

Supplementary material

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Tables

Table S1. Instrumental variables of OSA on asthma, adult-onset asthma, child-onset asthma and moderate-to-severe asthma (with SNPs reaching $P < 5 \times 10^{-8}$, $F > 10$).

Exposure	Outcome	SNP	Effect_allele	Other_allele	EAF	Beta	SE	P	F
OSA	Asthma	rs10507084	T	C	0.1795	0.0650	0.0097	1.81E-11	45.17
		rs10928510	G	A	0.1605	-0.0565	0.0103	4.35E-08	29.99
		rs11030374	G	T	0.4860	-0.0457	0.0075	9.14E-10	37.50
		rs113955098	A	G	0.0675	-0.0979	0.0153	1.74E-10	40.74
		rs114106239	T	C	0.0371	-0.1174	0.0205	9.80E-09	32.88
		rs11619393	C	T	0.0766	0.0775	0.0138	1.91E-08	31.58
		rs12485486	G	C	0.3406	0.0433	0.0078	3.38E-08	30.48
		rs12511115	C	G	0.2956	0.0473	0.0082	7.19E-09	33.48
		rs2016950	T	C	0.1580	-0.0573	0.0104	3.23E-08	30.57
		rs58570686	T	C	0.2006	-0.0538	0.0094	9.97E-09	32.85
		rs59333125	C	A	0.0807	-0.0764	0.0139	4.00E-08	30.15
		rs76229479	C	A	0.0988	-0.0729	0.0127	9.35E-09	32.97
OSA	Adult-onset asthma	rs10928510	G	A	0.1605	-0.0565	0.0103	4.35E-08	29.99
		rs114106239	T	C	0.0371	-0.1174	0.0205	9.80E-09	32.88
		rs11619393	C	T	0.0766	0.0775	0.0138	1.91E-08	31.58
		rs144468328	A	G	0.0568	-0.0917	0.0167	3.70E-08	30.30
		rs2016950	T	C	0.1580	-0.0573	0.0104	3.23E-08	30.57

		rs59333125	C	A	0.0807	-0.0764	0.0139	4.00E-08	30.15
		rs76229479	C	A	0.0988	-0.0729	0.0127	9.35E-09	32.97
OSA	Child-onset asthma	rs10928510	G	A	0.1605	-0.0565	0.0103	4.35E-08	29.99
		rs114106239	T	C	0.0371	-0.1174	0.0205	9.80E-09	32.88
		rs11619393	C	T	0.0766	0.0775	0.0138	1.91E-08	31.58
		rs144468328	A	G	0.0568	-0.0917	0.0167	3.70E-08	30.30
		rs2016950	T	C	0.1580	-0.0573	0.0104	3.23E-08	30.57
		rs59333125	C	A	0.0807	-0.0764	0.0139	4.00E-08	30.15
		rs76229479	C	A	0.0988	-0.0729	0.0127	9.35E-09	32.97
OSA	Moderate-to- severe asthma	rs10507084	T	C	0.1795	0.0650	0.0097	1.81E-11	45.17
		rs11030374	G	T	0.4860	-0.0457	0.0075	9.14E-10	37.50
		rs113955098	A	G	0.0675	-0.0979	0.0153	1.74E-10	40.74
		rs114106239	T	C	0.0371	-0.1174	0.0205	9.80E-09	32.88
		rs11619393	C	T	0.0766	0.0775	0.0138	1.91E-08	31.58
		rs12485486	G	C	0.3406	0.0433	0.0078	3.38E-08	30.48
		rs12511115	C	G	0.2956	0.0473	0.0082	7.19E-09	33.48
		rs144468328	A	G	0.0568	-0.0917	0.0167	3.70E-08	30.30
		rs2016950	T	C	0.1580	-0.0573	0.0104	3.23E-08	30.57
		rs58570686	T	C	0.2006	-0.0538	0.0094	9.97E-09	32.85
		rs59333125	C	A	0.0807	-0.0764	0.0139	4.00E-08	30.15
		rs76229479	C	A	0.0988	-0.0729	0.0127	9.35E-09	32.97

Abbreviations: OSA, obstructive sleep apnea; SNP, single-nucleotide polymorphisms; EAF, effect allele frequency; SE, standard error; F = F-Statistic.

Table S2. The MR analyses results of weighted median and MR-Egger methods between OSA and asthma.

Exposure	Outcome	MR analyses results			
		Method	nSNP	OR (95%CI)	p
OSA	Asthma	MR-Egger	12	1.41(0.96 to 2.07)	0.113
		Weighted median		1.05(0.92 to 1.19)	0.462
	Adult-onset asthma	MR-Egger	7	1.13(0.28 to 4.62)	0.868
		Weighted median		0.95(0.76 to 1.18)	0.619
	Child-onset asthma	MR-Egger	7	3.34(0.45 to 24.81)	0.292
		Weighted median		1.46(1.02 to 2.10)	0.041
	Moderate-to-severe asthma	MR-Egger	12	4.72(1.10 to 20.25)	0.063
		Weighted median		1.11(0.70 to 1.78)	0.650
Asthma	OSA	MR-Egger	66	1.10(0.98 to 1.24)	0.106
		Weighted median		1.04(0.99 to 1.10)	0.123
Adult-onset asthma		MR-Egger	13	1.22 (0.91 to 1.63)	0.216
		Weighted median		1.04(0.96 to 1.13)	0.381
Child-onset asthma		MR-Egger	41	1.00(0.95 to 1.06)	0.885
		Weighted median		1.01(0.98 to 1.04)	0.363
Moderate-to-severe asthma		MR-Egger	14	1.10(0.91 to 1.33)	0.358
		Weighted median		1.03(1.00 to 1.07)	0.075

Abbreviations: MR, Mendelian randomization; OSA, obstructive sleep apnea; SNP, single-nucleotide

polymorphisms; OR, odds ratio; CI, confidence interval.

Table S3. Heterogeneity and horizontal pleiotropy analyses between OSA and asthma.

Exposure	Outcome	Heterogeneity			Horizontal pleiotropy		
		Method	Cochran's Q	p	MR-egger intercept	p	
OSA	Asthma	MR-Egger	10.921	0.364	-0.016	0.190	
		IVW	13.080	0.288			
	Adult-onset asthma	MR-Egger	10.844	0.055	-0.007	0.900	
		IVW	10.883	0.092			
	Child-onset asthma	MR-Egger	9.413	0.094	-0.058	0.459	
		IVW	10.623	0.101			
	Moderate-to-severe asthma	MR-Egger	14.225	0.163	-0.09934	0.047	
		IVW	21.490	0.029			
	Asthma	OSA	MR-Egger	119.729	<0.001	-0.004	0.291
			IVW	121.852	<0.001		
	Adult-onset asthma	OSA	MR-Egger	22.290	0.022	-0.012	0.331
			IVW	24.390	0.018		
Child-onset asthma	OSA	MR-Egger	49.631	0.118	0.001	0.702	
		IVW	49.820	0.137			
Moderate-to-severe asthma	OSA	MR-Egger	15.761	0.202	-0.010	0.526	
		IVW	16.322	0.232			

Abbreviations: OSA, obstructive sleep apnea; IVW, inverse variance weighted method; MR, Mendelian randomization

Table S4. Instrumental variables of asthma, adult-onset asthma, child-onset asthma and moderate-to-severe asthma on OSA (with SNPs reaching $P < 5 \times 10^{-8}$, $F > 10$).

Exposure	Outcome	SNP	Effect_allele	Other_allele	EAf	Beta	SE	P	F
Asthma	OSA	rs10178845	A	G	0.2946	-0.0617	0.0072	8.22E-18	73.90
		rs10477741	G	T	0.1284	0.0743	0.0098	3.44E-14	57.47
		rs10486391	G	A	0.4108	-0.0389	0.0067	5.13E-09	34.14
		rs10912564	T	C	0.3065	0.0393	0.0071	3.37E-08	30.48
		rs11042902	T	C	0.3075	0.0413	0.0071	6.17E-09	33.78
		rs11071559	T	C	0.1280	-0.0847	0.0098	4.21E-18	75.22
		rs11088309	G	C	0.1425	0.0605	0.0093	8.55E-11	42.13
		rs11178649	T	G	0.4072	-0.0429	0.0066	1.06E-10	41.70
		rs112267124	A	G	0.2342	0.0429	0.0077	2.55E-08	31.02
		rs11567923	CT	C	0.1932	0.0498	0.0084	2.95E-09	35.22
		rs117552144	T	C	0.0668	0.0795	0.0138	8.51E-09	33.15
		rs117710327	A	C	0.0670	-0.1264	0.0134	3.84E-21	89.05
		rs11816044	A	G	0.3256	-0.0473	0.0070	1.20E-11	45.96
		rs12123821	T	C	0.0482	0.1457	0.0153	1.81E-21	90.54
		rs12365699	A	G	0.1667	-0.0535	0.0088	1.16E-09	37.04
		rs12964116	G	A	0.0355	0.1076	0.0177	1.08E-09	37.17
		rs13277355	G	A	0.7260	-0.0406	0.0073	3.09E-08	30.65
		rs1444782	A	G	0.4236	-0.0955	0.0066	2.14E-47	209.12

		rs148639908	AT	A	0.3536	-0.0707	0.0068	3.35E-25	107.56
		rs1608555	T	C	0.3585	0.0377	0.0068	3.14E-08	30.62
		rs1684466	A	G	0.6377	-0.0569	0.0070	4.92E-16	65.83
		rs16903574	G	C	0.0765	0.0866	0.0125	5.31E-12	47.57
		rs17454584	G	A	0.2186	0.0598	0.0079	3.52E-14	57.42
		rs1837253	C	T	0.7397	0.1084	0.0075	1.49E-47	209.84
		rs1870140	G	A	0.8458	-0.0498	0.0091	3.96E-08	30.17
		rs200491113	GTAGA	G	0.0320	-0.1288	0.0187	6.28E-12	47.24
		rs2296618	G	A	0.1353	-0.0619	0.0096	1.30E-10	41.30
		rs2412099	A	G	0.4214	-0.0513	0.0066	9.89E-15	59.92
		rs2477923	C	T	0.4633	-0.0361	0.0066	3.64E-08	30.33
		rs28498223	T	C	0.2808	0.0497	0.0073	1.05E-11	46.23
		rs3024971	G	T	0.1071	-0.1122	0.0106	4.67E-26	111.47
		rs34290285	A	G	0.2554	-0.0989	0.0075	1.38E-39	173.33
		rs35225972	A	G	0.6828	0.0438	0.0070	4.42E-10	38.92
		rs35320232	T	C	0.1188	-0.0558	0.0101	3.67E-08	30.32
		rs35441874	A	T	0.2471	-0.0825	0.0076	2.47E-27	117.30
		rs35570272	T	G	0.3963	0.0509	0.0067	2.91E-14	57.80
		rs35621564	G	A	0.3652	-0.0444	0.0068	7.50E-11	42.38
		rs368981	A	G	0.7089	0.0562	0.0072	7.57E-15	60.44
		rs3785356	T	C	0.2980	0.0563	0.0072	3.85E-15	61.77

		rs3827780	A	G	0.5551	-0.0369	0.0066	2.02E-08	31.48
		rs413214	A	G	0.6162	0.0469	0.0067	2.68E-12	48.91
		rs4722758	G	C	0.1996	0.0634	0.0081	7.21E-15	60.54
		rs4736639	C	G	0.2862	-0.0397	0.0072	4.05E-08	30.13
		rs4739738	A	G	0.6416	-0.0679	0.0068	1.86E-23	99.60
		rs4795401	G	A	0.5106	-0.1026	0.0065	1.16E-55	247.03
		rs479844	G	A	0.5547	0.0403	0.0066	7.70E-10	37.83
		rs4842921	A	G	0.3875	-0.0407	0.0067	1.17E-09	37.02
		rs56375023	A	G	0.2373	0.1035	0.0077	3.18E-41	180.84
		rs5743618	A	C	0.2257	-0.0664	0.0079	2.86E-17	71.43
		rs61816766	C	T	0.0332	0.1353	0.0187	4.51E-13	52.41
		rs72823641	A	T	0.1367	-0.1478	0.0096	2.56E-53	236.27
		rs7423358	C	T	0.7581	0.0430	0.0076	1.83E-08	31.67
		rs7626218	T	A	0.3952	-0.0414	0.0067	5.96E-10	38.33
		rs76493820	G	C	0.0580	0.0864	0.0141	8.21E-10	37.71
		rs7734635	G	A	0.1543	0.0768	0.0091	2.48E-17	71.72
		rs7770794	A	G	0.2858	0.0416	0.0072	8.81E-09	33.09
		rs78556180	T	G	0.1468	0.0507	0.0092	3.99E-08	30.15
		rs7936312	T	G	0.4768	0.0838	0.0065	9.54E-38	164.91
		rs7961712	A	G	0.8499	0.0565	0.0092	7.35E-10	37.93
		rs802731	G	C	0.2709	0.0479	0.0073	6.54E-11	42.65

		rs848	C	A	0.8179	-0.0963	0.0085	5.80E-30	129.31
		rs912131	G	A	0.7039	0.0581	0.0071	4.04E-16	66.22
		rs919826	C	T	0.4900	-0.0358	0.0065	4.65E-08	29.86
		rs9272226	T	C	0.6282	-0.0898	0.0095	2.37E-21	90.01
		rs981625	G	C	0.0650	0.0725	0.0132	4.16E-08	30.07
		rs992969	G	A	0.7476	-0.1199	0.0076	1.25E-56	251.46
Adult-onset asthma	OSA	rs1023518	G	T	NA	-0.0746	0.0105	1.20E-12	50.85
		rs118013485	G	A	NA	0.1015	0.0187	4.50E-08	29.51
		rs1474011	G	A	NA	-0.0597	0.0092	8.00E-11	42.02
		rs1775554	A	C	NA	0.1040	0.0093	2.90E-29	124.88
		rs17843580	A	G	NA	-0.1317	0.0179	8.80E-14	54.22
		rs1837253	T	C	NA	-0.0779	0.0105	8.80E-14	55.59
		rs3024971	T	G	NA	0.0972	0.0148	5.10E-11	43.02
		rs34290285	G	A	NA	0.0699	0.0105	3.40E-11	44.17
		rs56389811	C	T	NA	0.0647	0.0108	1.60E-09	36.00
		rs6454805	A	G	NA	0.0610	0.0096	1.50E-10	40.39
		rs6985449	G	A	NA	0.0584	0.0096	1.20E-09	36.67
		rs72743461	C	A	NA	-0.0787	0.0109	3.30E-13	52.63
rs7936312	G	T	NA	-0.0609	0.0092	6.30E-11	43.64		
Child-onset asthma	OSA	rs10066308	G	A	NA	-0.0901	0.0153	6.20E-09	34.71
		rs10791824	A	G	NA	-0.1042	0.0143	1.50E-13	53.35

		rs11236791	G	A	NA	-0.1877	0.0142	4.30E-39	175.20
		rs117137535	G	A	NA	-0.2877	0.0484	1.10E-09	35.38
		rs11727369	G	A	NA	-0.1070	0.0147	2.10E-13	53.09
		rs118013485	G	A	NA	0.1827	0.0287	1.40E-10	40.64
		rs12123821	C	T	NA	-0.4742	0.0330	5.30E-47	206.19
		rs12365699	G	A	NA	0.1387	0.0190	6.00E-13	53.47
		rs12413578	C	T	NA	0.1989	0.0229	2.20E-18	75.18
		rs12935657	G	A	NA	0.1450	0.0164	2.30E-18	78.23
		rs12964116	A	G	NA	-0.3261	0.0382	1.10E-17	72.85
		rs13277355	A	G	NA	0.0988	0.0159	2.50E-10	38.86
		rs17481562	C	T	NA	0.0838	0.0147	8.10E-09	32.73
		rs17728272	C	T	NA	-0.0975	0.0167	4.90E-09	34.03
		rs1837253	T	C	NA	-0.1804	0.0160	1.50E-29	126.77
		rs2066844	C	T	NA	-0.1818	0.0330	1.20E-08	30.32
		rs2252775	T	G	NA	-0.1746	0.0181	3.30E-22	93.43
		rs2255088	T	C	NA	-0.1042	0.0150	2.20E-12	47.92
		rs2738783	T	G	NA	-0.0957	0.0173	4.10E-08	30.54
		rs274949	G	A	NA	0.0791	0.0141	1.20E-08	31.31
		rs28688825	A	G	NA	0.2271	0.0258	2.00E-19	77.72
		rs3122929	C	T	NA	-0.1339	0.0144	1.00E-20	86.08
		rs34986765	T	C	NA	0.1662	0.0209	1.50E-15	63.11

		rs35449774	C	T	NA	-0.1912	0.0248	1.30E-15	59.58
		rs3785356	C	T	NA	-0.1120	0.0155	2.90E-13	52.25
		rs4574025	C	T	NA	-0.0876	0.0142	5.10E-10	38.06
		rs4739738	G	A	NA	0.1144	0.0147	7.90E-15	60.22
		rs4833103	A	C	NA	0.1195	0.0144	1.50E-16	69.18
		rs56062135	C	T	NA	-0.1728	0.0166	2.90E-25	107.79
		rs6454805	A	G	NA	0.0915	0.0147	1.50E-10	38.64
		rs6489785	T	C	NA	0.0965	0.0145	1.10E-11	44.61
		rs6664108	T	C	NA	-0.0890	0.0153	5.10E-09	33.94
		rs6868082	C	T	NA	-0.1412	0.0248	6.10E-09	32.37
		rs7209400	C	T	NA	-0.0872	0.0142	1.10E-09	37.67
		rs78147778	T	C	NA	0.1522	0.0164	9.40E-21	86.49
		rs7918084	C	T	NA	-0.0813	0.0142	3.60E-09	32.78
		rs8069176	G	A	NA	0.3124	0.0141	1.60E-109	488.43
		rs892225	A	G	NA	-0.0862	0.0147	2.40E-09	34.58
		rs928412	A	G	NA	0.2295	0.0162	2.90E-47	200.85
		rs9828592	T	C	NA	-0.0963	0.0142	5.00E-12	46.03
		rs9893132	A	G	NA	-0.0853	0.0147	2.50E-09	33.42
Moderate-to-severe asthma	OSA	rs112502960	A	G	0.359	0.134	0.023	6.05E-09	33.94
		rs11603634	G	A	0.504	0.124	0.0223	2.30E-08	30.92
		rs12479210	T	C	0.387	0.183	0.0225	4.77E-16	66.15

		rs13274782	C	A	0.623	-0.132	0.0228	7.29E-09	33.52
		rs1438673	T	C	0.492	-0.169	0.0221	2.11E-14	58.47
		rs144829310	T	G	0.164	0.207	0.0297	3.68E-12	48.57
		rs34290285	A	G	0.257	-0.193	0.0251	1.41E-14	59.12
		rs3749833	C	T	0.261	0.161	0.0249	1.14E-10	41.80
		rs61840192	A	G	0.427	-0.167	0.0224	8.42E-14	55.58
		rs703816	C	T	0.434	0.151	0.0222	1.18E-11	46.26
		rs7203459	C	T	0.246	-0.206	0.0255	7.83E-16	65.26
		rs72743461	A	C	0.236	0.167	0.0258	1.03E-10	41.90
		rs7523907	T	C	0.541	0.135	0.0224	1.64E-09	36.32
		rs7936312	T	G	0.474	0.134	0.022	1.09E-09	37.10

Abbreviations: OSA, obstructive sleep apnea; SNP, single-nucleotide polymorphisms; EAF, effect allele frequency; SE, standard error; F = F-Statistic

Figures

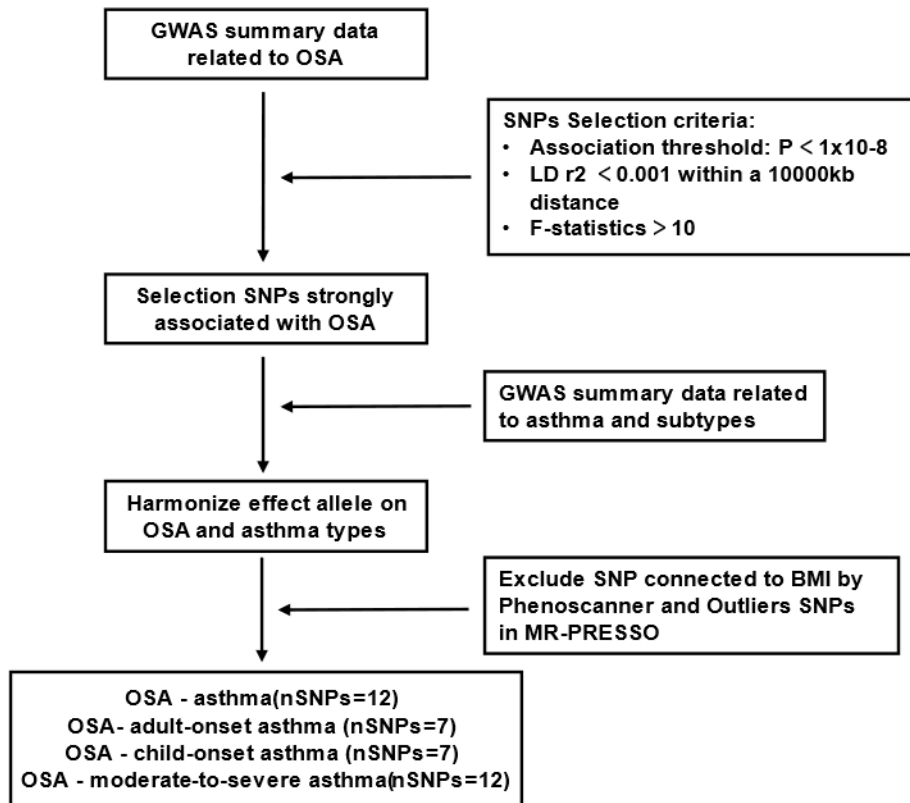


Figure S1. Detailed genetic instrument screening flowchart for the causal associations of OSA on asthma, adult-onset asthma, child-onset asthma and moderate-to-severe asthma.

Abbreviations: GWAS, genome-wide association study; OSA, obstructive sleep apnea; SNP, single-nucleotide polymorphisms; LD, linkage disequilibrium; BMI, body mass index; MR-PRESSO, Mendelian randomization - pleiotropy residual sum and outlier

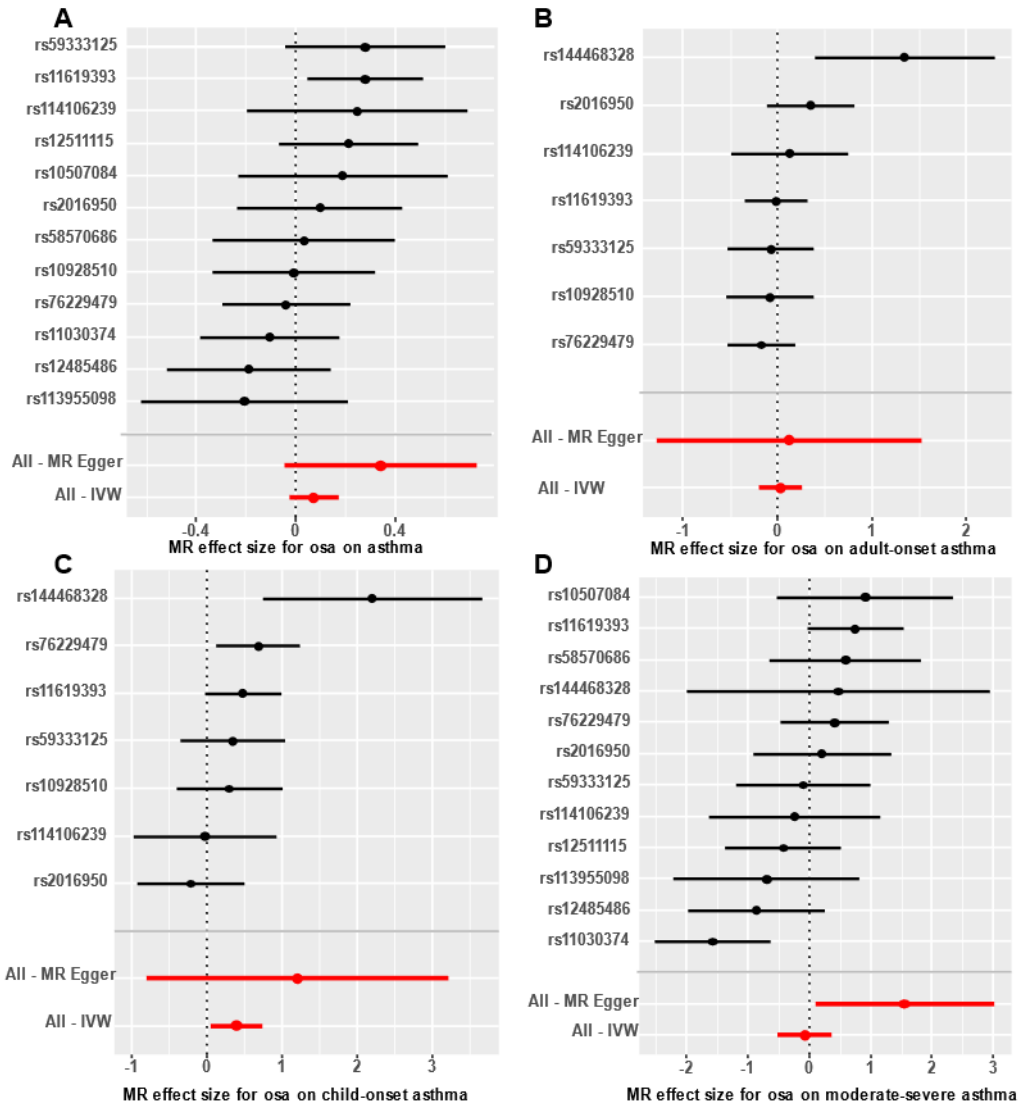


Figure S2. The forest plots of the MR effect size. A) the forest plots of the MR effect size for OSA on asthma; B) the forest plots of the MR effect size for OSA on adult-onset asthma; C) the forest plots of the MR effect size for OSA on child-onset asthma; D) the forest plots of the MR effect size for OSA on moderate-to-severe asthma.

Abbreviations: OSA, obstructive sleep apnea; MR, Mendelian randomization; IVW, inverse variance weighted method

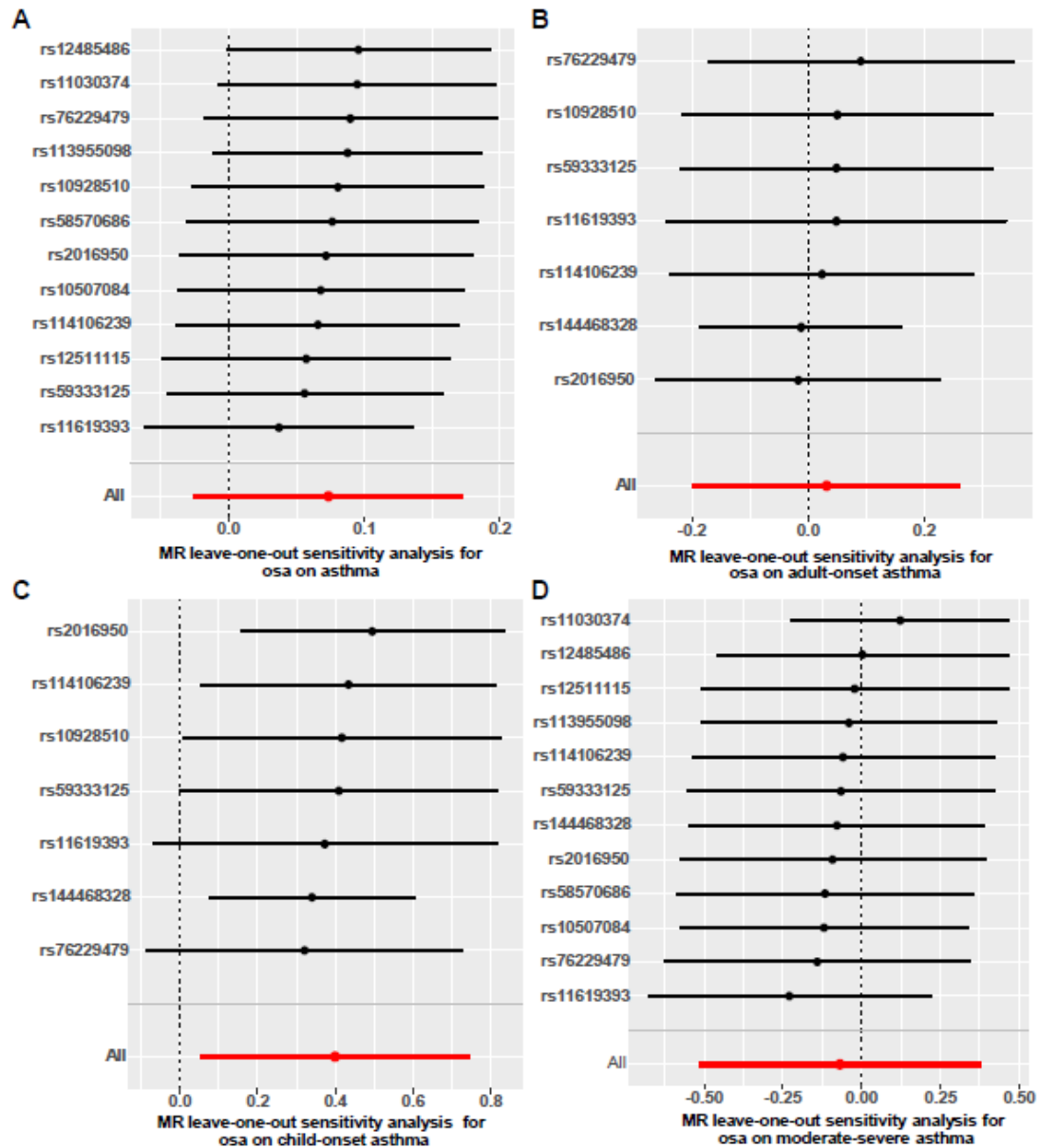


Figure S3. The MR leave-one-out sensitivity analysis. A) the MR leave-one-out sensitivity analysis for OSA on asthma; B) the MR leave-one-out sensitivity analysis for OSA on adult-onset asthma; C) the MR leave-one-out sensitivity analysis for OSA on child-onset asthma; D) the MR leave-one-out sensitivity analysis for OSA on moderate-to-severe asthma.

Abbreviations: OSA, obstructive sleep apnea; MR, Mendelian randomization.

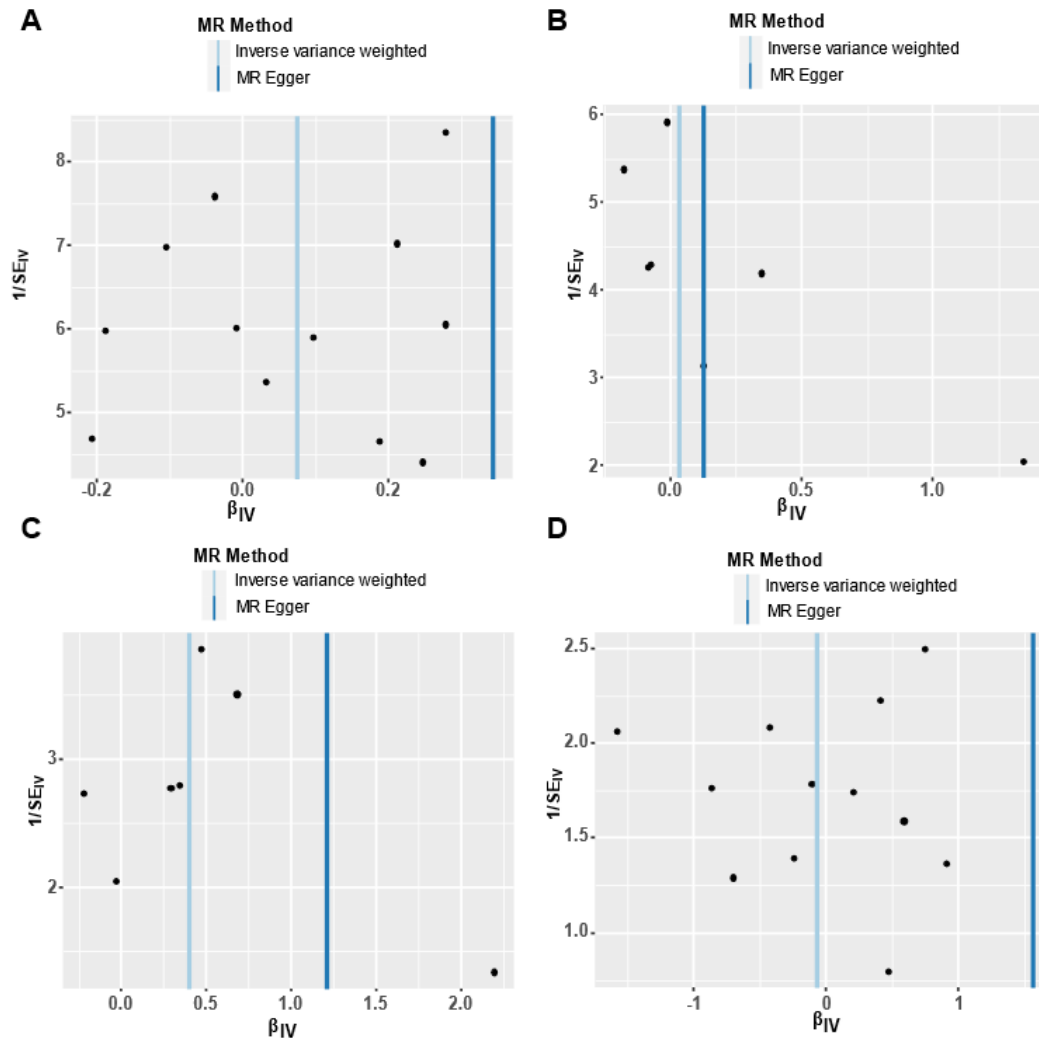


Figure S4. The funnel plots. A) the funnel plot of the causal effect of OSA on asthma; B) the funnel plot of the causal effect of OSA on adult-onset asthma; C) the funnel plot of the causal effect of OSA on child-onset asthma; D) the funnel plot of the causal effect of OSA on moderate-to-severe asthma.

Abbreviations: OSA, obstructive sleep apnea; MR, Mendelian randomization; IV, instrumental variables.

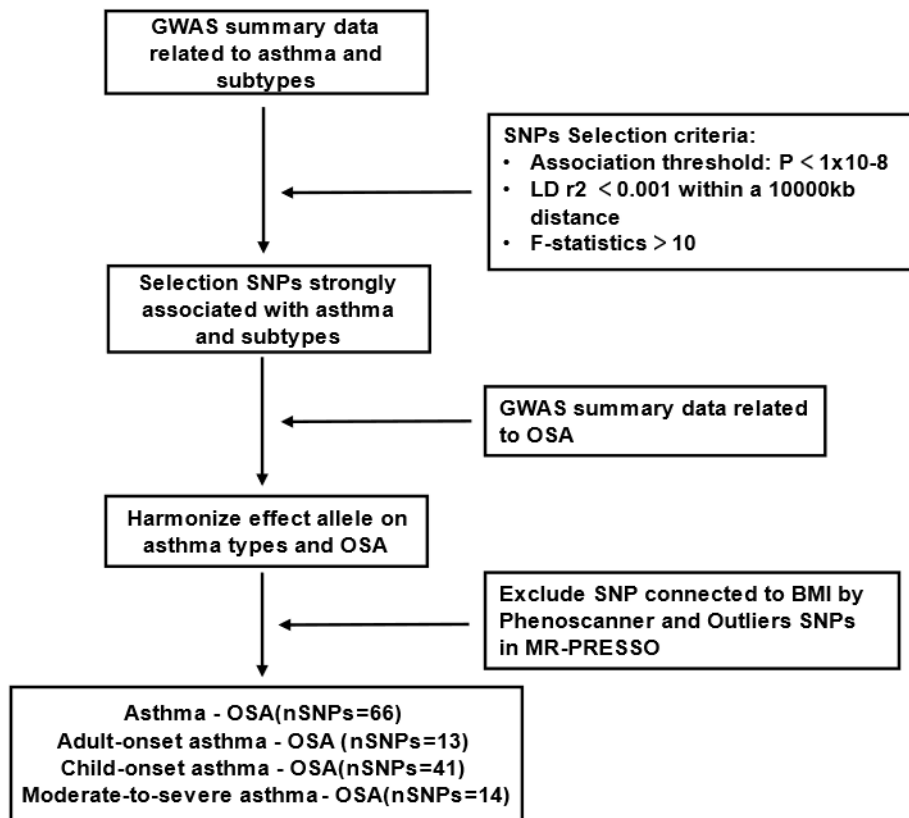


Figure S5. Detailed genetic instrument screening flowchart for the causal associations of asthma, adult-onset asthma, child-onset asthma and moderate-to-severe asthma on OSA.

Abbreviations: GWAS, genome-wide association study; OSA, obstructive sleep apnea; SNP, single-nucleotide polymorphisms; LD, linkage disequilibrium; BMI, body mass index; MR-PRESSO, Mendelian randomization - pleiotropy residual sum and outlier.

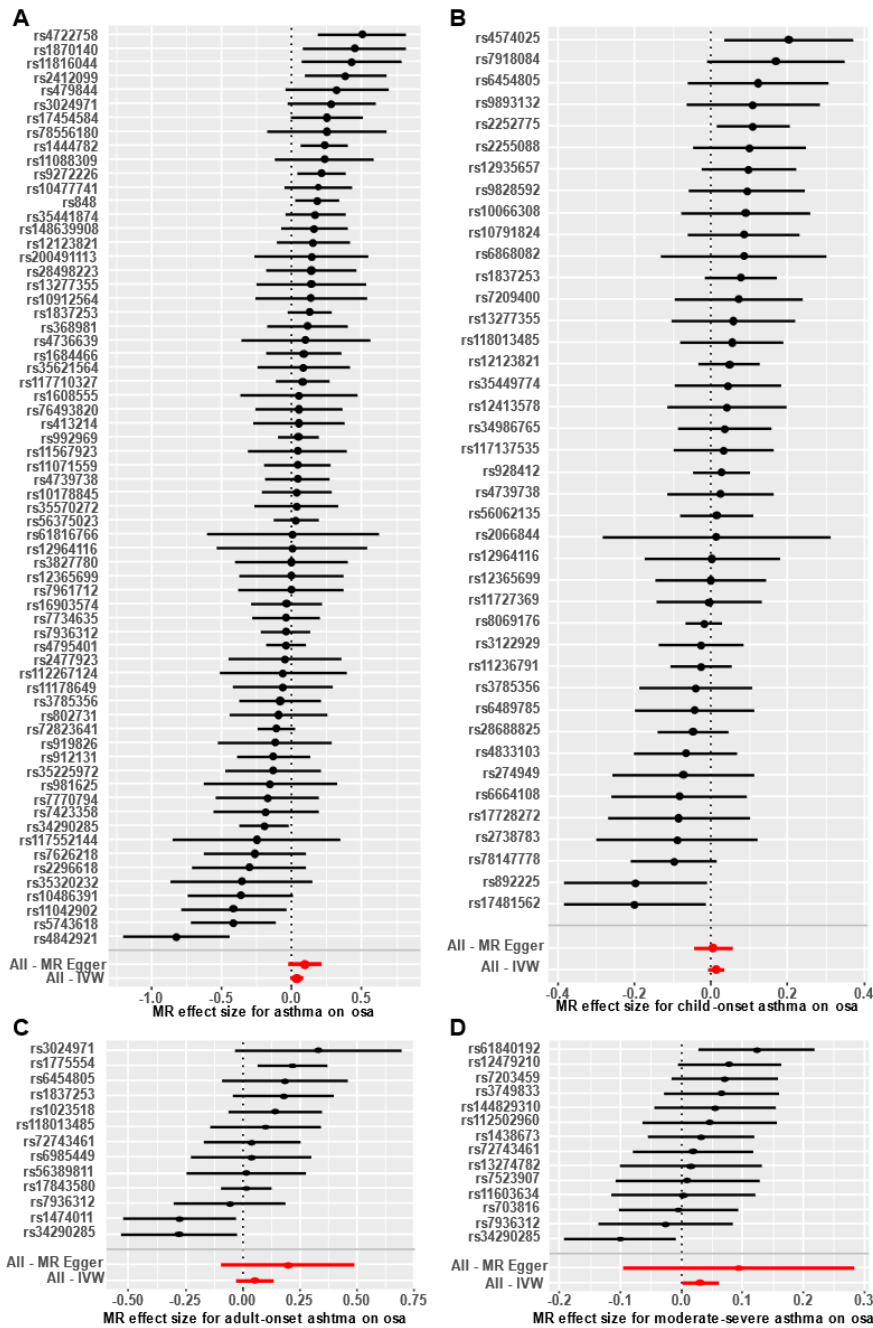


Figure S6. The forest plots of the MR effect size. A) the forest plots of the MR effect size for asthma on OSA; B) the forest plots of the MR effect size for child-onset asthma on OSA; C) the forest plots of the MR effect size for adult-onset asthma on OSA; D) the forest plots of the MR effect size for moderate-to-severe asthma on OSA.

Abbreviations: OSA, obstructive sleep apnea; MR, Mendelian randomization; IVW, inverse variance weighted method.

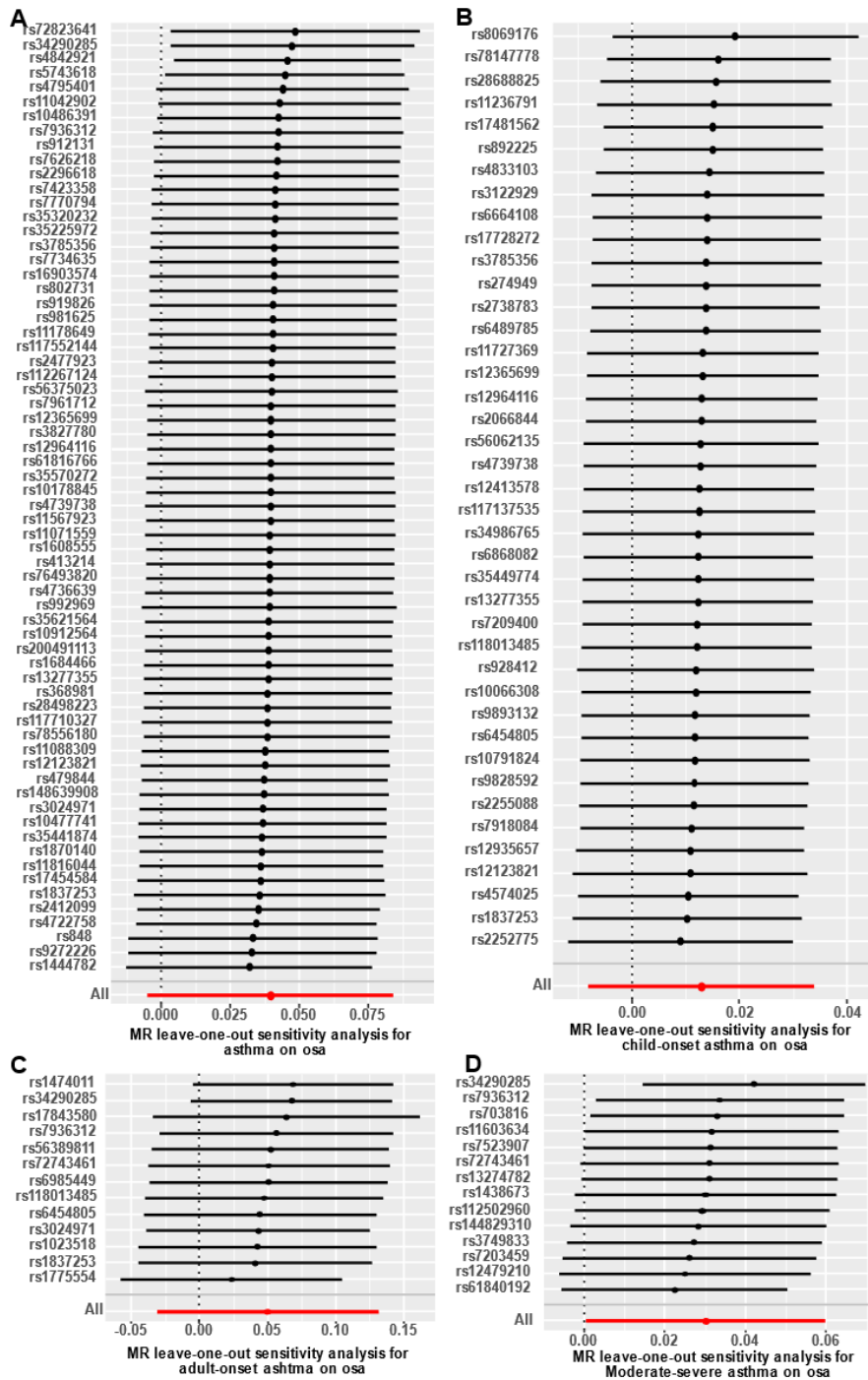


Figure S7. The MR leave-one-out sensitivity analysis. A) the MR leave-one-out sensitivity analysis for asthma on OSA; B) the MR leave-one-out sensitivity analysis for child-onset asthma on OSA; C) the MR leave-one-out sensitivity analysis for adult-onset asthma on OSA; D) the MR leave-one-out sensitivity analysis for moderate-to-severe asthma on OSA.

Abbreviations: OSA, obstructive sleep apnea; MR, Mendelian randomization.

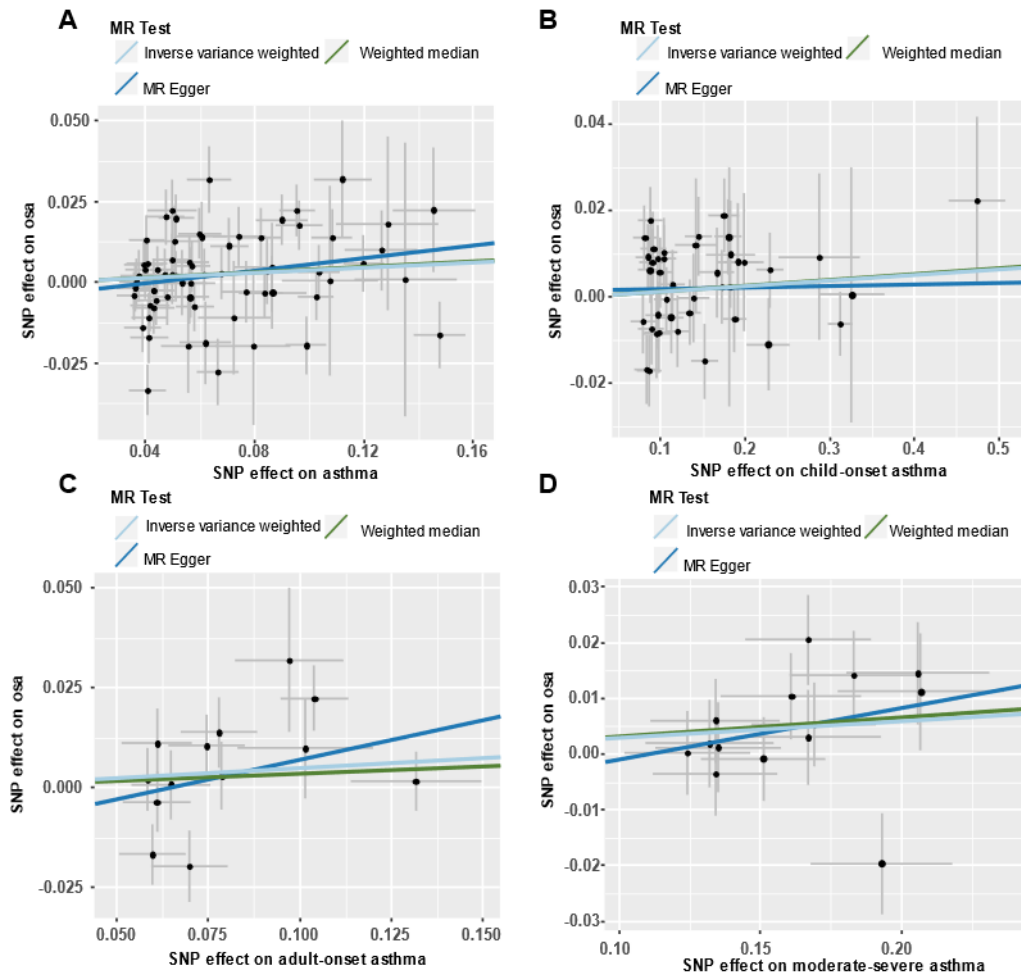


Figure S8. The scatter plots. A) the scatter plots of SNP effect for asthma on OSA; B) the scatter plots of SNP effect for child-onset asthma on OSA; C) the scatter plots of SNP effect for adult-onset asthma on OSA; D) the scatter plots of SNP effect for moderate-to-severe asthma on OSA.

Abbreviations: OSA, obstructive sleep apnea; MR, Mendelian randomization; SNP, single-nucleotide polymorphisms.

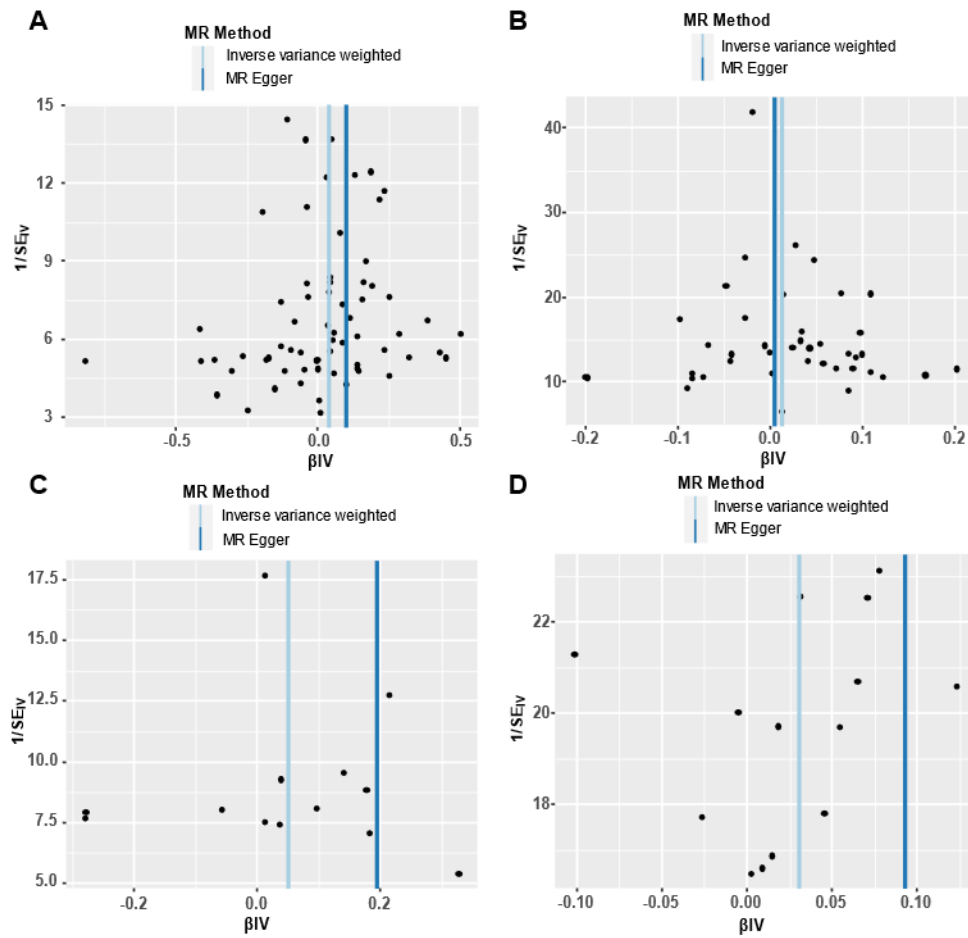


Figure S9. The funnel plots. A) the funnel plot of the causal effect of asthma on OSA; B) the funnel plot of the causal effect of child-onset asthma on OSA; C) the funnel plot of the causal effect of adult-onset asthma on OSA; D) the funnel plot of the causal effect of moderate-to-severe asthma on OSA.

Abbreviations: OSA, obstructive sleep apnea; MR, Mendelian randomization; IV, instrumental variables.