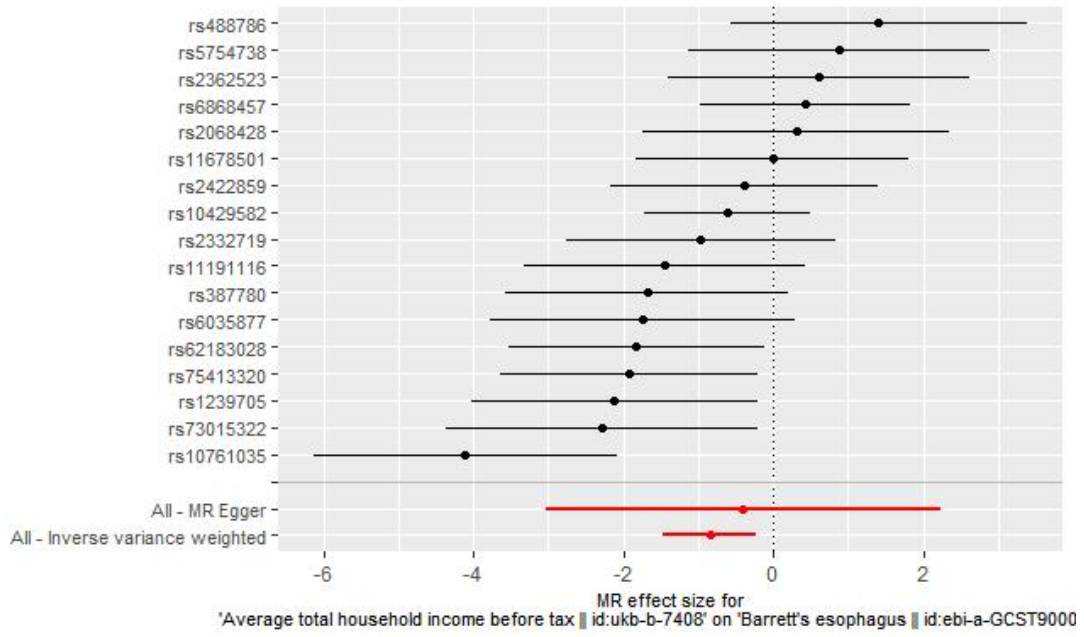
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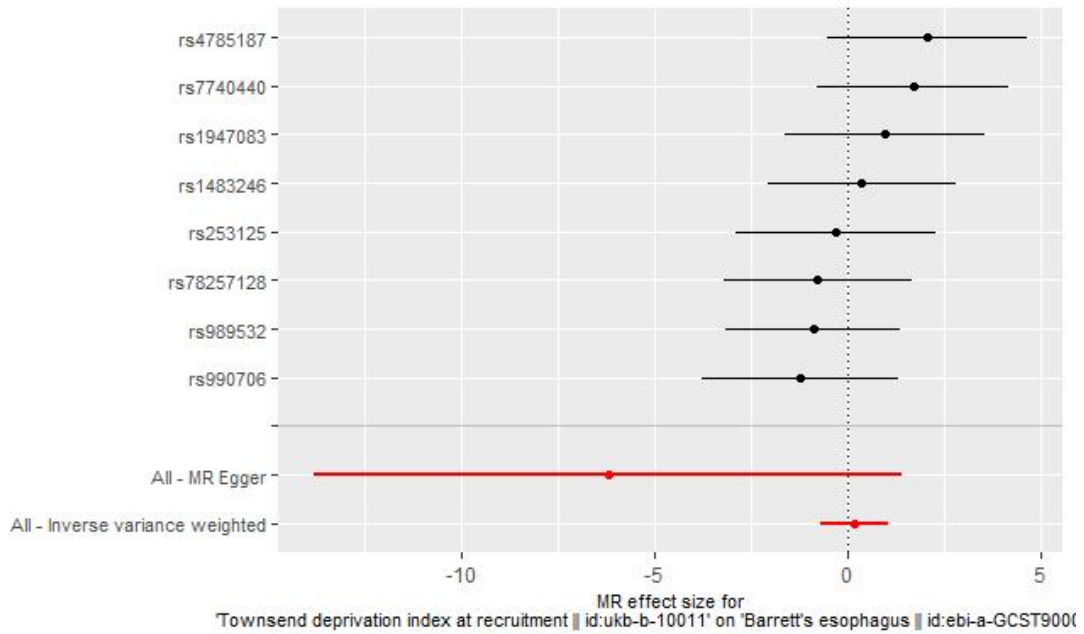
Supplementary Figure 31. MR, Mendelian Randomization.



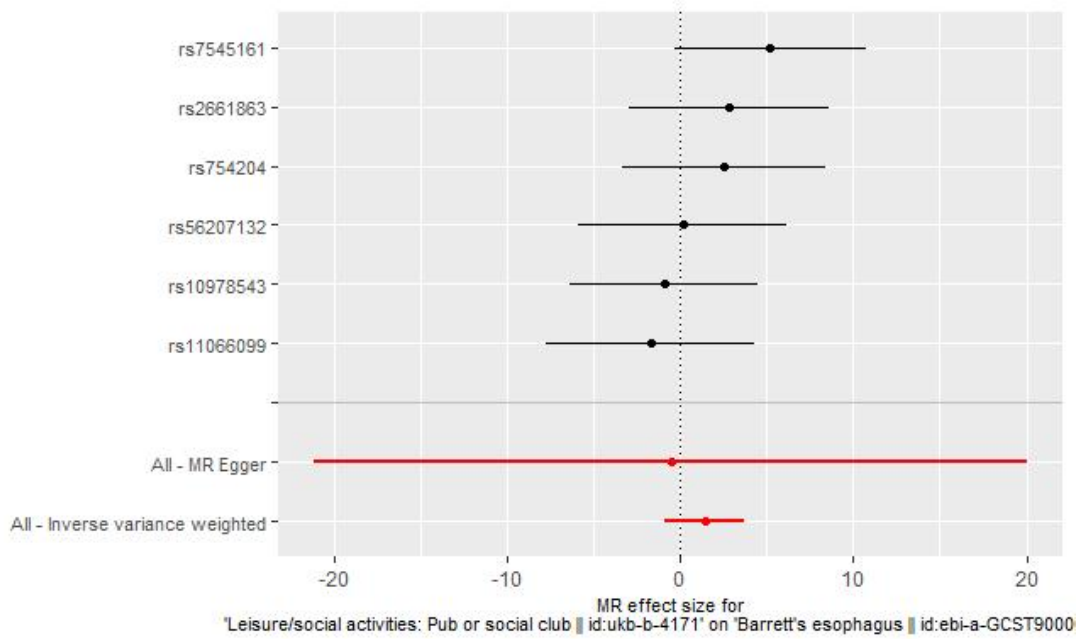
Supplementary Figure 32. MR, Mendelian Randomization.



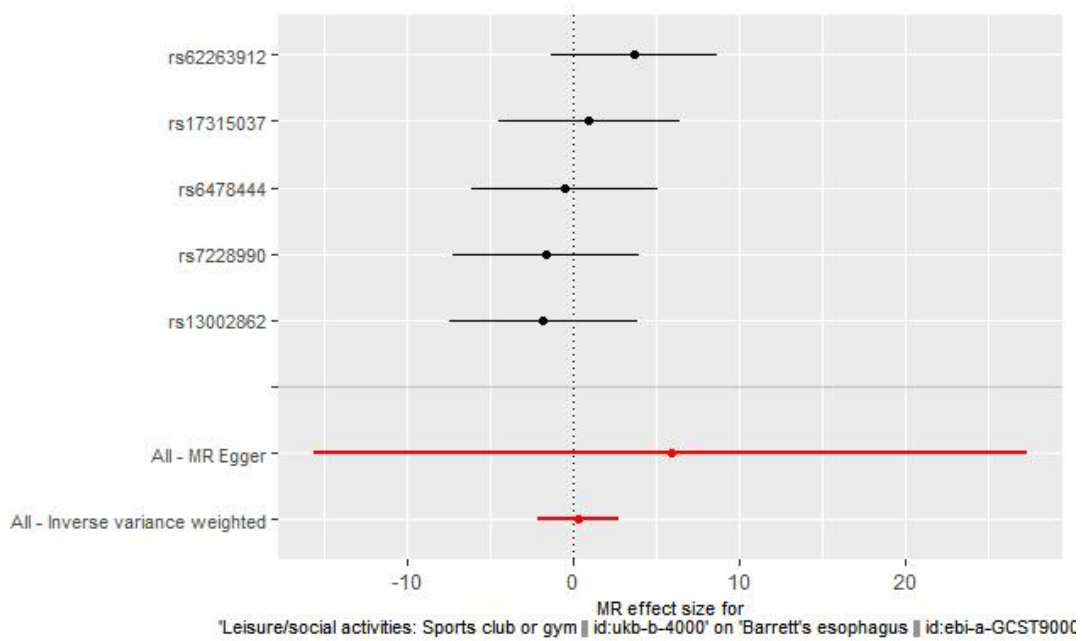
Supplementary Figure 33. MR, Mendelian Randomization.



Supplementary Figure 34. MR, Mendelian Randomization.

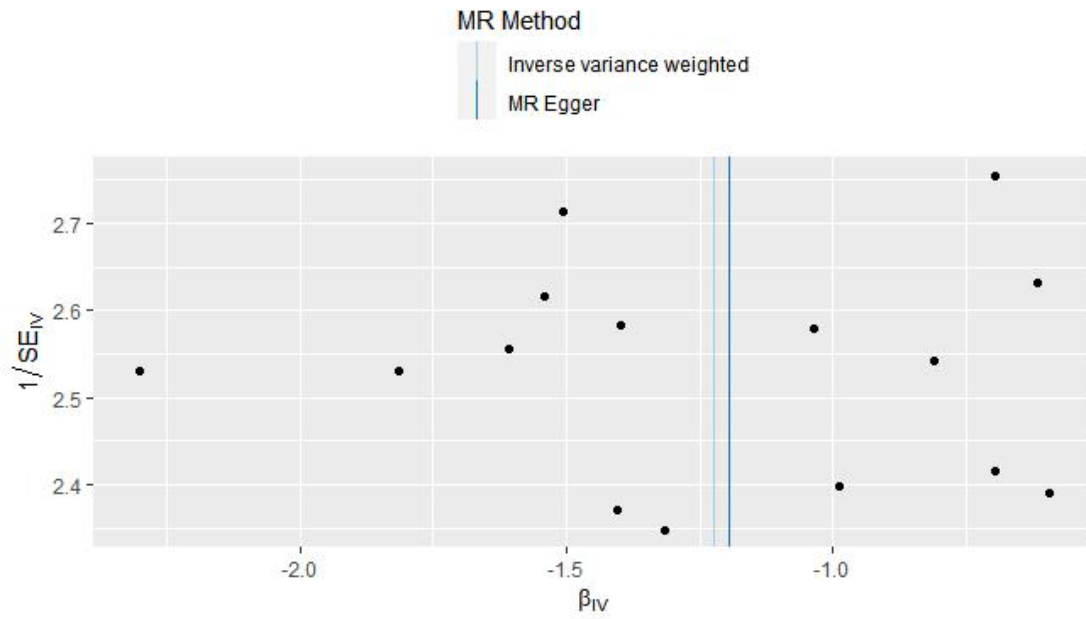


Supplementary Figure 35. MR, Mendelian Randomization.

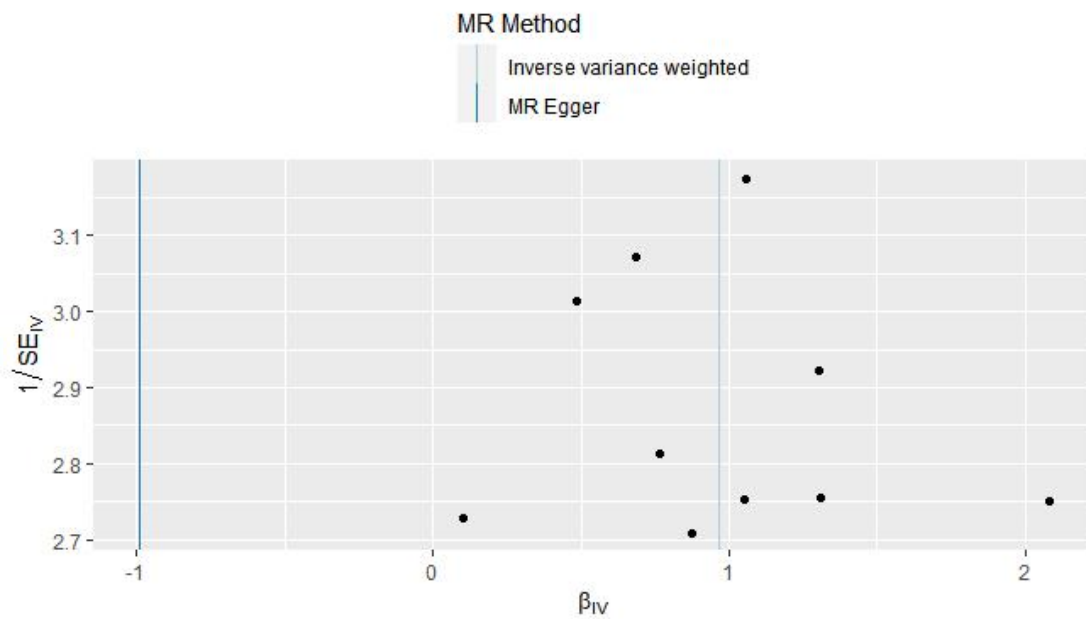


Supplementary Figure 36. MR, Mendelian Randomization.

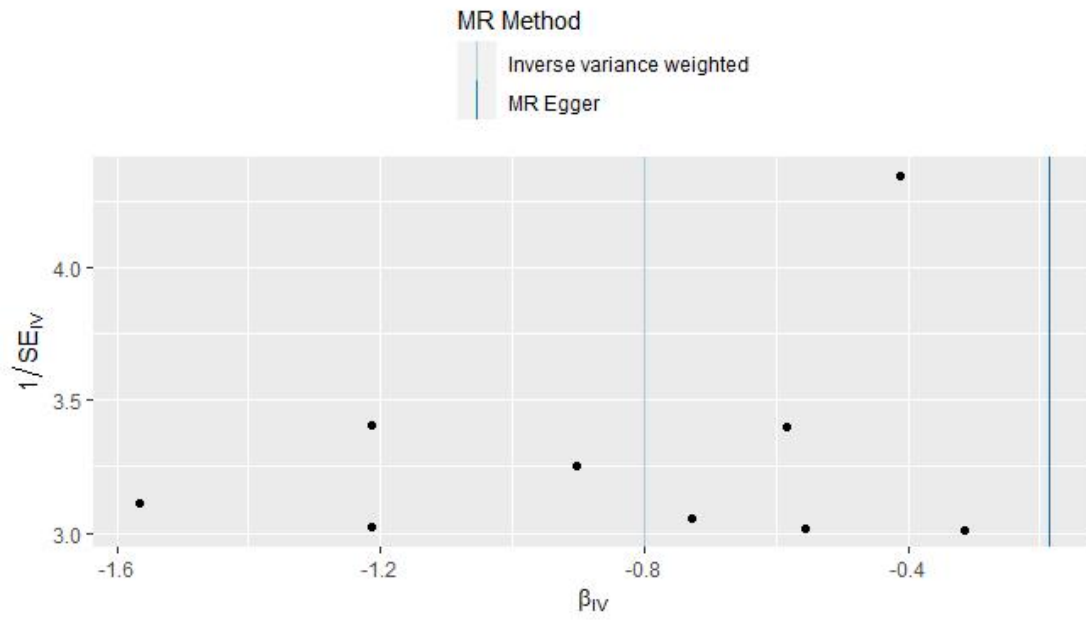
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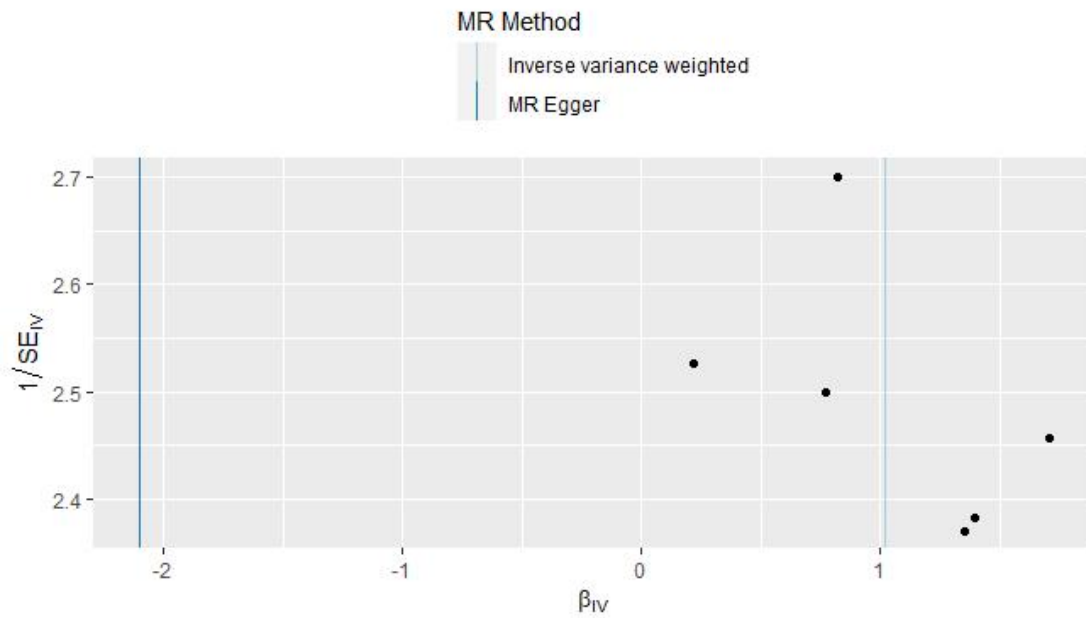
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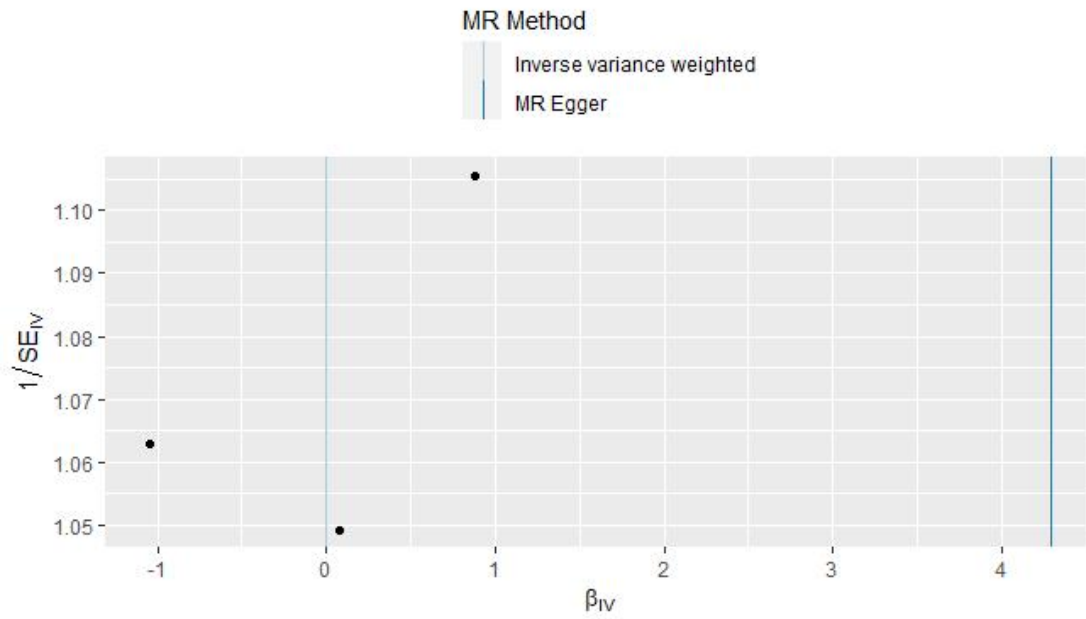
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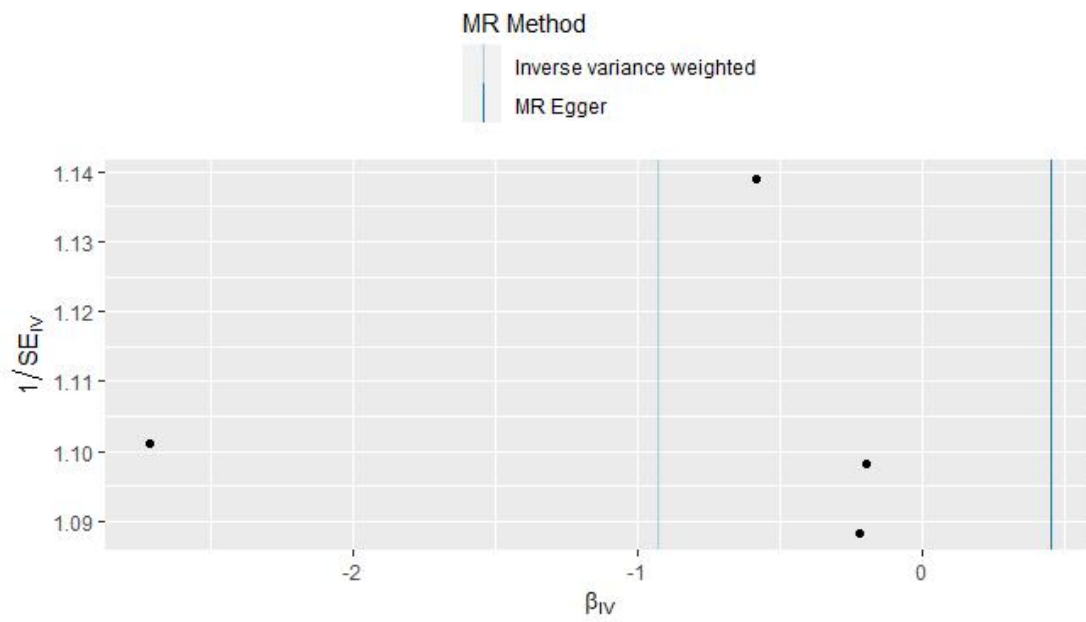
Supplementary Figure 39. SNP, single-nucleotide polymorphism; IV, Instrumental variable; SE: Standard Error; MR, Mendelian Randomization.



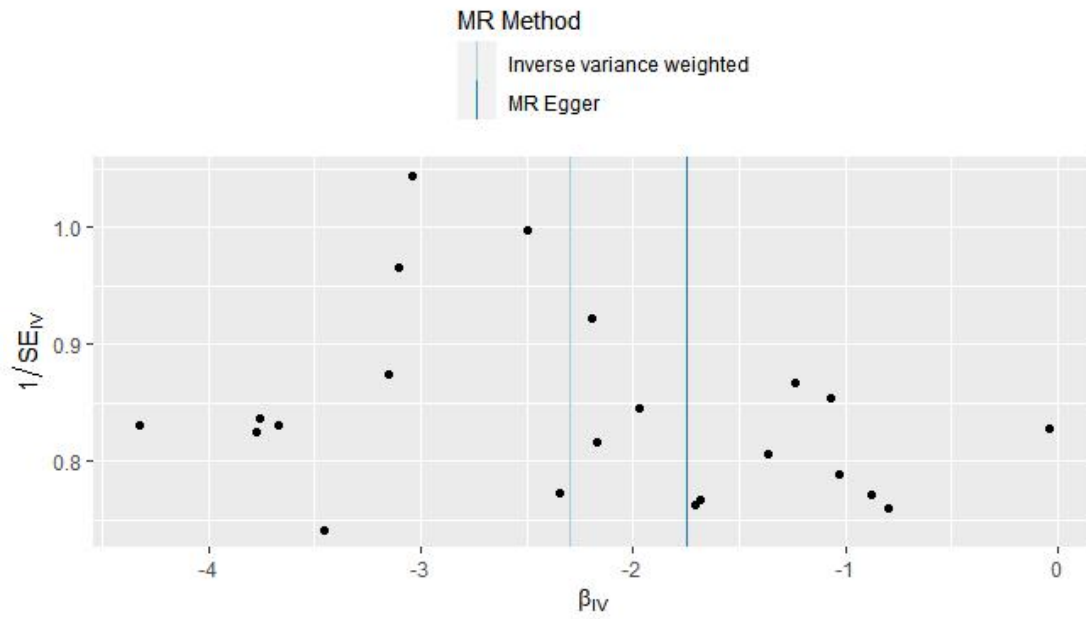
Supplementary Figure 40. SNP, single-nucleotide polymorphism; IV, Instrumental variable; SE: Standard Error; MR, Mendelian Randomization.



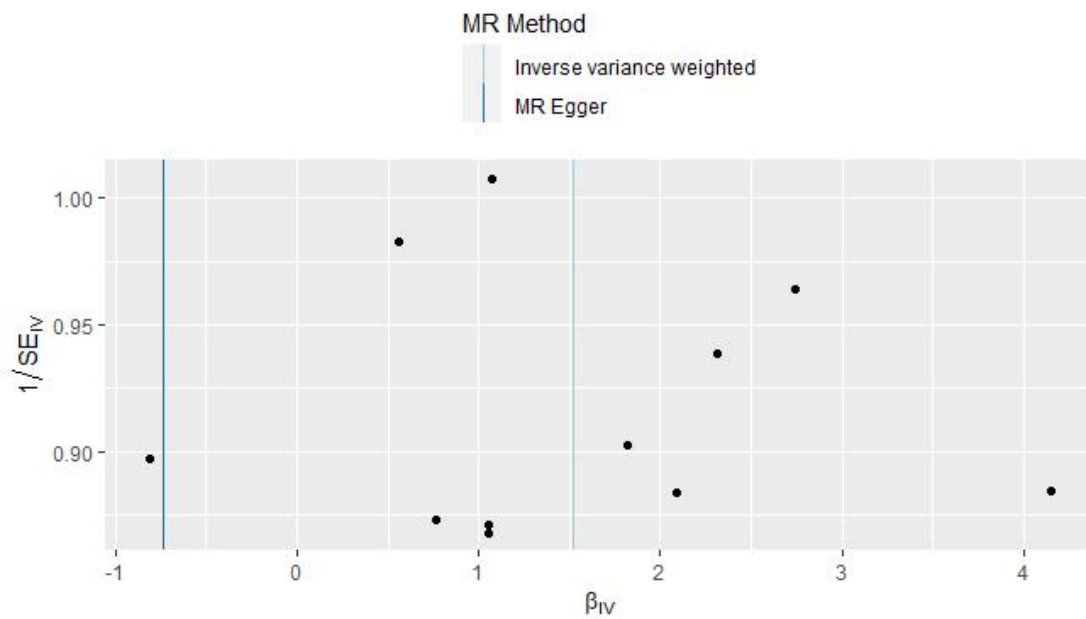
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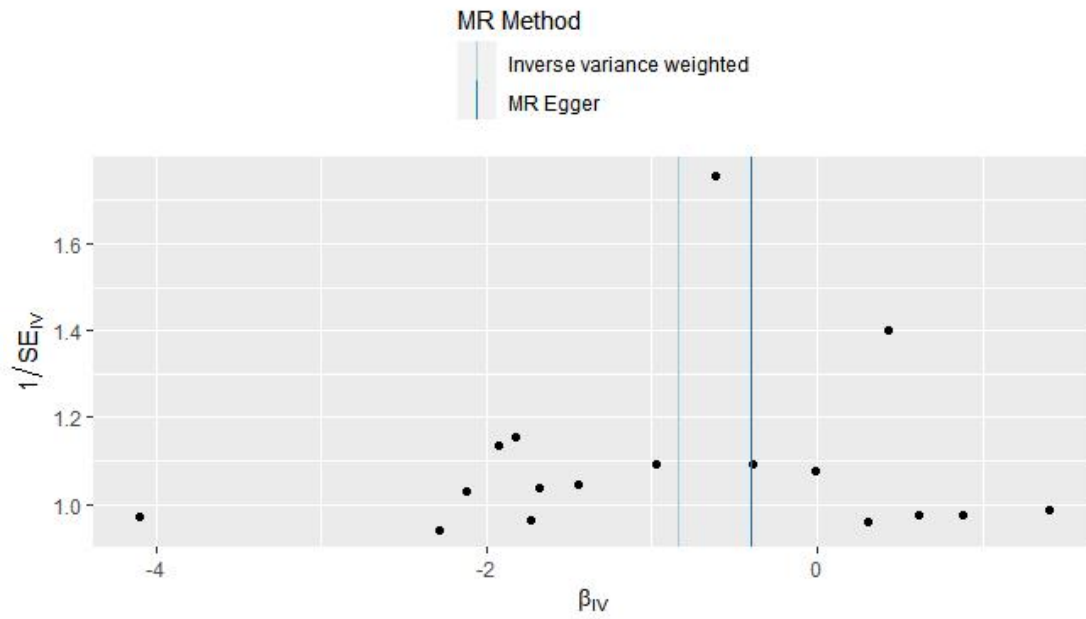
Supplementary Figure 42. SNP, single-nucleotide polymorphism; IV, Instrumental variable; SE: Standard Error; MR, Mendelian Randomization.



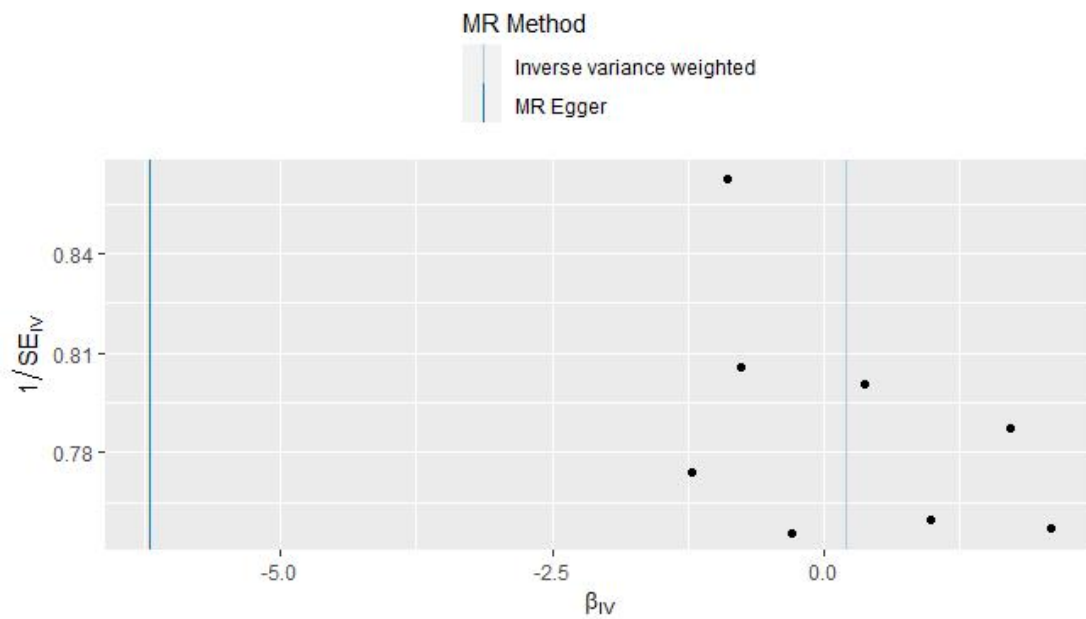
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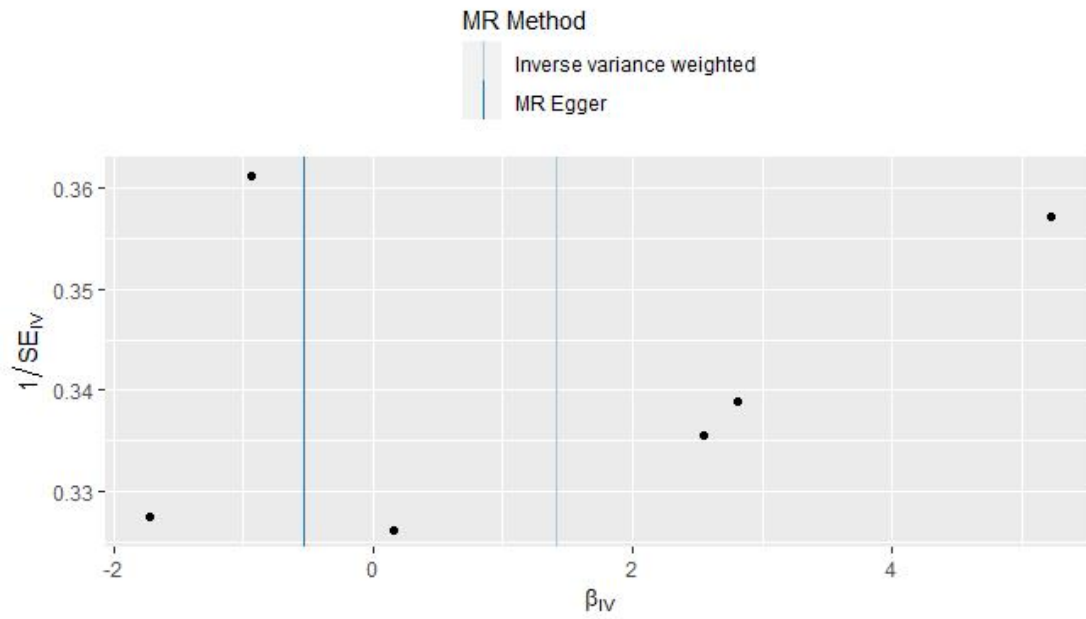
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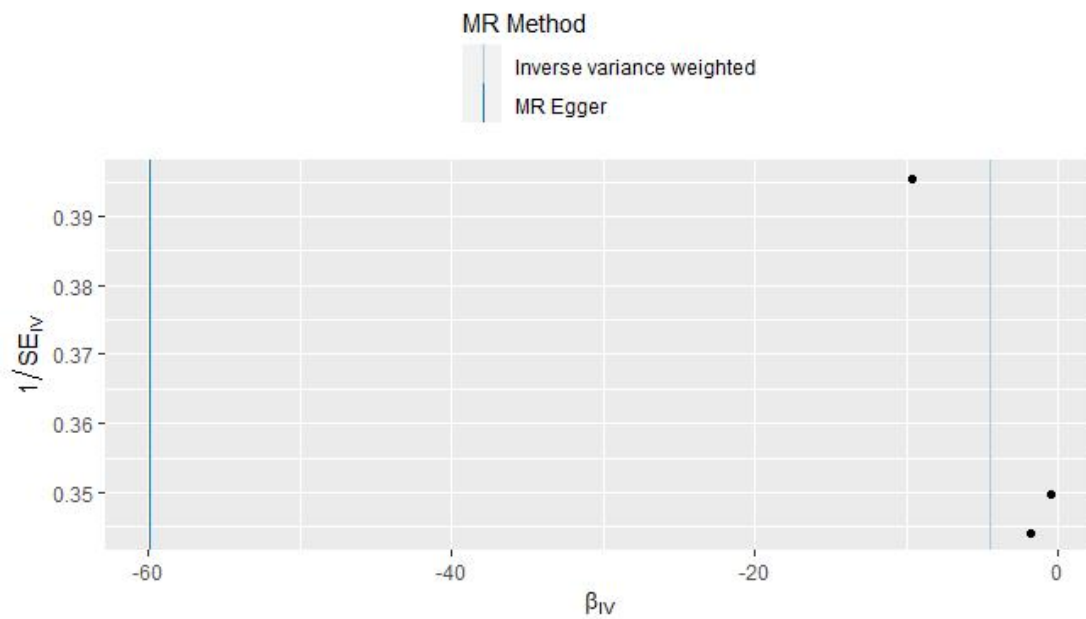
Supplementary Figure 45. SNP, single-nucleotide polymorphism; IV, Instrumental variable; SE: Standard Error; MR, Mendelian Randomization.



Supplementary Figure 46. SNP, single-nucleotide polymorphism; IV, Instrumental variable; SE: Standard Error; MR, Mendelian Randomization.



Supplementary Figure 47. SNP, single-nucleotide polymorphism; IV, Instrumental variable; SE: Standard Error; MR, Mendelian Randomization.



Supplementary Figure 48. SNP, single-nucleotide polymorphism; IV, Instrumental variable; SE: Standard Error; MR, Mendelian Randomization.

Supplementary Material

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Supplementary Table 1 Association of the SNPs used as candidate genetic instruments from the GWAS for Mendelian randomization analyses of Age completed full time education and risk of Gastroesophageal reflux disease.

	SNP	Related confounding phenotypes	effect_allele.exposure	other_allele.exposure	effect_allele.outcome	other_allele.outcome	beta.exposure	beta.outcome	se.outcome	sample_size.outcome	outcome	sample_size.exposure	pvalue.exposure	se.exposure	exposure
1	rs10189857	BMI	G	A	G	A	-0.0124054	0.0203421	0.00485316	602604	Gastroesophageal reflux disease	307897	2.70E-09	0.00208474	Age completed full time education
2	rs10760199	BMI	T	G	T	G	0.0115963	-0.0186891	0.00483678	602604	Gastroesophageal reflux disease	307897	2.50E-08	0.00208033	Age completed full time education

3	rs10953765	BMI	A	G	A	G	-0.0130933	0.0257032	0.00488839	602604	Gastroesophageal reflux disease	307897	4.90E-10	0.002104	Age completed full time education
4	rs11665242	ALCOHOL	G	A	G	A	-0.0125523	0.0317599	0.00488187	602604	Gastroesophageal reflux disease	307897	2.10E-09	0.00209622	Age completed full time education
5	rs13064576	BMI	T	C	T	C	0.0172696	-0.0427774	0.00529368	602604	Gastroesophageal reflux disease	307897	2.40E-14	0.00226489	Age completed full time education

6	rs13238996	BMI	G	A	G	A	-0.0133142	0.0259569	0.00548628	602604	Gastroesophageal reflux disease	307897	3.20E-08	0.00240789	Age completed full time education
7	rs1462163		T	C	T	C	-0.0127222	0.0131675	0.00493409	602604	Gastroesophageal reflux disease	307897	1.90E-09	0.00211969	Age completed full time education
8	rs1557341	ALCOHOL	C	A	C	A	0.0129858	-0.0349517	0.00502925	602604	Gastroesophageal reflux disease	307897	3.70E-09	0.00220266	Age completed full time education

9	rs17563464		A	C	A	C	-0.0148391	0.0120229	0.00583798	602604	Gastroesophageal reflux disease	307897	3.50E-09	0.00251248	Age completed full time education
10	rs178217		C	T	C	T	-0.0143669	0.0200742	0.0055639	602604	Gastroesophageal reflux disease	307897	2.10E-09	0.00239746	Age completed full time education
11	rs2588962	SMO KING	A	G	A	G	0.0150825	-0.0193965	0.00483127	602604	Gastroesophageal reflux disease	307897	4.10E-13	0.00207972	Age completed full time education

1 5	rs467 4403		G	T	G	T	-0.0127 249	0.0167 346	0.005 4189 9	602604	Gastroesophageal reflux disease	307897	4.90E- 08	0.002 3324	Age com plet ed full time edu cati on
1 6	rs473 1951		T	G	T	G	0.0153 215	-0.027 8152	0.006 0556	602604	Gastroesophageal reflux disease	307897	3.40E- 09	0.002 59236	Age com plet ed full time edu cati on
1 7	rs644 9503	SMO KING	A	G	A	G	0.0123 947	-0.009 65273	0.004 8140 5	602604	Gastroesophageal reflux disease	307897	2.60E- 09	0.002 08193	Age com plet ed full time edu cati on

18	rs6508344	A	G	A	G	-0.0115957	0.00687788	0.00484917	602604	Gastroesophageal reflux disease	307897	2.80E-08	0.00208724	Age completed full time education
19	rs6679399	C	A	C	A	0.0426608	-0.0296751	0.0154884	602604	Gastroesophageal reflux disease	307897	3.00E-10	0.00677016	Age completed full time education
20	rs67209586	A	G	A	G	-0.0117953	0.0116753	0.00491632	602604	Gastroesophageal reflux disease	307897	2.40E-08	0.00211341	Age completed full time education

2 1	rs681 9127 0	SMO KING	C	A	C	A	0.0166 103	-0.021 12	0.005 7590 2	602604	Gastroesophageal reflux disease	307897	2.50E- 11	0.002 48918	Age com plet ed full time edu cati on Age com plet ed full time edu cati on
2 2	rs693 1604		T	C	T	C	0.0136 265	-0.020 4973	0.005 0225 9	602604	Gastroesophageal reflux disease	307897	1.10E- 10	0.002 1131	Age com plet ed full time edu cati on Age com plet ed full time edu cati on
2 3	rs711 0786		T	C	T	C	0.0127 141	-0.019 6005	0.004 8601 3	602604	Gastroesophageal reflux disease	307897	1.20E- 09	0.002 09121	Age com plet ed full time edu cati on

2	rs733		G	C	G	C	0.0121	-0.013	0.004	602604	Gastroesophageal	307897	6.20E-	0.002	Age
4	5432						373	8862	8378		reflux disease		09	08869	com
									3						plet
															ed
															full
															time
															edu
															cati
															on
															Age
															com
															plet
2	rs776		C	T	C	T	-0.0227	0.0365	0.008	602604	Gastroesophageal	307897	2.10E-	0.003	ed
5	8758						349	404	8969		reflux disease		09	79371	full
									8						time
															edu
															cati
															on
															Age
															com
															plet
															ed
															full
															time
															edu
															cati
															on
2	rs789	ALCO	G	A	G	A	0.0145	-0.019	0.004	602604	Gastroesophageal	307897	6.20E-	0.002	ed
6	6518	HOL					245	5954	8192		reflux disease		12	11298	full
									4						time
															edu
															cati
															on

27	rs9655780	ALCOHOL	A	G	A	G	-0.0174579	0.0217935	0.00646314	602604	Gastroesophageal reflux disease	307897	4.30E-10	0.00279646	Age completed full time education
28	rs9866630		A	G	A	G	-0.0126597	0.00781251	0.00481209	602604	Gastroesophageal reflux disease	307897	1.00E-09	0.0020719	Age completed full time education

Supplementary Table 2 Association of the SNPs used as candidate genetic instruments from the GWAS for Mendelian randomization analyses of Job involves heavy manual or physical work and risk of Gastroesophageal reflux disease.

SN	P	Relat ed confo undi ng phen otype s	effect_all ele.expos ure	other_all ele.expos ure	effect_all ele.outco me	other_all ele.outco me	beta.e xposu re	beta. outco me	se.o utco me	samplesi ze.outco me	pval. outco me	outcome	pval.e xposu re	samplesi ze.expos ure	se.ex posu re	exp osu re
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1	rs10 8115 8	Alcohol	T	C	T	C	0.0169 887	-0.000 13351	0.004 8923	602604	0.9782 28	Gastroesopha geal reflux disease	2.70E- 12	263615	0.002 4299 6	Job invo lves heav y man ual or phys ical wor k Job invo lves heav
2	rs10 8206 25		C	T	C	T	-0.016 0068	-0.016 8521	0.005 8133 6	602604	0.0037 4516	Gastroesopha geal reflux disease	2.90E- 08	263615	0.002 8851 5	y man ual or phys ical wor

3	rs1130889		G	C	G	C	-0.0249218	-0.00252268	0.00913744	602604	0.782485	Gastroesophageal reflux disease	4.50E-08	263615	0.00455725	Job involves heavy manual or physical work
4	rs11663824	Alcohol	A	C	A	C	0.0136375	0.0318018	0.00492016	602604	1.02E-10	Gastroesophageal reflux disease	2.50E-08	263615	0.00244806	Job involves heavy manual or physical work

5	rs11678979	BMI	C	T	C	T	-0.0149934	-0.0331273	0.00543865	602604	1.12E-09	Gastroesophageal reflux disease	3.00E-08	263615	0.00270637	Job involves heavy manual or physical work Job involves heavy manual
6	rs11726786	Alcohol	G	T	G	T	0.0165951	0.00575011	0.00498646	602604	0.248851	Gastroesophageal reflux disease	2.40E-11	263615	0.00248344	Job involves heavy manual or physical work Job involves heavy manual
7	rs11756123		T	A	T	A	-0.0137486	-0.0287505	0.00499782	602604	8.79E-09	Gastroesophageal reflux disease	3.20E-08	263615	0.00248658	Job involves heavy manual

														or phys ical wor k		
														Job invo lves heav y man ual or phys ical wor k		
8	rs13 2509 96		C	G	C	G	-0.013 3122	0.0098 0948	0.004 8185 2	602604	0.0417 715	Gastroesopha geal reflux disease	2.70E- 08	263615	0.002 3930 7	Job invo lves heav y man ual or phys ical wor k Job invo lves heav y man ual or phys ical wor k
9	rs13 7005 9	BMI	G	A	G	A	0.0180 816	0.0401 347	0.005 6884 8	602604	1.72E- 12	Gastroesopha geal reflux disease	1.80E- 10	263615	0.002 8349 2	Job invo lves heav y man ual or phys ical wor k

10	rs20 91329		G	A	G	A	-0.0158895	-0.0077522	0.0052737	602604	0.141569	Gastroesophageal reflux disease	2.00E-09	263615	0.00265008	Job involves heavy manual or physical work Job involves heavy manual
11	rs23 18540	BMI	G	T	G	T	-0.0142827	-0.0255283	0.00487905	602604	1.67E-07	Gastroesophageal reflux disease	3.70E-09	263615	0.00242247	Job involves heavy manual or physical work Job involves heavy manual
12	rs28 19348	BMI	C	T	C	T	0.0145582	0.0252013	0.00501888	602604	5.13E-07	Gastroesophageal reflux disease	5.60E-09	263615	0.00249731	Job involves heavy manual

1	rs34														or phys ical wor k	
3	7007 31		A	G	A	G	0.0197 694	-0.006 11605	0.007 0170 2	602604	0.3834 26	Gastroesopha geal reflux disease	1.50E- 08	263615	0.003 4944 5	Job invo lves heav y man ual or phys ical wor k Job invo lves heav y man ual or phys ical wor k
1	rs35															
4	9991 62	BMI	G	C	G	C	-0.024 8598	-0.042 6913	0.005 2233 2	602604	3.00E- 16	Gastroesopha geal reflux disease	7.40E- 22	263615	0.002 5873	Job invo lves heav y man ual or phys ical wor k

15	rs3785354	Alcohol	T	C	T	C	0.0135824	0.0237887	0.00494509	602604	1.50E-06	Gastroesophageal reflux disease	3.70E-08	263615	0.0024672	Job involves heavy manual or physical work Job involves heavy manual
16	rs4580876	BMI	A	G	A	G	-0.0220715	-0.0338177	0.00482026	602604	2.29E-12	Gastroesophageal reflux disease	3.00E-20	263615	0.0023945	Job involves heavy manual or physical work Job involves heavy manual
17	rs4731992		G	A	G	A	-0.0170407	-0.0222119	0.00582934	602604	0.000138759	Gastroesophageal reflux disease	4.00E-09	263615	0.002895	Job involves heavy manual

18	rs62511803	A	G	A	G	-0.021702	-0.0145097	0.00689064	602604	0.035229	Gastroesophageal reflux disease	7.50E-10	263615	0.00343968	or physical work Job involves heavy manual or physical work Job involves heavy manual or physical work
19	rs6544763	C	T	C	T	0.0139692	0.0182768	0.005072	602604	0.000314007	Gastroesophageal reflux disease	3.20E-08	263615	0.00252586	or physical work Job involves heavy manual or physical work

20	rs7108077	G	A	G	A	-0.0134395	-0.0117868	0.00496158	602604	0.0175194	Gastroesophageal reflux disease	4.90E-08	263615	0.00246345	Job involves heavy manual or physical work Job involves heavy manual
21	rs7467480	A	T	A	T	-0.0155085	-0.0163904	0.00488544	602604	0.000793816	Gastroesophageal reflux disease	1.70E-10	263615	0.0024292	Job involves heavy manual or physical work Job involves heavy manual
22	rs8054111	G	A	G	A	-0.015349	-0.0117556	0.0054579	602604	0.0312507	Gastroesophageal reflux disease	1.20E-08	263615	0.0026932	Job involves heavy manual

● **Supplementary Table 3** Association of the SNPs used as candidate genetic instruments from the GWAS for Mendelian randomization analyses of Average total household income before tax and risk of Gastroesophageal reflux disease.

SNP	Related confounding phenotypes	effect_al lele.exposure	other_al lele.exposure	effect_al lele.outcome	other_al lele.outcome	beta. exposure	beta. outcome	samples ize.outcome	pval. outcome	outcome	outcome.deprecatd	pval. exposure	samples ize.exposure	se.e xposure	exp osure
1	rs10761035	A	G	A	G	0.0186402	-0.0226412	602604	0.000241035	Gastroesophageal reflux disease	Gastroesophageal reflux disease	3.70E-08	397751	0.00338512	Average total household income before tax

2	rs11588857	Alcohol	A	G	A	G	0.0213402	-0.0127023	602604	0.0315435	Gastroesophageal reflux disease	Gastroesophageal reflux disease	4.90E-11	397751	0.00324615	Average total household income before tax
3	rs11665242	Alcohol	G	A	G	A	-0.0175478	0.0317599	602604	7.73E-11	Gastroesophageal reflux disease	Gastroesophageal reflux disease	6.00E-11	397751	0.00268166	Average total household income before tax
4	rs12692596	BMI	T	C	T	C	-0.0154093	0.0198715	602604	6.52E-05	Gastroesophageal reflux disease	Gastroesophageal reflux disease	1.70E-08	397751	0.00273347	Average total household income before

																re tax
																Ave rage total hou sh old inco me befo re tax Ave rage total hou sh old inco me befo re tax
5	rs13 002 946	BMI	A	T	A	T	0.0205 047	-0.033 6393	602604	6.50E -10	Gastroesoph ageal reflux disease	Gastroesophag eal reflux disease	7.30E- 12	397751	0.002 9928 5	
6	rs14 213 34	BMI	C	A	C	A	0.0162 948	-0.020 2427	602604	3.12E -05	Gastroesoph ageal reflux disease	Gastroesophag eal reflux disease	1.00E- 09	397751	0.002 6702 8	

																				Average total household income before tax
7	rs14 553 50	A	T	A	T	-0.017 2341	0.015 1799	602604	0.001 6761	Gastroesophageal reflux disease	Gastroesophageal reflux disease	9.20E-11	397751	0.002 6596 1						
8	rs20 684 28	T	C	T	C	0.0169 724	-0.009 41417	602604	0.094 1369	Gastroesophageal reflux disease	Gastroesophageal reflux disease	4.20E-08	397751	0.003 0951 5						
9	rs23 327 19	G	A	G	A	-0.018 3042	0.022 2214	602604	3.58E-05	Gastroesophageal reflux disease	Gastroesophageal reflux disease	5.70E-10	397751	0.002 9532 3						

10	rs2422859	G	T	G	T	0.0163711	-0.00956311	602604	0.0469732	Gastroesophageal reflux disease	Gastroesophageal reflux disease	6.20E-10	397751	0.00264718	Average total household income before tax
11	rs387780	C	T	C	T	0.0167299	-0.0150838	602604	0.00335714	Gastroesophageal reflux disease	Gastroesophageal reflux disease	3.30E-09	397751	0.00282732	Average total household income before tax

															Average total household income before tax	
1 2	rs57 547 38		G	A	G	A	-0.016 2464	0.011 8154	602604	0.026 3937	Gastroesophageal reflux disease	Gastroesophageal reflux disease	2.70E-08	397751	0.002 9203 8	
1 3	rs60 358 77		C	A	C	A	-0.014 5138	0.004 55135	602604	0.345 124	Gastroesophageal reflux disease	Gastroesophageal reflux disease	4.30E-08	397751	0.002 6504 2	
1 4	rs66 993 97	BMI	G	A	G	A	-0.019 0757	0.020 122	602604	5.77E-05	Gastroesophageal reflux disease	Gastroesophageal reflux disease	3.50E-12	397751	0.002 7415 3	

15	rs6868457		C	T	C	T	0.0209797	-0.00864939	602604	0.0730685	Gastroesophageal reflux disease	Gastroesophageal reflux disease	3.10E-15	397751	0.0026601	Average total household income before tax
16	rs7700107	BMI	C	A	C	A	-0.0228296	0.0355854	602604	3.81E-07	Gastroesophageal reflux disease	Gastroesophageal reflux disease	2.50E-09	397751	0.00382992	Average total household income before tax

17	rs784256	BMI	A	G	A	G	-0.0253813	0.0289491	602604	2.70E-06	Gastroesophageal reflux disease	Gastroesophageal reflux disease	7.90E-14	397751	0.00339684	Average total household income before tax
18	rs9388490		T	C	T	C	0.015105	-0.0236637	602604	1.06E-06	Gastroesophageal reflux disease	Gastroesophageal reflux disease	1.50E-08	397751	0.00266861	Average total household income before tax
19	rs9556958	BMI	T	C	T	C	-0.0153409	0.027291	602604	1.60E-08	Gastroesophageal reflux disease	Gastroesophageal reflux disease	8.50E-09	397751	0.0026641	Average total household income before

- **Supplementary Table 4** Association of the SNPs used as candidate genetic instruments from the GWAS for Mendelian randomization analyses of Townsend deprivation index at recruitment and risk of Gastroesophageal reflux disease.

SNP	Related confounding phenotypes	effect_all ele.exposure	other_all ele.exposure	effect_all ele.outcome	other_all ele.outcome	beta.e xposure	beta. outcome	se.o outcome	samplesi ze.outcome	pval. outcome	outcome	pval.e xposure	se.ex posure	samplesi ze.exposure	exp osure
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1	rs113 3452 85 BMI	C	T	C	T	0.0163 127	0.0200 155	0.007 1161 4	602604	0.0049 1281	Gastroesophageal reflux disease	3.20E-08	0.002 9509 4	462464	Townsend deprivation index at recruitment
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2	rs11855821	BMI	A	G	A	G	-0.0125981	-0.0259592	0.00543947	602604	1.82E-06	Gastroesophageal reflux disease	3.90E-08	0.00229259	462464	Townsend deprivation index at recruitment
3	rs1483246		C	T	C	T	-0.0121102	-0.0093388	0.00484509	602604	0.05392	Gastroesophageal reflux disease	3.10E-09	0.00204409	462464	Townsend deprivation index at recruitment
4	rs1947083		A	G	A	G	0.0118662	0.0160533	0.00500619	602604	0.00134273	Gastroesophageal reflux disease	1.90E-08	0.0021105	462464	Townsend deprivation index at recr

5	rs2403326	BMI	G	A	G	A	0.0115465	0.0191822	0.00481194	602604	6.71E-05	Gastroesophageal reflux disease	1.20E-08	0.00202703	462464	uitment Townsend deprivation index at recruitment Townsend deprivation index at recruitment
6	rs253125		C	T	C	T	0.013174	-0.00570351	0.00556832	602604	0.305703	Gastroesophageal reflux disease	1.90E-08	0.0023432	462464	

7	rs3865018	BMI	T	C	T	C	-0.0134594	-0.0178233	0.0054528	602604	0.00108059	Gastroesophageal reflux disease	4.20E-09	0.00229086	462464	Townsend deprivation index at recruitment
8	rs4785187		A	G	A	G	0.0137996	0.0192606	0.00579202	602604	0.000883019	Gastroesophageal reflux disease	1.50E-08	0.00243703	462464	Townsend deprivation index at recruitment
9	rs6931604	Alcohol	T	C	T	C	-0.0121903	-0.0204973	0.00502259	602604	4.48E-05	Gastroesophageal reflux disease	4.10E-09	0.00207309	462464	Townsend deprivation index at recr

10	rs704067	BMI	A	G	A	G	0.0120267	0.0226494	0.00485438	602604	3.07E-06	Gastroesophageal reflux disease	3.90E-09	0.0020424	462464	uitment
11	rs7740440		A	G	A	G	0.011847	0.0202381	0.00482118	602604	2.70E-05	Gastroesophageal reflux disease	5.70E-09	0.00203391	462464	Townsend deprivation index at recruitment

1 2	rs782 5712 8	T	C	T	C	-0.016 7416	-0.003 64373	0.006 6265 3	602604	0.5824 09	Gastroesopha geal reflux disease	2.40E- 09	0.002 8067 6	462464	Tow nsen d depr ivati on inde x at recr uitm ent Tow nsen d depr ivati on inde x at recr
1 3	rs989 532	G	A	G	A	0.0138 559	0.0113 503	0.005 1313 6	602604	0.0269 699	Gastroesopha geal reflux disease	7.40E- 11	0.002 1275 6	462464	Tow nsen d depr ivati on inde x at recr uitm ent Tow nsen d depr ivati on inde x at recr
1 4	rs990 706	T	C	T	C	0.0155 869	-0.012 9805	0.006 4345 7	602604	0.0436 626	Gastroesopha geal reflux disease	7.90E- 09	0.002 7014 1	462464	Tow nsen d depr ivati on inde x at recr

Supplementary Table 5 Association of the SNPs used as candidate genetic instruments from the GWAS for Mendelian randomization analyses of Leisure/social activities: Pub or social club and risk of Gastroesophageal reflux disease

SNP	Related confounding phenotypes	effect_all ele.exposure	other_all ele.exposure	effect_all ele.outcome	other_all ele.outcome	beta.e xposure	beta.outcome	se.outcome	samplesize.outcome	pval.outcome	outcome	pvalue.xposure	se.exposure	samplesize.exposure	exposure
1 rs1066099		G	C	G	C	0.00651032	-0.0147389	0.00633095	602604	0.0199081	Gastroesophageal reflux disease	4.60E-08	0.00119092	461369	Leisure/social activities: Pub or social club

2	rs139920	BMI	T	C	T	C	0.00614932	0.00712136	0.00481379	602604	0.139042	Gastroesophageal reflux disease	1.20E-11	0.00090753	461369	Leisure/social activities: Pub or social club Leisure/social activities: Pub or social club
3	rs2661863		C	T	C	T	-0.00537368	0.0056056	0.00505625	602604	0.267583	Gastroesophageal reflux disease	1.90E-08	0.000956722	461369	Leisure/social activities: Pub or social club Leisure/social activities: Pub or social club
4	rs754204		T	C	T	C	0.00507247	0.000413709	0.00483499	602604	0.931812	Gastroesophageal reflux disease	3.00E-08	0.000915201	461369	Leisure/social activities: Pub or social club

5	rs75 4516 1		T	C	T	C	-0.006 87787	-0.006 04065	0.006 2211 7	602604	0.3315 57	Gastroesopha geal reflux disease	4.20E- 09	0.001 1701 8	461369	Leisu re/soc ial activi ties: Pub or social club Leisu re/soc ial activi ties: Pub or social club Leisu re/soc ial activi ties: Pub or social club Leisu re/soc ial activi ties: Pub or social club
6	rs78 0094	Alcohol	C	T	C	T	0.0051 697	-0.003 84079	0.004 9459	602604	0.4374 18	Gastroesopha geal reflux disease	2.70E- 08	0.000 9301 37	461369	Leisu re/soc ial activi ties: Pub or social club Leisu re/soc ial activi ties: Pub or social club Leisu re/soc ial activi ties: Pub or social club
7	rs94 0159 3	BMI	C	A	C	A	-0.005 31642	-0.034 7468	0.004 8223 2	602604	5.79E- 13	Gastroesopha geal reflux disease	5.30E- 09	0.000 9107 46	461369	Leisu re/soc ial activi ties: Pub or social club

Supplementary Table 6 Association of the SNPs used as candidate genetic instruments from the GWAS for Mendelian randomization analyses of Leisure/social activities: Sports club or gym and risk of Gastroesophageal reflux disease.

SN	P	Related confounding phenotypes	effect_all ele.exposure	other_all ele.exposure	effect_al lele.outcome	other_all ele.outcome	beta.e xposure	beta. outcome	se.o utcome	samples ize.outcome	pval. outcome	outcome	se.ex posure	samplesi ze.exposure	pval.e xposure	expo sure
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1	rs11 7120 56	BMI	C	T	C	T	-0.005 97808	0.0424 557	0.004 8354 8	602604	1.63E- 18	Gastroesopha geal reflux disease	0.000 9605 55	461369	4.90E- 10	Leisu re/soc ial activi ties: Sport s club or gym Leisu re/soc ial activi ties: Sport s club or gym
2	rs13 0028 62		A	C	A	C	0.0060 452	-0.001 17087	0.005 5049 7	602604	0.8315 66	Gastroesopha geal reflux disease	0.001 0953 7	461369	3.40E- 08	Leisu re/soc ial activi ties: Sport s club or gym

3	rs17 3150 37		C	T	C	T	-0.007 88121	0.0045 8221	0.006 9191 6	602604	0.5078 11	Gastroesopha geal reflux disease	0.001 3926 2	461369	1.50E- 08	Leisu re/soc ial activi ties: Sport s club or gym Leisu re/soc ial activi ties: Sport s club or gym Leisu re/soc ial activi ties: Sport s club or gym Leisu re/soc ial activi ties: Sport s club or gym
4	rs62 2639 12	Smoki ng	A	G	A	G	-0.006 11858	-0.003 39804	0.005 0045 2	602604	0.4971 41	Gastroesopha geal reflux disease	0.000 9922 44	461369	7.00E- 10	Leisu re/soc ial activi ties: Sport s club or gym Leisu re/soc ial activi ties: Sport s club or gym Leisu re/soc ial activi ties: Sport s club or gym Leisu re/soc ial activi ties: Sport s club or gym
5	rs64 7844 4		G	A	G	A	0.0055 0414	-0.001 21552	0.005 0577 5	602604	0.8100 77	Gastroesopha geal reflux disease	0.001 0037 3	461369	4.20E- 08	Leisu re/soc ial activi ties: Sport s club or gym Leisu re/soc ial activi ties: Sport s club or gym Leisu re/soc ial activi ties: Sport s club or gym Leisu re/soc ial activi ties: Sport s club or gym

6	rs728990	G	C	G	C	-0.00580003	0.0157475	0.00526749	602604	0.00279364	Gastroesophageal reflux disease	0.00106034	461369	4.50E-08	Leisure/social activities: Sports club or gym
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- Supplementary Table 7 Association of the SNPs used as candidate genetic instruments from the GWAS for Mendelian randomization analyses of Age completed full time education and risk of Barrett's esophagus.

SNP	Related confounding phenotypes	effect_al lele.exposure	other_al lele.exposure	effect_al lele.outcome	other_al lele.outcome	beta. exposure	beta. outcome	se.outcome	samples. outcome	pval. outcome	outcome	samples. exposure	pval. exposure	se.exposure	exposure
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1	rs10 189 857	BMI	G	A	G	A	-0.012 4054	0.031 531	0.015 1383	56429	0.037 264	Barrett's esophagus id:ebi-a-GCST900 00515	307897	2.70E- 09	0.002 0847 4	Age com plet ed full time edu cati on	
2	rs10 760 199	BMI	T	G	T	G	0.0115 963	0.003 42634	0.015 179	56429	0.821 413	Barrett's esophagus id:ebi-a-GCST900 00515	307897	2.50E- 08	0.002 0803 3	Age com plet ed full time edu cati on	
3	rs11 665 242	Alcohol	G	A	G	A	-0.012 5523	0.047 4094	0.015 2082	56429	0.001 82478	Barrett's esophagus id:ebi-a-GCST900 00515	307897	2.10E- 09	0.002 0962 2	Age com plet ed full time edu cati on	

4	rs14 621 63	T	C	T	C	-0.012 7222	0.013 7455	0.015 4459	56429	0.373 513	Barrett's esophagus id:ebi-a-GCST900 00515	307897	1.90E- 09	0.002 1196 9	Age com plet ed full time edu cati on Age com plet ed full time edu cati on
5	rs17 563 464	A	C	A	C	-0.014 8391	0.015 247	0.018 8083	56429	0.417 565	Barrett's esophagus id:ebi-a-GCST900 00515	307897	3.50E- 09	0.002 5124 8	Age com plet ed full time edu cati on Age com plet ed full time edu cati on
6	rs17 821 7	C	T	C	T	-0.014 3669	0.052 7652	0.017 3023	56429	0.002 29145	Barrett's esophagus id:ebi-a-GCST900 00515	307897	2.10E- 09	0.002 3974 6	Age com plet ed full time edu cati on

7	rs25 889 62	Smoking	A	G	A	G	0.0150 825	-0.037 6218	0.015 1151	56429	0.012 8097	Barrett's esophagus id:ebi-a-GCST900 00515	307897	4.10E- 13	0.002 0797 2	Age com plet ed full time edu cati on	
8	rs45 577 20		G	A	G	A	0.0119 687	-0.028 0723	0.015 5009	56429	0.070 1391	Barrett's esophagus id:ebi-a-GCST900 00515	307897	2.00E- 08	0.002 1339 3	Age com plet ed full time edu cati on	
9	rs46 744 03		G	T	G	T	-0.012 7249	0.043 9594	0.017 1779	56429	0.010 4954	Barrett's esophagus id:ebi-a-GCST900 00515	307897	4.90E- 08	0.002 3324	Age com plet ed full time edu cati on	

														Age completed full time education
10	rs4731951	T	G	T	G	0.0153215	-0.0503112	0.0187821	56429	0.00739129	Barrett's esophagus id:ebi-a-GCST90000515	307897	3.40E-09	0.00259236
11	rs6508344	A	G	A	G	-0.0115957	0.0197887	0.0152033	56429	0.19305	Barrett's esophagus id:ebi-a-GCST90000515	307897	2.80E-08	0.00208724
12	rs6679399	C	A	C	A	0.0426608	-0.0454615	0.0499448	56429	0.362698	Barrett's esophagus id:ebi-a-GCST90000515	307897	3.00E-10	0.00677016

1 3	rs67 295 86	A	G	A	G	-0.011 7953	0.010 3537	0.015 3002	56429	0.498 595	Barrett's esophagus id:ebi-a-GCST900 00515	307897	2.40E- 08	0.002 1134 1	Age com plet ed full time edu cati on Age com plet ed full time edu cati on
1 4	rs71 107 86	T	C	T	C	0.0127 141	-0.047 7787	0.015 2041	56429	0.001 67517	Barrett's esophagus id:ebi-a-GCST900 00515	307897	1.20E- 09	0.002 0912 1	Age com plet ed full time edu cati on Age com plet ed full time edu cati on
1 5	rs77 687 58	C	T	C	T	-0.022 7349	0.049 2636	0.027 8694	56429	0.077 117	Barrett's esophagus id:ebi-a-GCST900 00515	307897	2.10E- 09	0.003 7937 1	Age com plet ed full time edu cati on

SNP	Allele 1	Allele 2	Allele 3	Allele 4	Beta	SE	P-value	SE	SE	Sample size	P-value	Outcome	P-value	Sample size	SE	Exposure
rs9655780	A	G	A	G	-0.0174579	0.021526	0.0201497	56429	0.285386	Barrett's esophagus id:ebi-a-GCST90000515	307897	4.30E-10	0.00279646	Age completed full time education		
rs9866630	A	G	A	G	-0.0126597	0.024975	0.0149754	56429	0.0953674	Barrett's esophagus id:ebi-a-GCST90000515	307897	1.00E-09	0.0020719	Age completed full time education		

● Supplementary Table 8 Association of the SNPs used as candidate genetic instruments from the GWAS for Mendelian randomization analyses of Job involves heavy manual or physical work and risk of Barrett's esophagus.

SNP	Related confounding phenotype	effect_all ele.exposure	other_all ele.exposure	effect_all ele.outcome	other_all ele.outcome	beta.e xposure	beta.o tcome	se.ou tcome	samplesi ze.outcome	pval.o tcome	outcome	pval.e xposure	samplesi ze.exposure	se.ex posure	exp osure
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1	rs1081158	Alcohol	T	C	T	C	0.0169887	0.00386911	0.0152839	56429	0.800152	Barrett's esophagus	2.70E-12	263615	0.00242996	Job involves heavy manual or physical work
2	rs10820625		C	T	C	T	-0.0160068	-0.0663494	0.018092	56429	0.000245092	Barrett's esophagus	2.90E-08	263615	0.00288515	Job involves heavy manual or physical work
3	rs11130889		G	C	G	C	-0.0249218	-0.0261838	0.0286138	56429	0.360152	Barrett's esophagus	4.50E-08	263615	0.00455725	Job involves heavy manual

4	rs11663824	Alcohol	A	C	A	C	0.0136375	0.0335832	0.015306	56429	0.0282273	Barrett's esophagus	2.50E-08	263615	0.00244806	or physical work Job involves heavy manual or physical work Job involves heavy manual or physical work
5	rs11678979	BMI	C	T	C	T	-0.0149934	-0.0531341	0.0172002	56429	0.0020729	Barrett's esophagus	3.00E-08	263615	0.00270637	or physical work Job involves heavy manual or physical work

6	rs11726786	Alcohol	G	T	G	T	0.0165951	0.0153067	0.0155479	56429	0.324876	Barrett's esophagus	2.40E-11	263615	0.00248344	Job involves heavy manual or physical work Job involves heavy manual
7	rs11756123		T	A	T	A	-0.0137486	-0.0104674	0.0157484	56429	0.506266	Barrett's esophagus	3.20E-08	263615	0.00248658	Job involves heavy manual or physical work Job involves heavy manual
8	rs13250996		C	G	C	G	-0.0133122	0.0250578	0.0151571	56429	0.0982902	Barrett's esophagus	2.70E-08	263615	0.00239307	Job involves heavy manual

9	rs1370059	BMI	G	A	G	A	0.0180816	0.0486319	0.0177771	56429	0.00622587	Barrett's esophagus	1.80E-10	263615	0.00283492	or physical work Job involves heavily manual or physical work Job involves heavily manual or physical work
10	rs2091329		G	A	G	A	-0.0158895	-0.043619	0.0164801	56429	0.00812643	Barrett's esophagus	2.00E-09	263615	0.00265008	Job involves heavily manual or physical work

1	rs23	BMI	G	T	G	T	-0.0142	-0.034	0.015	56429	0.0222	Barrett's esophag us	3.70E- 09	263615	0.002	Job invo lves heav y man ual or phys ical wor k Job invo lves heav y man ual or phys ical wor k Job invo lves heav y man ual
1	1854 0						827	8159	2291		459		09	42247		
1	rs28	BMI	C	T	C	T	0.0145	0.0322	0.015	56429	0.0403	Barrett's esophag us	5.60E- 09	263615	0.002	man ual or phys ical wor k Job invo lves heav y man ual or phys ical wor k Job invo lves heav y man ual
1	1934 8						582	053	7062		172		09	49731		
1	rs34		A	G	A	G	0.0197	-0.015	0.022	56429	0.4686	Barrett's esophag us	1.50E- 08	263615	0.003	lves heav y man ual
1	7007 31						694	9721	0407		58		08	49445		

14	rs35999162	BMI	G	C	G	C	-0.0248598	-0.0494108	0.01634	56429	0.00249523	Barrett's esophagus	7.40E-22	263615	0.0025873	or physical work Job involves heavy manual or physical work Job involves heavy manual or physical work
15	rs3785354	BMI	T	C	T	C	0.0135824	0.0135052	0.0154584	56429	0.382312	Barrett's esophagus	3.70E-08	263615	0.0024672	Job involves heavy manual or physical work

16	rs4580876	BMI	A	G	A	G	-0.0220715	-0.0660802	0.0151042	56429	1.21E-05	Barrett's esophagus	3.00E-20	263615	0.0023945	Job involves heavy manual or physical work Job involves heavy manual
17	rs4731992		G	A	G	A	-0.0170407	-0.039451	0.0181492	56429	0.0297276	Barrett's esophagus	4.00E-09	263615	0.002895	Job involves heavy manual or physical work Job involves heavy manual
18	rs62511803		A	G	A	G	-0.0211702	-0.0119118	0.0215452	56429	0.580349	Barrett's esophagus	7.50E-10	263615	0.00343968	Job involves heavy manual

19	rs6544763	C	T	C	T	0.0139692	0.0292379	0.0158076	56429	0.0643695	Barrett's esophagus	3.20E-08	263615	0.00252586	or physical work Job involves heavy manual or physical work Job involves heavy manual or physical work
20	rs7108077	G	A	G	A	-0.0134395	-0.0141655	0.0154855	56429	0.360316	Barrett's esophagus	4.90E-08	263615	0.00246345	or physical work Job involves heavy manual or physical work Job involves heavy manual or physical work

2 1	rs74 6748 0	A	T	A	T	-0.0155 085	-0.016 5796	0.015 3925	56429	0.2814 26	Barrett's esophag us	1.70E- 10	263615	0.002 4292	Job invo lves heav y man ual or phys ical wor k Job invo lves heav y man ual or phys ical wor k
2 2	rs80 5411 1	G	A	G	A	-0.0153 49	-0.027 8481	0.017 0007	56429	0.1014 09	Barrett's esophag us	1.20E- 08	263615	0.002 6932	

- Supplementary Table 9 Association of the SNPs used as candidate genetic instruments from the GWAS for Mendelian randomization analyses of Average total household income before tax and risk of Barrett's esophagus.

SNP	Relat ed confo undi ng phen otype s	effect_all ele.expos ure	other_all ele.expos ure	effect_all ele.outco me	other_all ele.outco me	beta.e xposu re	beta. outco me	se.o utco me	samplesi ze.outco me	pval. outco me	outcome	pval.e xposu re	samplesi ze.expos ure	se.ex posu re	exp osu re
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1	rs104 2958 2	C	T	C	T	0.0270 261	-0.016 5796	0.015 3925	56429	0.2814 26	Barrett's esophagus	7.60E- 24	397751	0.002 68405	Ave rag e tota l hou seh old inc om e bef ore tax Ave rag e tota l hou seh old inc
2	rs107 6103 5	A	G	A	G	0.0186 402	-0.076 484	0.019 207	56429	6.83E- 05	Barrett's esophagus	3.70E- 08	397751	0.003 38512	

3	rs111 9111 6		T	C	T	C	-0.016 3993	0.0229 312	0.015 6668	56429	0.1432 8	Barrett's esophagus	3.50E- 09	397751	0.002 77643	ome e bef ore tax Ave rag e tota l hou seh old inc om e bef ore tax Ave rag e tota l hou seh old inc om e bef ore tax Ave rag e tota l hou seh old inc om e bef
4	rs115 8885 7	Alcohol	A	G	A	G	0.0213 402	0.0072 9364	0.018 2288	56429	0.6890 69	Barrett's esophagus	4.90E- 11	397751	0.003 24615	

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																Ave rag e tota l hou sh old inc om e bef ore tax Ave rag e tota l hou sh old inc om e bef
5	rs116 6524 2	Alcohol	G	A	G	A	-0.017 5478	0.0474 094	0.015 2082	56429	0.0018 2478	Barrett's esophagus	6.00E- 11	397751	0.002 68166	
6	rs116 7850 1		C	T	C	T	-0.051 7926	0.0033 8915	0.048 2575	56429	0.9440 1	Barrett's esophagus	1.20E- 09	397751	0.008 51645	

																ore tax
																Ave rag e tota l hou seh old inc om e bef ore tax Ave rag e tota l
7	rs117 1433 7	Alcohol	A	G	A	G	0.0153 807	-0.038 4626	0.015 5466	56429	0.0133 607	Barrett's esophagus	9.40E- 09	397751	0.002 67881	hou seh old inc om e bef ore tax Ave rag e tota l
8	rs118 7775 8	Alcohol	G	T	G	T	-0.020 3602	0.0533 468	0.015 8799	56429	0.0007 81124	Barrett's esophagus	1.20E- 12	397751	0.002 86697	hou seh old inc om e bef

9	rs1191743	BMI	T	C	T	C	0.0227135	-0.0525662	0.0165358	56429	0.00147816	Barrett's esophagus	3.10E-15	397751	0.00288021	ore tax Ave rag e tota l hou seh old inc om e bef ore tax Ave rag e tota l hou seh old inc om e bef
10	rs12309705		G	A	G	A	0.0155639	-0.0363754	0.0151036	56429	0.0160232	Barrett's esophagus	4.70E-09	397751	0.00265785	

1	rs126															ore
1	9259	BMI	T	C	T	C	-0.015	0.0476	0.015	56429	0.0021	Barrett's	1.70E-	397751	0.002	tax
	6						4093	95	5212		1997	esophagus	08		73347	Ave

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1	rs128															
2	8378	BMI	T	C	T	C	-0.018	-0.003	0.014	56429	0.8048	Barrett's	1.40E-	397751	0.002	
	8						8574	70028	9768		56	esophagus	12		66308	

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1	rs130	BMI	A	T	A	T	0.0205	-0.053	0.017	56429	0.0020	Barrett's	7.30E-	397751	0.002	sh
3	0294						047	1401	2051		109	esophagus	12		99285	old
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1	rs145														
5	5350	A	T	A	T	-0.017 2341	0.0171 412	0.015 168	56429	0.2584 4	Barrett's esophagus	9.20E- 11	397751	0.002 65961	Ave rag e tota l hou seh old inc om e bef ore tax Ave rag e tota l hou seh old inc om e bef
1	rs206														
6	8428	T	C	T	C	0.0169 724	0.0051 8713	0.017 6429	56429	0.7687 52	Barrett's esophagus	4.20E- 08	397751	0.003 09515	

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3042 633 7613

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Barrett's
esophagus

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08

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19	rs242 2859		G	T	G	T	0.0163 711	-0.006 30733	0.014 9776	56429	0.6736 68	Barrett's esophagus	6.20E- 10	397751	0.002 64718	Ave rag e tota l hou seh old inc om e bef ore tax Ave rag e tota l hou seh old inc om e bef
20	rs282 0314	BMI	C	A	C	A	-0.016 5601	0.0396 095	0.016 1309	56429	0.0140 689	Barrett's esophagus	2.90E- 09	397751	0.002 78855	

2	rs387						0.0167	-0.028	0.016		0.0813	Barrett's	3.30E-			ore
1	780		C	T	C	T	299	0818	1118	56429	448	esophagus	09	397751	0.002	tax
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2	rs411						-0.017	0.0103	0.015		0.5097	Barrett's	1.10E-			hou
2	5668	BMI	A	G	A	G	9965	173	6503	56429	44	esophagus	10	397751	0.002	seh
																old
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														Ave rag e tota l hou sh old inc om e bef ore tax Ave rag e tota l
2	rs488					0.0206	0.0290	0.020						
3	786	T	C	T	C	878	769	9333	56429	0.1648	Barrett's esophagus	6.70E- 09	397751	0.003 56762
														hou sh old inc om e bef ore tax Ave rag e tota l
2	rs575					-0.016	-0.014	0.016						
4	4738	G	A	G	A	2464	3007	6343	56429	0.3899	Barrett's esophagus	2.70E- 08	397751	0.002 92038
														hou sh old inc om e bef

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																Ave rag e tota l hou seh old inc om e bef ore tax Ave rag e tota l hou seh old inc om e bef
2 7	rs621 8302 8			T	G	T	G	-0.018 9832	0.0346 632	0.016 4578	56429	0.0351 876	Barrett's esophagus	3.20E- 11	397751	0.002 86114
2 8	rs642 9636	Smoki ng		T	G	T	G	0.0192 858	-0.030 9935	0.016 9206	56429	0.0669 962	Barrett's esophagus	5.00E- 11	397751	0.002 93518

														ore tax		
														Ave rag e tota l hou seh old inc om e bef ore tax Ave rag e tota l hou seh old inc om e bef		
2 9	rs669 9397	BMI	G	A	G	A	-0.019 0757	0.0214 816	0.015 4816	56429	0.1652 72	Barrett's esophagus	3.50E- 12	397751	0.002 74153	
3 0	rs686 8457		C	T	C	T	0.0209 797	0.0089 3787	0.014 9911	56429	0.5510 35	Barrett's esophagus	3.10E- 15	397751	0.002 6601	

3	rs730														ore
1	1532	T	G	T	G	-0.027	0.0620	0.028	56429	0.0317	Barrett's	4.10E-	397751	0.004	tax
	2					1853	315	879		154	esophagus	08		95368	Ave
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3	rs770	BMI	C	A	C	A	-0.022	0.0929	0.021	56429	2.11E-	Barrett's	2.50E-	397751	0.003	ore
3	0107						8296	077	843		05	esophagus	09		82992	tax
																Ave
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3	rs789																Ave rag e tota l hou
5	6518	BMI	G	A	G	A	0.0148 13	-0.045 1136	0.015 04	56429	0.0027 0352	Barrett's esophagus	4.10E- 08	397751	0.002 70047	sh old inc om e bef ore tax	
																Ave rag e tota l	
3	rs938	Nervo	T	C	T	C	0.0151 05	-0.021 958	0.015 1386	56429	0.1469 3	Barrett's esophagus	1.50E- 08	397751	0.002 66861	hou sh old inc om e bef	
6	8490	us															

37	rs9556958	BMI	T	C	T	C	-0.0153409	0.0294665	0.0152257	56429	0.0529529	Barrett's esophagus	8.50E-09	397751	0.0026641	ore tax Ave rag e tota l hou seh old inc om e bef ore tax Ave rag e tota l hou seh old inc om e bef
38	rs968050	Alcohol	T	C	T	C	0.0223829	-0.0465845	0.014979	56429	0.00187098	Barrett's esophagus	3.10E-17	397751	0.00265073	

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39	rs9891103	Alcohol	T	C	T	C	-0.0234517	-0.0236481	0.0180562	56429	0.1903	Barrett's esophagus	9.40E-14	397751	0.00314818
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- Supplementary Table 10 Association of the SNPs used as candidate genetic instruments from the GWAS for Mendelian randomization analyses of Townsend deprivation index at recruitment and risk of Barrett's esophagus.

SNP	Relat ed confo undi ng phen otype	effect_all ele.expos ure	other_all ele.expos ure	effect_all ele.outco me	other_all ele.outco me	beta.e xposu re	beta.o utco me	se.o utco me	samplesi ze.outco me	pval.o utco me	outco me	pval.e xposu re	se.ex posu re	samplesi ze.expos ure	exp osu re
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1	rs113 3452 85	BMI	C	T	C	T	0.0163 127	0.0008 26945	0.022 6093	56429	0.9708 24	Barrett's esophag us	3.20E- 08	0.002 95094	462464	Tow nsen d depri vatio n inde x at recru itme nt Tow nsen d depri vatio n inde x at recru itme nt
2	rs118 5582 1	BMI	A	G	A	G	-0.012 5981	-0.034 3493	0.017 2571	56429	0.0465 415	Barrett's esophag us	3.90E- 08	0.002 29259	462464	Tow nsen d depri vatio n inde x at recru itme nt

3	rs1483246		C	T	C	T	-0.0121102	-0.00456071	0.0151265	56429	0.763029	Barrett's esophagus	3.10E-09	0.00204409	462464	Townsend deprivation index at recruitment
4	rs1947083		A	G	A	G	0.0118662	0.0116892	0.01562	56429	0.454248	Barrett's esophagus	1.90E-08	0.0021105	462464	Townsend deprivation index at recruitment
5	rs2403326	BMI	G	A	G	A	0.0115465	0.0163561	0.015033	56429	0.276588	Barrett's esophagus	1.20E-08	0.00202703	462464	Townsend deprivation index at recruitment

6	rs253125		C	T	C	T	0.013174	-0.00381172	0.0174319	56429	0.826912	Barrett's esophagus	1.90E-08	0.0023432	462464	itment Townsend deprivation index at recruitment Townsend deprivation index at recruitment
7	rs3865018	BMI	T	C	T	C	-0.0134594	-0.0387711	0.0171256	56429	0.0235787	Barrett's esophagus	4.20E-09	0.00229086	462464	

8	rs478 5187		A	G	A	G	0.0137 996	0.0287 684	0.018 2185	56429	0.1143 18	Barrett's esophag us	1.50E- 08	0.002 43703	462464	Tow nsen d depri vatio n inde x at recru itme nt Tow nsen d depri vatio n inde x at recru
9	rs693 1604	Alcohol	T	C	T	C	-0.012 1903	-0.042 3081	0.015 579	56429	0.0066 1317	Barrett's esophag us	4.10E- 09	0.002 07309	462464	Tow nsen d depri vatio n inde x at recru itme nt Tow nsen d depri vatio n inde x at recru
10	rs704 067	BMI	A	G	A	G	0.0120 267	0.0589 608	0.015 3505	56429	0.0001 22543	Barrett's esophag us	3.90E- 09	0.002 0424	462464	Tow nsen d depri vatio n inde x at recru

1	rs774	A	G	A	G	0.0118	0.0202	0.015	56429	0.1774	Barrett's esophag us	5.70E- 09	0.002	462464	itme nt Tow nsen d depri vatio n inde x at recru itme nt Tow nsen d depri vatio n inde x at recru itme nt
1	0440					47	887	0443		65		03391			
1	rs782	T	C	T	C	-0.016	0.0127	0.020	56429	0.5386	Barrett's esophag us	2.40E- 09	0.002	462464	
2	5712 8					7416	768	782		85		80676			

1	rs989					0.0138	-0.012	0.016			Barrett's				Tow
3	532	G	A	G	A	559	2055	0622	56429	0.4473	esophag	7.40E-	0.002	462464	nsen
										2	us	11	12756		d
															depri
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- Supplementary Table 11 Association of the SNPs used as candidate genetic instruments from the GWAS for Mendelian randomization analyses of Leisure/social activities: Pub or social club and risk of Barrett's esophagus.

SNP	Related confounder	effect_all ele.exposure	other_all ele.exposure	effect_all ele.outcome	other_all ele.outcome	beta.e xposure	beta.o utcome	se.o utcome	samplesize.outcome	pval.outcome	outcome	pval.e xposure	se.exposure	samplesize.exposure	exposure
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1	rs10 9785 43		G	A	G	A	-0.005 94347	0.0055 3832	0.016 4536	56429	0.7364 16	Barrett's esophag us	4.00E- 09	0.001 01	461369	Leisu re/soc ial activit ies: Pub or social club Leisu re/soc ial activit ies: Pub or social club Leisu re/soc ial activit ies: Pub or social
2	rs11 0660 99		G	C	G	C	0.0065 1032	-0.011 1791	0.019 881	56429	0.5739 13	Barrett's esophag us	4.60E- 08	0.001 19092	461369	Leisu re/soc ial activit ies: Pub or social club Leisu re/soc ial activit ies: Pub or social
3	rs12 4725 55	Smoki ng	G	T	G	T	0.0054 8379	0.0169 719	0.015 1147	56429	0.2614 89	Barrett's esophag us	1.70E- 09	0.000 91026 3	461369	Leisu re/soc ial activit ies: Pub or social

																club
																Leisu
																re/soc
																ial
4	rs139920	BMI	T	C	T	C	0.00614932	0.0186796	0.0151511	56429	0.217618	Barrett's esophagus	1.20E-11	0.00090753	461369	activit
																ies:
																Pub
																or
																social
																club
																Leisu
																re/soc
																ial
5	rs2661863		C	T	C	T	-0.00537368	-0.0150832	0.015858	56429	0.341535	Barrett's esophagus	1.90E-08	0.000956722	461369	activit
																ies:
																Pub
																or
																social
																club
																Leisu
																re/soc
																ial
6	rs35864506	Alcohol	G	T	G	T	0.0082214	0.0275618	0.0224755	56429	0.220084	Barrett's esophagus	2.00E-09	0.00137156	461369	activit
																ies:
																Pub
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																social club
7	rs36030660	BMI	C	T	C	T	-0.00593371	0.0160957	0.0172789	56429	0.351582	Barrett's esophagus	6.80E-09	0.00102383	461369	Leisure/social activities: Pub or social club
8	rs56207132		T	C	T	C	0.0067597	0.00105641	0.0207268	56429	0.959351	Barrett's esophagus	3.60E-08	0.00122705	461369	Leisure/social activities: Pub or social club
9	rs6969458	Smoking	A	G	A	G	0.00721591	0.0131922	0.015857	56429	0.405436	Barrett's esophagus	3.50E-15	0.00091688	461369	Leisure/social activities: Pub or

															social club	
10	rs754204		T	C	T	C	0.00507247	0.0129037	0.0151179	56429	0.393362	Barrett's esophagus	3.00E-08	0.000915201	461369	Leisure/social activities: Pub or social club
11	rs7545161		T	C	T	C	-0.00687787	-0.0358937	0.0192523	56429	0.0622687	Barrett's esophagus	4.20E-09	0.00117018	461369	Leisure/social activities: Pub or social club
12	rs780094	Alcohol	C	T	C	T	0.0051697	0.00571426	0.0153858	56429	0.71034	Barrett's esophagus	2.70E-08	0.000930137	461369	Leisure/social activities: Pub or

social club

1	rs94	Smoking	C	A	C	A	-0.005	-0.048	0.015	56429	0.0011	Barrett's esophagus	5.30E-09	0.00091074	461369	Leisure/social activities: Pub or social club
3	01593						31642	8776	0461		6011					

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● Supplementary Table 12 Association of the SNPs used as candidate genetic instruments from the GWAS for Mendelian randomization analyses of Leisure/social activities: Sports club or gymDataset and risk of Barrett's esophagus.

SNP	Related confounding phen	effect_all ele.exposure	other_all ele.exposure	effect_all ele.outcome	other_all ele.outcome	beta.e xposure	beta.o utcome	se.o utcome	samplesi ze.outcome	pval. outcome	outcome	se.exposure	samplesi ze.exposure	pval.e xposure	expo sure
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1	rs11712056	BMI	C	T	C	T	-0.00597808	0.0578611	0.015117	56429	0.00012942	Barrett's esophagus	0.000960555	461369	4.90E-10	Leisure/social activities: Sports club or gym
2	rs13002862		A	C	A	C	0.0060452	-0.0108781	0.0175674	56429	0.535771	Barrett's esophagus	0.00109537	461369	3.40E-08	Leisure/social activities: Sports club or gym
3	rs6478444		G	A	G	A	0.00550414	-0.00295881	0.015738	56429	0.850874	Barrett's esophagus	0.00100373	461369	4.20E-08	Leisure/social activities: Sports club or

- Supplementary Table 13 UVMR analyse for genetically causal associations of Age completed full time education with BMI.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI)
1	Body mass index	Age completed full time education	MR Egger	32	0.698	1.16 (0.55, 2.44)
2	Body mass index	Age completed full time education	Weighted median	32	0.002	0.76 (0.64, 0.91)
3	Body mass index	Age completed full time education	Inverse variance weighted	32	4.32E-05	0.74 (0.64, 0.85)
4	Body mass index	Age completed full time education	Simple mode	32	0.247	0.80 (0.56, 1.16)
5	Body mass index	Age completed full time education	Weighted mode	32	0.198	0.80 (0.58, 1.11)

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- Supplementary Table 14 UVMR analyse for genetically causal associations of Age completed full time education with MDD.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI)
1	Major Depressive Disorder	Age completed full time education	MR Egger	35	0.668	0.74 (0.19, 2.91)
2	Major Depressive Disorder	Age completed full time education	Weighted median	35	0.009	0.64 (0.46, 0.89)
3	Major Depressive Disorder	Age completed full time education	Inverse variance weighted	35	0.002	0.63 (0.47, 0.84)
4	Major Depressive Disorder	Age completed full time education	Simple mode	35	0.189	0.57 (0.25, 1.30)
5	Major Depressive Disorder	Age completed full time education	Weighted mode	35	0.068	0.50 (0.24, 1.03)

- Supplementary Table 15 UVMR analyse for genetically causal associations of Age completed full time education with Cigarettes smoked per day.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI)
1	Cigarettes smoked per day	Age completed full time education	MR Egger	36	0.391	0.74 (0.37, 1.46)
2	Cigarettes smoked per day	Age completed full time education	Weighted median	36	<0.001	0.67 (0.54, 0.83)

3	Cigarettes smoked per day	Age completed full time education	Inverse variance weighted	36	1.93E-08	0.62 (0.52, 0.73)
4	Cigarettes smoked per day	Age completed full time education	Simple mode	36	0.218	0.73 (0.45, 1.19)
5	Cigarettes smoked per day	Age completed full time education	Weighted mode	36	0.219	0.76 (0.50, 1.17)

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• Supplementary Table 16 UVMR analyse for genetically causal associations of Age completed full time education with Alcoholic drinks per week.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI)
1	Alcoholic drinks per week	Age completed full time education	MR Egger	36	0.960	1.01 (0.75, 1.35)
2	Alcoholic drinks per week	Age completed full time education	Weighted median	36	0.869	0.99 (0.92, 1.08)
3	Alcoholic drinks per week	Age completed full time education	Inverse variance weighted	36	0.492	1.03 (0.95, 1.10)
4	Alcoholic drinks per week	Age completed full time education	Simple mode	36	0.658	0.96 (0.79, 1.16)
5	Alcoholic drinks per week	Age completed full time education	Weighted mode	36	0.575	0.95 (0.79, 1.14)

● Supplementary Table 17 UVMR analyse for genetically causal associations of Average total household income before tax with Sleep duration.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI)
1	Sleep duration	Age completed full time education	MR Egger	39	0.650	1.09 (0.76, 1.54)
2	Sleep duration	Age completed full time education	Weighted median	39	0.577	1.02 (0.96, 1.08)
3	Sleep duration	Age completed full time education	Inverse variance weighted	39	0.548	1.03 (0.94, 1.12)
4	Sleep duration	Age completed full time education	Simple mode	39	0.804	1.02 (0.90, 1.15)
5	Sleep duration	Age completed full time education	Weighted mode	39	0.738	1.02 (0.91, 1.14)

● Supplementary Table 18 UVMR analyse for genetically causal associations of Average total household income before tax with BMI.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI)
1	Body mass index	Average total household income before tax	MR Egger	34	0.275	1.28 (0.83, 1.97)
2	Body mass index	Average total household income before tax	Weighted median	34	<0.001	0.81 (0.72, 0.90)
3	Body mass index	Average total household income before tax	Inverse variance weighted	34	3.66E-09	0.77 (0.71, 0.84)
4	Body mass index	Average total household income before tax	Simple mode	34	0.133	0.84 (0.68, 1.05)
5	Body mass index	Average total household income before tax	Weighted mode	34	0.112	0.83 (0.67, 1.04)

● Supplementary Table 19 UVMR analyse for genetically causal associations of Average total household income before tax with MDD.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI)
1	Major Depressive Disorder	Average total household income before tax	MR Egger	42	0.706	1.18 (0.51, 2.69)
2	Major Depressive Disorder	Average total household income before tax	Weighted median	42	0.001	0.69 (0.55, 0.86)
3	Major Depressive Disorder	Average total household income before tax	Inverse variance weighted	42	4.85E-05	0.68 (0.56, 0.82)
4	Major Depressive Disorder	Average total household income before tax	Simple mode	42	0.162	0.66 (0.37, 1.17)
5	Major Depressive Disorder	Average total household income before tax	Weighted mode	42	0.640	0.88 (0.52, 1.49)

- Supplementary Table 20 UVMR analyse for genetically causal associations of Average total household income before tax with Cigarettes smoked per day.

	Outcome	Exposure	Method	nSNP	Pval	OR (95% CI)
1	Cigarettes smoked per day	Average total household income before tax	MR Egger	43	0.337	1.28 (0.78, 2.09)
2	Cigarettes smoked per day	Average total household income before tax	Weighted median	43	<0.001	0.75 (0.64, 0.88)
3	Cigarettes smoked per day	Average total household income before tax	Inverse variance weighted	43	1.91E-07	0.71 (0.63, 0.81)
4	Cigarettes smoked per day	Average total household income before tax	Simple mode	43	0.177	0.76 (0.51, 1.13)
5	Cigarettes smoked per day	Average total household income before tax	Weighted mode	43	0.345	0.83 (0.58, 1.21)

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- Supplementary Table 21 UVMR analyse for genetically causal associations of Average total household income before tax with Alcoholic drinks per week.

	Outcome	Exposure	Method	nSNP	Pval	OR (95% CI)
1	Alcoholic drinks per week	Average total household income before tax	MR Egger	40	0.845	0.98 (0.80, 1.20)
2	Alcoholic drinks per week	Average total household income before tax	Weighted median	40	0.757	1.01 (0.95, 1.07)
3	Alcoholic drinks per week	Average total household income before tax	Inverse variance weighted	40	0.085	1.04 (0.99, 1.09)
4	Alcoholic drinks per week	Average total household income before tax	Simple mode	40	0.912	1.01 (0.89, 1.14)
5	Alcoholic drinks per week	Average total household income before tax	Weighted mode	40	0.798	0.99 (0.89, 1.10)

- Supplementary Table 22 UVMR analyse for genetically causal associations of Average total household income before tax with Sleep duration.

	Outcome	Exposure	Method	nSNP	Pval	OR (95% CI)
1	Sleep duration	Average total household income before tax	MR Egger	40	0.997	1.00 (0.85, 1.17)
2	Sleep duration	Average total household income before tax	Weighted median	40	0.024	1.05 (1.01, 1.10)
3	Sleep duration	Average total household income before tax	Inverse variance weighted	40	0.015	1.05 (1.01, 1.09)
4	Sleep duration	Average total household income before tax	Simple mode	40	0.214	1.06 (0.97, 1.15)
5	Sleep duration	Average total household income before tax	Weighted mode	40	0.183	1.05 (0.98, 1.14)

- Supplementary Table 23 UVMR analyse for genetically causal associations of BMI with Gastroesophageal reflux disease.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI))
1	Gastroesophageal reflux disease	Body mass index	MR Egger	63	0.003	1.44 (1.14, 1.80)
2	Gastroesophageal reflux disease	Body mass index	Weighted median	63	1.05E-32	1.68 (1.55, 1.83)
3	Gastroesophageal reflux disease	Body mass index	Inverse variance weighted	63	9.17E-41	1.65 (1.53, 1.77)
4	Gastroesophageal reflux disease	Body mass index	Simple mode	63	1.77E-07	1.73 (1.44, 2.08)
5	Gastroesophageal reflux disease	Body mass index	Weighted mode	63	3.17E-11	1.71 (1.50, 1.95)

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● Supplementary Table 24 UVMR analyse for genetically causal associations of MDD with Gastroesophageal reflux disease.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI))
1	Gastroesophageal reflux disease	Major Depressive Disorder	MR Egger	4	0.306	1.41 (0.86, 2.31)
2	Gastroesophageal reflux disease	Major Depressive Disorder	Weighted median	4	6.04E-09	1.46 (1.29, 1.67)
3	Gastroesophageal reflux disease	Major Depressive Disorder	Inverse variance weighted	4	1.68E-14	1.47 (1.33, 1.62)
4	Gastroesophageal reflux disease	Major Depressive Disorder	Simple mode	4	0.025	1.46 (1.22, 1.75)
5	Gastroesophageal reflux disease	Major Depressive Disorder	Weighted mode	4	0.019	1.46 (1.24, 1.71)

● Supplementary Table 25 UVMR analyse for genetically causal associations of Cigarettes smoked per day with Gastroesophageal reflux disease.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI))
1	Gastroesophageal reflux disease	Cigarettes smoked per day	MR Egger	6	0.428	0.93 (0.78, 1.10)
2	Gastroesophageal reflux disease	Cigarettes smoked per day	Weighted median	6	0.136	1.04 (0.99, 1.10)
3	Gastroesophageal reflux disease	Cigarettes smoked per day	Inverse variance weighted	6	0.266	1.09 (0.93, 1.28)
4	Gastroesophageal reflux disease	Cigarettes smoked per day	Simple mode	6	0.121	1.65 (0.97, 2.79)
5	Gastroesophageal reflux disease	Cigarettes smoked per day	Weighted mode	6	0.472	1.02 (0.97, 1.08)

● Supplementary Table 26 UVMR analyse for genetically causal associations of Alcoholic drinks per week with Gastroesophageal reflux disease.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI))
1	Gastroesophageal reflux disease	Alcoholic drinks per week	MR Egger	9	0.670	0.77 (0.24, 2.44)
2	Gastroesophageal reflux disease	Alcoholic drinks per week	Weighted median	9	0.380	0.87 (0.64, 1.19)
3	Gastroesophageal reflux disease	Alcoholic drinks per week	Inverse variance weighted	9	0.349	0.87 (0.65, 1.16)
4	Gastroesophageal reflux disease	Alcoholic drinks per week	Simple mode	9	0.953	1.02 (0.60, 1.71)
5	Gastroesophageal reflux disease	Alcoholic drinks per week	Weighted mode	9	0.795	0.95 (0.65, 1.39)

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● Supplementary Table 27 UVMR analyse for genetically causal associations of Sleep duration with Gastroesophageal reflux disease.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI))
1	Gastroesophageal reflux disease	Sleep duration	MR Egger	44	0.191	0.59 (0.27, 1.29)
2	Gastroesophageal reflux disease	Sleep duration	Weighted median	44	0.086	0.83 (0.67, 1.03)
3	Gastroesophageal reflux disease	Sleep duration	Inverse variance weighted	44	0.001	0.72 (0.59, 0.88)
4	Gastroesophageal reflux disease	Sleep duration	Simple mode	44	0.980	1.01 (0.63, 1.61)
5	Gastroesophageal reflux disease	Sleep duration	Weighted mode	44	0.482	0.88 (0.61, 1.27)

● Supplementary Table 28 UVMR analyse for genetically causal associations of BMI with Barrett's esophagus.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI))
1	Barrett's esophagus	Body mass index	MR Egger	63	0.050	1.81 (1.01, 3.23)
2	Barrett's esophagus	Body mass index	Weighted median	63	3.61E-05	1.71 (1.33, 2.21)
3	Barrett's esophagus	Body mass index	Inverse variance weighted	63	2.51E-10	1.87 (1.54, 2.27)
4	Barrett's esophagus	Body mass index	Simple mode	63	<0.001	3.22 (1.73, 5.99)
5	Barrett's esophagus	Body mass index	Weighted mode	63	0.089	1.55 (0.94, 2.55)

● Supplementary Table 29 UVMR analyse for genetically causal associations of MDD with Barrett's esophagus.

Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI))
Barrett's esophagus	Major Depressive Disorder	Inverse variance weighted	2	0.005	1.95 (1.22, 3.09)

- Supplementary Table 30 UVMR analyse for genetically causal associations of Cigarettes smoked per day with Barrett's esophagus.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI))
1	Barrett's esophagus	Cigarettes smoked per day	MR Egger	14	0.816	1.04 (0.77, 1.39)
2	Barrett's esophagus	Cigarettes smoked per day	Weighted median	14	0.072	1.16 (0.99, 1.36)
3	Barrett's esophagus	Cigarettes smoked per day	Inverse variance weighted	14	0.021	1.24 (1.03, 1.49)
4	Barrett's esophagus	Cigarettes smoked per day	Simple mode	14	0.721	1.08 (0.70, 1.68)
5	Barrett's esophagus	Cigarettes smoked per day	Weighted mode	14	0.149	1.14 (0.96, 1.34)

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- Supplementary Table 31 UVMR analyse for genetically causal associations of Alcoholic drinks per week with Barrett's esophagus.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI))
1	Barrett's esophagus	Alcoholic drinks per week	MR Egger	18	0.417	2.51 (0.29, 21.91)
2	Barrett's esophagus	Alcoholic drinks per week	Weighted median	18	0.219	1.56 (0.77, 3.19)
3	Barrett's esophagus	Alcoholic drinks per week	Inverse variance weighted	18	0.354	1.34 (0.72, 2.51)
4	Barrett's esophagus	Alcoholic drinks per week	Simple mode	18	0.308	2.10 (0.53, 8.43)
5	Barrett's esophagus	Alcoholic drinks per week	Weighted mode	18	0.241	1.78 (0.70, 4.52)

- Supplementary Table 32 UVMR analyse for genetically causal associations of Sleep duration with Barrett's esophagus.

	Outcome	Exposure	Method	nSNP	Pval	OR ((95% CI))
1	Barrett's esophagus	Sleep duration	MR Egger	23	0.070	0.00 (1.40E-05, 1.17)
2	Barrett's esophagus	Sleep duration	Weighted median	23	0.382	0.63 (0.22, 1.78)

3	Barrett's esophagus	Sleep duration	Inverse variance weighted	23	0.380	0.55 (0.14, 2.10)
4	Barrett's esophagus	Sleep duration	Simple mode	23	0.842	0.81 (0.10, 6.27)
5	Barrett's esophagus	Sleep duration	Weighted mode	23	0.870	0.87 (0.17, 4.51)

Supplementary Table 33 The results of the mediation effect test.

Exposure	Mediator	Outcome	Total Effect: β_c (95% CI) *	Direct Effect: β_a (95% CI) †	Direct Effect: β_b (95% CI) †	Mediation Effect (95% CI) §	Proportion mediated
Educational attainment	MDD	GERD	-1.468 (1.694, -1.242)	-0.465(-0.321, -0.143)	0.343(-0.059, 0.212)	-0.159 (-0.278, -0.057)	10.83%
Educational attainment	MDD	BE	-2.203 (-2.906, -1.501)	-0.465(-0.004, 0.043)	0.502(-0.142, 0.869)	-0.233 (-0.482, -0.053)	10.58%
Educational attainment	Smoking	BE	-2.203 (-2.906, -1.501)	0.161(-0.026, 0.029)	0.259(-0.26, 0.778)	-0.077 (-0.161, -0.005)	3.50%
Household income	Sleep	GERD	-0.048 (-1.074, -0.525)	-0.363(-0.066, -0.01)	-0.096(-0.631, 0.439)	0.017 (0.001, 0.041)	9.75%

*Total Effect β_c : the effect of educational attainment on the risk of EC, BE, and GERD. Only the results for which the total effect is statistically significant are shown here.

†Direct effect β_a : the effect of educational attainment on the risk of modifiable risk factors.

‡Direct effect β_b : the effect of modifiable risk factors on the risk of EC, BE, and GERD after adjusting two educational attainment traits.

§Mediation effect: $\beta_a \times \beta_b$; 95% CI of mediation effect: $\beta_a \times \beta_b \pm 1.96 \times \sqrt{\beta_b^2 \times se_a^2 + \beta_a^2 \times se_b^2}$.

Supplementary Table 34 Heterogeneity and pleiotropy evaluations for genetically causal associations of socioeconomic traits with Gastroesophageal reflux disease risk.

Exposure	Outcome	nSNP	Heterogeneity		Pleiotropy		
			Q	P	Intercept	SE	P
Age completed full time education	Gastroesophageal reflux disease	27	7.569	0.134	0.01	0.0541	0.342
Job involves heavy manual or physical work	Gastroesophageal reflux disease	10	20.339	0.016	0.032	0.013	0.041
Average total household income before tax	Gastroesophageal reflux disease	9	15.49	0.05	-0.011	0.022	0.649

Townsend deprivation index at recruitment	Gastroesophageal reflux disease	6	9.074	0.106	0.041	0.019	0.09
Leisure/social activities: Pub or social club	Gastroesophageal reflux disease	3	2.179	0.336	-0.024	0.025	0.512
Leisure/social activities: Sports club or gym	Gastroesophageal reflux disease	4	5.27	0.153	-0.009	0.034	0.825

Supplementary Table 35 Heterogeneity and pleiotropy evaluations for genetically causal associations of socioeconomic traits with Barrett's esophagus.

Exposure	Outcome	nSNP	Heterogeneity		Pleiotropy		
			Q	P	Intercept	SE	P
Age completed full time education	Barrett's esophagus	12	8.714	0.648	-0.011	0.019	0.579
Job involves heavy manual or physical work	Barrett's esophagus	11	13.894	0.178	0.037	0.038	0.353
Average total household income before tax	Barrett's esophagus	17	34.101	0.005	-0.009	0.026	0.736
Townsend deprivation index at recruitment	Barrett's esophagus	8	6.652	0.466	0.086	0.052	0.148
Leisure/social activities: Pub or social club	Barrett's esophagus	6	4.152	0.528	0.012	0.063	0.861
Leisure/social activities: Sports club or gym	Barrett's esophagus	3	6.978	0.031	0.324	0.498	0.633

Supplementary Table 36 Pleiotropy evaluations for genetically causal associations of Age completed full time education with modifiable risk factors.

Exposure	Outcome	nSNP	Pleiotropy		
			Intercept	SE	P
Age completed full time education	Body mass index	32	-0.006	0.005	0.237
Age completed full time education	Major Depressive Disorder	35	-0.002	0.01	0.814
Age completed full time education	Cigarettes smoked per day	36	-0.003	0.005	0.603
Age completed full time education	Alcoholic drinks per week	36	<0.001	0.002	0.904
Age completed full time education	Sleep duration]	39	-0.001	0.002	0.364

Supplementary Table 37 Pleiotropy evaluations for genetically causal associations of Average total household income before tax with modifiable risk factors.

Exposure	Outcome	nSNP	Pleiotropy
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			Intercept	SE	P
Average total household income before tax	Body mass index	34	-0.01	0.004	0.027
Average total household income before tax	Major Depressive Disorder	42	-0.011	0.008	0.191
Average total household income before tax	Cigarettes smoked per day	43	-0.012	0.005	0.021
Average total household income before tax	Alcoholic drinks per week	40	0.001	0.002	0.546
Average total household income before tax	Sleep duration]	40	0.001	0.002	0.687

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- Supplementary Table 38 Pleiotropy evaluations for genetically causal associations of modifiable risk factors with Gastroesophageal reflux disease.

Exposure	Outcome	nSNP	Pleiotropy		
			Intercept	SE	P
Body mass index	Gastroesophageal reflux disease	63	0.004	0.003	0.218
Major Depressive Disorder	Gastroesophageal reflux disease	4	0.002	0.013	0.88
Cigarettes smoked per day	Gastroesophageal reflux disease	6	0.019	0.008	0.067
Alcoholic drinks per week	Gastroesophageal reflux disease	9	0.002	0.009	0.833
Sleep duration]	Gastroesophageal reflux disease	44	-0.002	0.005	0.708

- Supplementary Table 39 Pleiotropy evaluations for genetically causal associations of modifiable risk factors with Barrett's esophagus.

Exposure	Outcome	nSNP	Pleiotropy		
			Intercept	SE	P
Body mass index	Barrett's esophagus	63	0.001	0.008	0.903
Major Depressive Disorder	Barrett's esophagus	2	0.015	0.01	0.154
Cigarettes smoked per day	Barrett's esophagus	14	-0.01	0.017	0.563
Alcoholic drinks per week	Barrett's esophagus	18	-0.01	0.017	0.563
Sleep duration]	Barrett's esophagus	23	-0.009	0.012	0.48