

Tables S1 Single nucleotide polymorphisms of daytime napping extracted from UK Biobank with statistically significant threshold

rsID	A1	A2	Beta	SE	EAF	P
rs60579048	G	T	-0.0120801	0.00192353	0.168441	3.39E-10
rs12140153	T	G	-0.0267869	0.00249768	0.0967607	7.87E-27
rs1843815	T	A	0.0080935	0.00144695	0.546169	2.23E-08
rs35039375	G	A	0.0144459	0.00250586	0.0922067	8.18E-09
rs2250377	G	A	-0.0153252	0.00152035	0.661574	6.82E-24
rs17369061	C	T	-0.0117463	0.00215139	0.128356	4.77E-08
rs4971718	T	C	0.00900348	0.00143818	0.501816	3.85E-10
rs2390669	C	A	-0.0125148	0.00216027	0.128988	6.91E-09
rs11125776	G	T	-0.0146443	0.00204936	0.145705	8.96E-13
rs12615434	T	C	0.0127252	0.00227285	0.113286	2.16E-08
rs908442	T	A	-0.0110406	0.00146731	0.408422	5.31E-14
rs13033444	G	A	0.01082	0.00160282	0.283377	1.47E-11
rs253662	C	T	0.0103879	0.0018335	0.810216	1.47E-08
rs12506659	T	C	-0.00892164	0.00144688	0.485703	7.01E-10
rs6854055	T	G	0.0122474	0.00166173	0.746635	1.71E-13
rs1968557	T	C	-0.00800284	0.0014414	0.494653	2.82E-08
rs2431108	C	T	0.013171	0.00153176	0.329053	8.10E-18
rs10875622	A	G	0.00979286	0.00145848	0.575866	1.89E-11
rs742787	C	T	-0.0102286	0.00148994	0.370452	6.65E-12
rs12193281	C	T	-0.00979444	0.00153092	0.331103	1.58E-10
rs2653349	G	A	-0.0166983	0.00174928	0.783617	1.36E-21
rs614987	C	A	0.0120846	0.00148376	0.61521	3.82E-16
rs11761181	C	T	0.0108149	0.00171574	0.228682	2.92E-10
rs12535424	A	G	-0.014507	0.00255031	0.087217	1.28E-08
rs285793	A	G	-0.00867653	0.00144812	0.538181	2.08E-09
rs2555571	G	T	-0.00789435	0.00144244	0.519615	4.43E-08
rs11138082	C	T	0.0141577	0.00178528	0.204972	2.19E-15
rs12682981	G	A	-0.0101414	0.00165954	0.254182	9.91E-10
rs17502738	C	T	-0.0102645	0.00181595	0.195985	1.58E-08
rs11258652	A	C	-0.0100428	0.00169325	0.237578	3.01E-09
rs10840017	G	A	-0.0100288	0.00175656	0.229946	1.14E-08
rs1836124	T	C	-0.0086352	0.0015721	0.298829	3.96E-08
rs174541	C	T	0.0101442	0.00149822	0.360594	1.28E-11
rs35011311	T	G	-0.00895823	0.00163987	0.266754	4.69E-08
rs1983336	A	G	0.0178914	0.00147118	0.405028	5.08E-34
rs2769916	A	G	0.0085258	0.00155807	0.689264	4.45E-08
rs12147887	T	C	0.0108139	0.00185585	0.184888	5.65E-09
rs2370926	C	T	-0.00835538	0.00149826	0.366603	2.45E-08
rs17158413	A	G	0.0104177	0.00169363	0.238506	7.71E-10
rs114488427	T	C	0.0122401	0.00220696	0.120362	2.92E-08
rs8050478	A	G	-0.0079374	0.00143999	0.500264	3.55E-08
rs112520848	C	G	0.00811376	0.00148611	0.386015	4.77E-08
rs3935190	A	G	0.00873751	0.0014508	0.534346	1.72E-09
rs12451365	C	T	0.0110612	0.00178363	0.204513	5.60E-10
rs2033103	T	C	0.00867968	0.00144735	0.452251	2.01E-09
rs962247	A	G	-0.00911236	0.00145269	0.476597	3.55E-10
rs17723754	T	C	-0.0137289	0.00145817	0.427454	4.75E-21
rs3810484	G	A	-0.0080557	0.00144848	0.443578	2.68E-08
rs2836918	C	T	0.00908323	0.00159998	0.285281	1.37E-08

A1: Effect Allele; A2: Alternative Allele; Beta: beta coefficient; SE: standard error of beta coefficient; EAF: Effect Allele Frequency; P: P value of the meta-analysis.

Table S2 Single nucleotide polymorphisms of sleep duration extracted from UK Biobank with statistically significant threshold

rsID	A1	A2	Beta	SE	EAF	P
rs7556815	A	G	2.443	0.164	0.219	1.30E-49
rs75539574	C	A	2.175	0.244	0.086	6.90E-19
rs12607679	T	C	1.208	0.156	0.738	8.30E-15
rs915416	C	G	1.156	0.15	0.29	9.90E-15
rs9940646	C	G	1.017	0.137	0.578	1.20E-13
rs13109404	T	G	1.872	0.264	0.928	1.40E-12
rs8050478	G	A	0.96	0.136	0.5	1.70E-12
rs56372231	T	C	1.017	0.144	0.334	2.20E-12
rs13088093	G	T	0.976	0.144	0.336	7.00E-12
rs2079070	C	G	1.053	0.154	0.265	7.50E-12
rs34556183	A	G	1.015	0.151	0.72	2.30E-11
rs3095508	C	A	0.921	0.138	0.594	3.10E-11
rs34731055	T	C	1.168	0.177	0.181	3.70E-11
rs73219758	G	A	0.984	0.15	0.708	5.60E-11
rs10973207	T	G	1.226	0.187	0.158	6.00E-11
rs2139261	G	C	1.122	0.174	0.749	8.50E-11
rs4592416	G	A	0.881	0.136	0.464	9.30E-11
rs365663	A	G	0.878	0.137	0.546	1.00E-10
rs1517572	C	A	0.879	0.138	0.581	1.50E-10
rs7915425	T	C	1.144	0.179	0.175	2.00E-10
rs330088	C	T	0.868	0.137	0.547	2.70E-10
rs8038326	A	G	0.955	0.152	0.727	2.80E-10
rs460692	C	T	1.263	0.2	0.137	3.60E-10
rs9382445	T	C	0.872	0.14	0.623	4.80E-10
rs4767550	G	A	0.858	0.139	0.414	6.30E-10
rs11885663	T	C	0.973	0.157	0.248	8.60E-10
rs1991556	G	A	0.994	0.163	0.774	1.00E-09
rs1057703	G	T	1.164	0.192	0.147	1.10E-09
rs4128364	C	T	0.876	0.143	0.339	1.40E-09
rs61796569	T	C	0.927	0.154	0.27	1.50E-09
rs10483350	G	A	1.042	0.172	0.195	1.50E-09
rs7115226	A	C	1.594	0.261	0.074	1.70E-09
rs269054	A	T	0.819	0.138	0.422	2.10E-09
rs112230981	A	G	1.892	0.314	0.95	2.20E-09
rs11602180	C	T	1.095	0.184	0.837	2.30E-09
rs2192528	A	G	0.802	0.136	0.48	2.70E-09
rs12246842	A	G	0.804	0.136	0.46	3.90E-09
rs205024	T	C	0.83	0.14	0.384	3.90E-09
rs12567114	A	G	0.89	0.152	0.276	4.30E-09
rs7616632	T	G	0.792	0.136	0.522	4.30E-09
rs6575005	T	C	0.934	0.159	0.758	4.40E-09
rs1776776	T	C	1.198	0.205	0.874	4.90E-09
rs11621908	C	T	1.446	0.25	0.917	5.60E-09
rs10421649	A	T	0.798	0.138	0.557	6.90E-09
rs2072727	T	C	0.795	0.137	0.436	7.90E-09
rs113113059	T	C	0.968	0.164	0.78	8.40E-09
rs374153	C	T	1.057	0.186	0.158	9.10E-09
rs151014368	A	G	0.966	0.169	0.206	9.10E-09
rs62120041	T	C	1.567	0.274	0.934	9.60E-09
rs7503199	C	T	0.885	0.154	0.734	1.00E-08
rs1939455	G	T	1.226	0.214	0.879	1.20E-08
rs7951019	G	T	2.213	0.391	0.032	1.20E-08
rs17732997	C	G	0.776	0.137	0.569	1.20E-08
rs61985058	T	C	1.116	0.194	0.143	1.30E-08
rs17427571	A	G	0.83	0.146	0.684	1.30E-08
rs7806045	T	C	0.887	0.158	0.755	1.40E-08
rs35531607	C	T	0.77	0.136	0.474	1.50E-08
rs7644809	T	C	0.784	0.138	0.422	1.60E-08
rs9345234	C	A	0.781	0.138	0.578	1.80E-08
rs12791153	T	A	1.413	0.253	0.081	1.90E-08
rs1263056	A	G	0.768	0.137	0.519	2.00E-08
rs55658675	C	T	0.788	0.142	0.645	2.00E-08
rs11567976	T	C	0.768	0.137	0.571	2.10E-08
rs180769	T	C	0.763	0.138	0.425	2.30E-08
rs1553132	G	A	0.87	0.155	0.258	2.50E-08
rs9903973	C	T	0.766	0.136	0.467	2.60E-08
rs11614986	A	G	0.983	0.177	0.821	2.70E-08
rs2231265	G	A	0.897	0.162	0.772	2.70E-08
rs174560	C	T	0.815	0.146	0.314	2.80E-08
rs10173260	C	T	0.77	0.139	0.606	2.90E-08
rs72804080	G	A	1.068	0.192	0.15	2.90E-08
rs12611523	A	G	0.758	0.137	0.545	3.10E-08
rs11643715	G	C	0.834	0.15	0.291	3.20E-08
rs4538155	T	C	0.779	0.142	0.647	3.60E-08
rs34354917	C	A	0.825	0.15	0.71	3.90E-08
rs80193650	G	A	1.01	0.184	0.162	4.10E-08
rs10761674	C	T	0.74	0.136	0.477	4.20E-08
rs11190970	G	A	0.923	0.169	0.799	4.60E-08

A1: Effect Allele; A2: Alternative Allele; Beta: beta coefficient; SE: standard error of beta coefficient; EAF: Effect Allele Frequency; P: P value of the meta-analysis.

Table S3 Single nucleotide polymorphisms of depression extracted from UK Biobank with statistically significant threshold

rsID	A1	A2	Beta	SE	EAF	P
rs301799	T	C	-0.03	0	0.57	1.36E-12
rs1002656	T	C	-0.03	0	0.7	3.74E-12
rs1466887	T	C	-0.02	0	0.55	4.12E-08
rs11579246	A	G	0.04	0.01	0.91	5.71E-10
rs1890946	T	C	-0.02	0	0.47	2.68E-11
rs10789214	T	C	0.02	0	0.57	4.44E-08
rs2568958	A	G	0.04	0	0.62	8.47E-25
rs113188507	A	G	0.02	0	0.28	1.87E-08
rs10913112	T	C	-0.03	0	0.38	3.40E-13
rs72710803	A	C	-0.04	0.01	0.91	5.29E-11
rs169235	A	G	-0.02	0	0.75	2.98E-08
rs17641524	T	C	-0.03	0	0.21	1.52E-13
rs12052908	A	T	-0.02	0	0.53	4.44E-10
rs1568452	T	C	0.02	0	0.39	8.12E-12
rs7585722	T	C	-0.03	0	0.85	2.68E-08
rs1226412	T	C	0.03	0	0.79	3.46E-09
rs62188629	A	G	0.02	0	0.31	7.13E-10
rs4346585	T	C	-0.02	0	0.7	7.13E-10
rs13084037	A	G	-0.02	0	0.77	7.08E-09
rs7624336	T	G	0.02	0	0.21	3.96E-08
rs141954845	A	G	0.02	0	0.39	8.15E-10
rs6783233	T	C	0.02	0	0.28	2.90E-08
rs1095626	T	C	-0.03	0	0.58	7.13E-14
rs7685686	A	G	0.02	0	0.58	2.57E-08
rs34937911	T	C	0.03	0.01	0.88	4.13E-08
rs45510091	A	G	0.04	0.01	0.95	1.83E-08
rs35553410	T	C	-0.02	0	0.75	1.42E-09
rs7659414	A	C	-0.02	0	0.58	1.20E-08
rs60157091	T	C	0.02	0	0.52	1.42E-08
rs3099439	T	C	-0.03	0	0.53	5.05E-15
rs10061069	C	G	-0.03	0	0.22	8.15E-11
rs30266	A	G	0.03	0	0.33	1.45E-16
rs11135349	A	C	-0.03	0	0.47	6.04E-17
rs200949	A	G	0.05	0.01	0.87	2.53E-19
rs9363467	T	C	0.02	0	0.6	6.44E-11
rs7758630	A	T	-0.02	0	0.41	5.56E-10
rs1933802	C	G	-0.02	0	0.45	2.57E-10
rs2876520	C	G	-0.02	0	0.53	2.29E-10
rs725616	T	C	0.02	0	0.36	1.87E-08
rs2029865	A	T	-0.02	0	0.45	1.20E-08
rs3823624	T	C	0.03	0	0.81	1.99E-09
rs2043539	A	G	0.03	0	0.42	9.89E-15
rs2247523	C	G	-0.02	0	0.53	4.38E-09
rs16887442	T	C	0.02	0	0.43	8.62E-09
rs58104186	A	G	0.02	0	0.47	1.82E-11
rs7807677	T	C	0.02	0	0.55	1.82E-11
rs7837935	T	G	-0.03	0	0.15	3.34E-09
rs67436663	C	G	-0.03	0	0.24	9.37E-10
rs1354115	A	C	0.02	0	0.62	7.08E-09
rs1982277	T	C	0.03	0	0.76	1.45E-11
rs263645	A	T	0.02	0	0.54	3.70E-10
rs3793577	A	G	-0.02	0	0.47	8.41E-11
rs59283172	A	G	-0.03	0.01	0.11	1.02E-08
rs7030813	T	C	0.03	0	0.37	3.07E-12
rs10817969	T	G	0.03	0	0.72	3.11E-11
rs913930	A	G	-0.02	0	0.64	2.42E-08
rs2670139	T	C	-0.03	0	0.76	1.21E-10
rs997934	T	C	0.02	0	0.38	4.81E-08
rs1021363	A	G	0.03	0	0.35	4.41E-16
rs1448938	A	G	0.02	0	0.42	1.30E-09
rs2509805	T	C	0.02	0	0.32	9.17E-09
rs198457	T	C	-0.03	0	0.19	2.99E-10
rs58621819	A	T	-0.02	0	0.79	1.57E-08
rs7117514	A	G	-0.02	0	0.54	7.29E-09
rs7932640	T	C	0.03	0	0.44	1.62E-15
rs61902811	A	G	-0.03	0	0.37	1.40E-12
rs2187490	T	G	-0.03	0.01	0.91	3.82E-08
rs57344483	A	G	-0.04	0.01	0.93	1.82E-08
rs78337797	T	G	0.03	0.01	0.88	3.37E-08
rs56314503	T	G	-0.03	0	0.75	2.95E-10
rs10774600	T	C	-0.03	0	0.17	3.39E-08
rs3213572	A	G	0.02	0	0.47	7.61E-10
rs1409379	T	C	0.02	0	0.76	1.67E-09
rs1343605	A	C	0.03	0	0.38	6.23E-18
rs9592461	A	G	0.02	0	0.49	9.10E-10
rs9545360	A	C	-0.03	0	0.18	5.02E-09
rs4772087	T	C	0.02	0	0.37	3.91E-10
rs61990288	A	G	-0.03	0	0.51	1.68E-13
rs1956373	T	G	-0.02	0	0.74	2.06E-08
rs1152578	T	C	-0.02	0	0.44	6.36E-10
rs1045430	T	G	-0.03	0	0.48	7.31E-13
rs10149470	A	G	-0.03	0	0.49	3.72E-14
rs8037355	T	C	-0.02	0	0.56	3.94E-11
rs34488670	T	C	-0.03	0	0.79	6.03E-09
rs7193263	A	G	-0.02	0	0.67	4.33E-10
rs7198928	T	C	0.02	0	0.62	4.45E-11
rs7200826	T	C	0.03	0	0.26	3.74E-12
rs56887639	A	G	-0.03	0	0.73	1.51E-12
rs12923444	A	C	-0.02	0	0.56	1.30E-09
rs75581564	A	G	0.03	0.01	0.12	3.17E-08
rs12967855	A	G	0.03	0	0.33	1.18E-12
rs7227069	A	G	0.02	0	0.43	1.50E-11
rs12967143	C	G	-0.03	0	0.7	3.70E-16
rs7241572	A	G	0.03	0	0.2	2.70E-10
rs33431	T	C	0.02	0	0.61	4.81E-08
rs143186028	T	G	0.03	0	0.18	2.29E-09
rs12624433	A	G	0.02	0	0.26	7.44E-09
rs5995992	T	C	-0.03	0	0.72	1.30E-11

A1: Effect Allele; A2: Alternative Allele; Beta: beta coefficient; SE: standard error of beta coefficient; EAF: Effect Allele Frequency; P: P value of the meta-analysis.

Appendix 1 The definition of each outcomes

1)Heart failure

Heart failure refers to a group of syndromes in which the ventricular filling and/or ejection function is impaired due to various cardiac structural or functional diseases, and the volume of cardiac excretion fails to meet the needs of the body's tissue metabolism, with the clinical manifestations of stagnation of the pulmonary circulation and/or the body circulation, and insufficient perfusion of blood to organs and tissues (1).

2)Hypertension

Hypertension was defined as a diagnosis of hypertension when systolic blood pressure was measured at greater than or equal to 140 mmHg and/or diastolic blood pressure at greater than or equal to 90 mmHg on more than 3 occasions on non-consecutive days (2).

3)Stroke

Stroke is defined as an acute cerebral blood circulation disorder in patients with cerebrovascular disease caused by various triggering factors, which is clinically manifested as a one-off or permanent brain dysfunction in terms of symptoms and signs (3).

4)Atrial fibrillation

Based on the duration of atrial fibrillation (AF) episodes, AF has been described in four main clinical patterns, including paroxysmal AF, persistent AF, "longstanding" persistent AF, and permanent AF (4).

5)Arrhythmia

Arrhythmia is due to the abnormal excitation of sinoatrial node or excitation generated outside sinoatrial node, that is, the origin of heart activity and/or conduction disorder lead to abnormal frequency and/or rhythm of heart beating (5).

6)Conduction disorders

Conduction disorders refers to sinus rhythm, atrial rhythm and ventricular rhythm, which stop or cannot be transmitted in the process of conduction, including sinus atrial block, atrioventricular block, indoor block and bundle branch block (6).

7)Coronary atherosclerosis

Coronary atherosclerosis is characterized by lipid deposition and changes in the vessel wall, and is often accompanied by inflammation and vascular matrix remodeling in discrete coronary plaques (7).

8)Myocardial infarction

Myocardial infarction is an occlusion of a coronary artery that interrupts blood flow, causing partial necrosis of part of the myocardium due to severe and persistent ischemia (8).

9)Non-ischemic cardiomyopathy

Non-ischemic cardiomyopathy are diseases of the heart muscle other than ischemic cardiomyopathy (9). Non-ischemic cardiomyopathy include dilated cardiomyopathy, alcoholic cardiomyopathy, perinatal cardiomyopathy, tachycardia, restrictive cardiomyopathy, hypertrophic cardiomyopathy, and others.

10)Non-rheumatic valve diseases

Non-rheumatic heart disease is a structural alteration of the heart valves due to non-immune factors such as chronic hypoxia and hypertension (10). These factors may cause myocardial damage, inflammatory responses, and fibrotic processes that in turn affect valve function.

11)Pulmonary embolism

Pulmonary embolism refers to a group of clinical syndromes or diseases caused by endogenous or exogenous embolus blocking the pulmonary artery or its branches causing dysfunction of the pulmonary circulation and the right heart, including air embolism, fat embolism, and pulmonary thromboembolism (11).

12)Aortic aneurysm

Pathological dilatation of the aorta beyond 50% of the normal vessel diameter is called an aortic aneurysm (12). Aortic aneurysms are classified as true aortic aneurysms and pseudo aortic aneurysms. True aneurysms are widening of the vessel involving the 3-layered structure of the vessel wall. Pseudoaneurysms are localized ruptures of the artery that are sealed by a blood clot or adjacent tissue.

13)Dissection of aorta

Dissection of aorta occurs when there is a tear in the inner lining of the arterial wall and blood enters the arterial wall through the tear to form a hematoma and further strips the inner and middle lining of the aorta (12).

14)Peripheral vascular disease

Peripheral vascular disease is a chronic ischemic disease of the limbs, and clinically, vascular diseases other than cardiovascular and cerebrovascular diseases are collectively referred to as peripheral vascular diseases. Peripheral vascular disease includes diseases of arteries, veins and lymphatic system (13).

15)Coronary artery disease

Coronary artery disease is a type of ischemic heart disease. Coronary arteries are the arteries responsible for supplying blood to the heart. When coronary arteries become narrowed or occluded, it can lead to myocardial ischemia, hypoxia or necrosis, triggering discomfort such as chest pain and tightness in the chest (14).

References

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Table S4 Estimates of genetical liability to daytime napping, sleep duration, and depression on cardiovascular disease in univariable Mendelian randomization

Disease	Exposure	Source	Number of used SNPs	IVW			Weighted median		MR-Egger		MR-PRESSO [†]		
				Cochran's Q P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	Outliers	OR (95% CI)	P value
Heart failure	Daytime napping	FinnGen	46	0.004	1.366 (1.013, 1.842)	0.041*	1.370 (0.954, 1.968)	0.088	2.193 (0.689, 6.983)	0.191	NA	NA	NA
Heart failure	Sleep duration	FinnGen	66	0.141	0.995 (0.993, 0.998)	2.69E-04*	0.996 (0.993, 1.000)	0.053	1.001 (0.992, 1.010)	0.804	1	0.995 (0.993, 0.998)	9.84E-05
Heart failure	Depression	FinnGen	10	0.179	0.980 (0.733, 1.310)	0.891	0.920 (0.651, 1.299)	0.636	0.807 (0.149, 4.373)	0.810	NA	NA	NA
Hypertension	Daytime napping	FinnGen	48	0.286	1.620 (0.961, 2.730)	0.070	2.185 (1.072, 4.453)	0.031	0.588 (0.062, 5.606)	0.647	NA	NA	NA
Hypertension	Sleep duration	FinnGen	70	0.008	1.000 (0.994, 1.006)	1.000	0.999 (0.991, 1.006)	0.701	0.996 (0.974, 1.019)	0.754	NA	NA	NA
Hypertension	Depression	FinnGen	10	0.845	1.236 (0.788, 1.939)	0.356	1.247 (0.701, 2.217)	0.453	1.261 (0.108, 14.649)	0.858	NA	NA	NA
Stroke	Daytime napping	FinnGen	48	5.14E-04	1.245 (0.867, 1.790)	0.235	1.101 (0.720, 1.683)	0.657	5.802 (1.479, 22.762)	0.015	1	1.195 (0.85, 1.68)	0.311
Stroke	Sleep duration	FinnGen	70	0.055	0.998 (0.995, 1.001)	0.142	0.998 (0.994, 1.002)	0.399	1.000 (0.990, 1.011)	0.942	NA	NA	NA
Stroke	Depression	FinnGen	10	0.812	0.989 (0.751, 1.303)	0.940	1.001 (0.697, 1.436)	0.997	0.403 (0.092, 1.773)	0.264	NA	NA	NA
Atrial fibrillation	Daytime napping	FinnGen	48	5.04E-05	1.069 (0.813, 1.406)	0.632	1.084 (0.793, 1.481)	0.613	1.011 (0.343, 2.980)	0.984	NA	NA	NA
Atrial fibrillation	Sleep duration	FinnGen	69	<0.001	0.998 (0.995, 1.001)	0.250	0.998 (0.995, 1.001)	0.254	1.000 (0.989, 1.011)	0.976	4	0.999 (0.997, 1.001)	0.389
Atrial fibrillation	Depression	FinnGen	10	0.789	1.298 (1.065, 1.583)	0.010*	1.363 (1.035, 1.796)	0.028	1.626 (0.579, 4.566)	0.383	NA	NA	NA
Arrhythmia	Daytime napping	FinnGen	48	0.785	0.996 (0.989, 1.003)	0.284	0.998 (0.987, 1.008)	0.671	0.986 (0.959, 1.014)	0.344	NA	NA	NA
Arrhythmia	Sleep duration	FinnGen	70	0.323	1.000 (1.000, 1.000)	0.268	1.000 (1.000, 1.000)	0.406	1.000 (1.000, 1.000)	0.064	NA	NA	NA
Arrhythmia	Depression	FinnGen	10	0.972	1.003 (0.996, 1.010)	0.393	1.003 (0.994, 1.012)	0.497	1.008 (0.973, 1.045)	0.677	NA	NA	NA
Conduction disorders	Daytime napping	FinnGen	48	0.549	1.268 (0.656, 2.449)	0.481	1.16 (0.451, 2.984)	0.758	2.393 (0.177, 32.374)	0.515	NA	NA	NA
Conduction disorders	Sleep duration	FinnGen	70	0.128	0.995 (0.988, 1.002)	0.171	1.000 (0.990, 1.010)	0.976	0.997 (0.971, 1.023)	0.795	NA	NA	NA
Conduction disorders	Depression	FinnGen	10	0.576	0.573 (0.293, 1.118)	0.102	0.706 (0.273, 1.824)	0.472	0.058 (0.001, 2.733)	0.186	NA	NA	NA
Coronary atherosclerosis	Daytime napping	FinnGen	48	0.066	1.918 (1.257, 2.927)	0.003*	2.320 (1.357, 3.966)	0.002	1.282 (0.239, 6.880)	0.774	NA	NA	NA
Coronary atherosclerosis	Sleep duration	FinnGen	70	0.009	0.996 (0.992, 1.001)	0.089	0.996 (0.990, 1.001)	0.138	0.990 (0.975, 1.006)	0.228	NA	NA	NA
Coronary atherosclerosis	Depression	FinnGen	10	0.727	0.924 (0.637, 1.342)	0.679	1.082 (0.668, 1.754)	0.748	2.252 (0.261, 19.411)	0.481	NA	NA	NA
Myocardial infarction	Daytime napping	FinnGen	47	1.38E-04	1.505 (1.025, 2.211)	0.037*	1.530 (1.002, 2.334)	0.049	4.245 (0.927, 19.448)	0.069	2	1.468 (1.047, 2.057)	0.031
Myocardial infarction	Sleep duration	FinnGen	70	0.055	0.998 (0.995, 1.001)	0.110	0.996 (0.992, 1.000)	0.051	0.994 (0.983, 1.005)	0.297	NA	NA	NA
Myocardial infarction	Depression	FinnGen	10	0.130	0.910 (0.663, 1.251)	0.563	0.907 (0.61, 1.35)	0.632	0.264 (0.048, 1.453)	0.165	NA	NA	NA
Non-ischemic cardiomyopathy	Daytime napping	FinnGen	48	0.583	1.449 (0.944, 2.224)	0.090	2.102 (1.120, 3.945)	0.021	3.761 (0.691, 20.479)	0.132	NA	NA	NA
Non-ischemic cardiomyopathy	Sleep duration	FinnGen	70	0.981	1.001 (0.996, 1.005)	0.804	1.001 (0.994, 1.007)	0.860	1.003 (0.988, 1.019)	0.690	NA	NA	NA
Non-ischemic cardiomyopathy	Depression	FinnGen	10	0.005	1.729 (0.851, 3.512)	0.130	1.063 (0.556, 2.031)	0.854	0.103 (0.002, 4.755)	0.279	1	1.407 (0.742, 2.668)	0.327
Non-rheumatic valve diseases	Daytime napping	FinnGen	48	0.021	0.651 (0.370, 1.145)	0.136	0.784 (0.382, 1.606)	0.506	1.622 (0.173, 15.182)	0.674	1	0.715 (0.425, 1.203)	0.213
Non-rheumatic valve diseases	Sleep duration	FinnGen	70	0.585	0.996 (0.991, 1.000)	0.057	0.997 (0.990, 1.004)	0.409	0.999 (0.982, 1.016)	0.892	NA	NA	NA
Non-rheumatic valve diseases	Depression	FinnGen	10	0.071	1.205 (0.642, 2.260)	0.561	0.956 (0.469, 1.946)	0.901	2.501 (0.055, 112.867)	0.650	NA	NA	NA
Pulmonary embolism	Daytime napping	FinnGen	48	0.835	1.460 (0.752, 2.835)	0.263	2.006 (0.801, 5.024)	0.137	5.246 (0.382, 72.099)	0.221	NA	NA	NA
Pulmonary embolism	Sleep duration	FinnGen	70	0.505	0.997 (0.991, 1.004)	0.410	0.995 (0.985, 1.004)	0.249	1.008 (0.984, 1.032)	0.524	NA	NA	NA
Pulmonary embolism	Depression	FinnGen	10	0.231	0.868 (0.402, 1.874)	0.719	0.760 (0.288, 2.009)	0.580	2.677 (0.026, 270.955)	0.687	NA	NA	NA
Aortic aneurysm	Daytime napping	FinnGen	47	0.481	1.051 (0.533, 2.073)	0.887	0.703 (0.253, 1.951)	0.498	12.799 (0.879, 186.29)	0.069	NA	NA	NA
Aortic aneurysm	Sleep duration	FinnGen	70	0.133	1.001 (0.994, 1.008)	0.777	1.001 (0.991, 1.012)	0.814	1.019 (0.992, 1.046)	0.170	NA	NA	NA
Aortic aneurysm	Depression	FinnGen	10	0.372	1.087 (0.552, 2.139)	0.810	1.627 (0.644, 4.113)	0.303	8.919 (0.218, 365.548)	0.281	NA	NA	NA
Dissection of aorta	Daytime napping	FinnGen	48	0.963	0.749 (0.109, 5.155)	0.769	0.696 (0.045, 10.791)	0.796	0.255 (0.000, 520.914)	0.727	NA	NA	NA
Dissection of aorta	Sleep duration	FinnGen	70	0.130	1.012 (0.992, 1.033)	0.235	1.019 (0.989, 1.050)	0.216	0.999 (0.926, 1.078)	0.975	NA	NA	NA
Dissection of aorta	Depression	FinnGen	10	0.777	1.976 (0.278, 14.066)	0.496	1.560 (0.111, 21.947)	0.742	777.876 (0.009, 64146795.850)	0.282	NA	NA	NA
Peripheral vascular disease	Daytime napping	FinnGen	48	0.939	2.076 (0.565, 7.622)	0.271	1.612 (0.267, 9.729)	0.603	4.556 (0.027, 774.086)	0.566	NA	NA	NA
Peripheral vascular disease	Sleep duration	FinnGen	70	0.150	0.984 (0.971, 0.997)	0.019*	0.973 (0.954, 0.992)	0.005	0.961 (0.913, 1.011)	0.126	NA	NA	NA
Peripheral vascular disease	Depression	FinnGen	10	0.779	1.212 (0.323, 4.547)	0.776	1.721 (0.299, 9.908)	0.543	0.007 (0.000, 14.525)	0.239	NA	NA	NA
Coronary artery disease	Daytime napping	FinnGen	46	3.88E-05	1.519 (1.130, 2.043)	0.006*	1.567 (1.095, 2.241)	0.014	3.024 (0.964, 9.484)	0.064	1	1.467 (1.118, 1.924)	0.008
Coronary artery disease	Sleep duration	FinnGen	66	0.002	0.997 (0.994, 0.999)	0.006*	0.997 (0.994, 1.000)	0.047	1.006 (0.998, 1.015)	0.153	1	0.996 (0.994, 0.998)	0.001
Coronary artery disease	Depression	FinnGen	10	0.290	1.072 (0.864, 1.330)	0.530	1.103 (0.846, 1.440)	0.468	1.268 (0.397, 4.049)	0.699	NA	NA	NA

*, Estimates with P<0.05 in IVW analysis are reported. †, Outlier-corrected estimate. NA, not available (if no outliers were detected). OR, odd ratio; CI, confidence interval; IVW, inverse variance weighted; MR, Mendelian randomization; MR-PRESSO, Mendelian Randomization Pleiotropy RESidual Sum and Outlier.

Table S5 Estimates of daytime napping on cardiovascular diseases mediated by multiple mediators

Cardiovascular diseases	Adjustment for body mass index		Adjustment for smoking initiation		Adjustment for type 2 diabetes mellitus		Adjustment for body mass index, smoking initiation and type 2 diabetes	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Heart failure	1.379 (1.026, 1.853)	0.033*	1.353 (1.038, 1.763)	0.025*	1.291 (0.924, 1.804)	0.134	1.184 (0.879, 1.595)	0.266
Hypertension	1.370 (0.785, 2.390)	0.268	1.103 (0.700, 1.737)	0.673	1.303 (0.768, 2.209)	0.326	1.234 (0.713, 2.138)	0.453
Stroke	1.329 (0.959, 1.840)	0.087	1.165 (0.866, 1.566)	0.313	1.115 (0.821, 1.516)	0.486	1.162 (0.846, 1.596)	0.355
Atrial fibrillation	0.900 (0.690, 1.173)	0.435	1.141 (0.907, 1.436)	0.260	0.988 (0.741, 1.318)	0.936	0.827 (0.633, 1.080)	0.163
Arrhythmia	0.998 (0.990, 1.006)	0.567	1.001 (0.994, 1.009)	0.692	0.999 (0.991, 1.006)	0.683	0.997 (0.989, 1.005)	0.429
Conduction disorders	1.500 (0.758, 2.970)	0.244	1.388 (0.780, 2.470)	0.265	1.199 (0.633, 2.273)	0.577	1.203 (0.604, 2.398)	0.599
Coronary atherosclerosis	1.187 (0.789, 1.787)	0.410	1.277 (0.895, 1.822)	0.177	1.248 (0.784, 1.986)	0.349	1.211 (0.793, 1.852)	0.376
Myocardial infarction	1.329 (0.919, 1.923)	0.131	1.157 (0.833, 1.606)	0.384	1.393 (0.903, 2.148)	0.134	1.240 (0.849, 1.813)	0.266
Non-ischemic cardiomyopathy	1.296 (0.827, 2.030)	0.258	1.125 (0.716, 1.767)	0.610	1.173 (0.695, 1.977)	0.550	1.142 (0.711, 1.834)	0.583
Non-rheumatic valve diseases	1.126 (0.666, 1.905)	0.657	0.592 (0.363, 0.965)	0.036*	0.727 (0.419, 1.262)	0.258	0.919 (0.525, 1.608)	0.766
Pulmonary embolism	1.733 (0.875, 3.430)	0.115	1.119 (0.610, 2.053)	0.716	0.649 (0.292, 1.440)	0.287	0.845 (0.393, 1.818)	0.666
Aortic aneurysm	1.362 (0.659, 2.818)	0.405	0.756 (0.404, 1.414)	0.381	1.360 (0.667, 2.770)	0.397	1.628 (0.786, 3.375)	0.190
Dissection of aorta	0.556 (0.078, 3.952)	0.557	0.578 (0.107, 3.114)	0.524	4.227 (0.517, 34.55)	0.179	1.755 (0.212, 14.544)	0.602
Peripheral vascular disease	0.825 (0.228, 2.991)	0.770	1.395 (0.462, 4.210)	0.554	0.393 (0.131, 1.185)	0.097	0.678 (0.182, 2.521)	0.562
Coronary artery disease	1.676 (1.256, 2.237)	4.52E-04*	1.381 (1.058, 1.801)	0.017*	1.412 (0.990, 2.013)	0.057	1.466 (1.083, 1.986)	0.013*

*, Estimates with P<0.05 are reported. The P value less than 0.05 means the associations of daytime napping with cardiovascular diseases were completely mediated by the mediator (s).

Table S6 Estimates of sleep duration on cardiovascular diseases mediated by multiple mediators

Cardiovascular diseases	Adjustment for body mass index		Adjustment for smoking initiation		Adjustment for type 2 diabetes		Adjustment for body mass index, smoking initiation and type 2 diabetes	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Heart failure	2.474 (1.219, 5.021)	0.012*	0.677 (0.190, 2.417)	0.548	2.287 (0.589, 8.873)	0.232	2.325 (1.157, 4.675)	0.018*
Hypertension	1.872 (0.528, 6.634)	0.331	1.771 (0.249, 12.592)	0.568	0.771 (0.151, 3.940)	0.754	1.949 (0.610, 6.228)	0.260
Stroke	1.175 (0.551, 2.505)	0.677	6.526 (1.768, 24.086)	0.005*	0.574 (0.200, 1.649)	0.303	1.656 (0.815, 3.369)	0.163
Atrial fibrillation	1.844 (0.979, 3.471)	0.058	0.874 (0.300, 2.543)	0.805	0.850 (0.275, 2.625)	0.777	1.569 (0.849, 2.900)	0.151
Arrhythmia	0.991 (0.973, 1.009)	0.311	1.000 (0.968, 1.034)	0.995	1.004 (0.977, 1.032)	0.753	0.989 (0.972, 1.008)	0.248
Conduction disorders	2.163 (0.453, 10.335)	0.334	0.480 (0.034, 6.756)	0.586	0.144 (0.016, 1.323)	0.087	0.621 (0.137, 2.808)	0.536
Coronary atherosclerosis	0.849 (0.332, 2.173)	0.733	0.598 (0.130, 2.748)	0.509	1.000 (0.208, 4.806)	>0.99	0.692 (0.271, 1.764)	0.440
Myocardial infarction	1.022 (0.430, 2.427)	0.961	1.228 (0.276, 5.458)	0.787	2.310 (0.607, 8.799)	0.220	1.150 (0.495, 2.674)	0.745
Non-ischemic cardiomyopathy	1.796 (0.635, 5.082)	0.270	0.606 (0.082, 4.499)	0.625	0.301 (0.053, 1.707)	0.175	0.609 (0.219, 1.696)	0.342
Non-rheumatic valve diseases	1.820 (0.534, 6.199)	0.338	0.413 (0.063, 2.701)	0.356	0.356 (0.059, 2.141)	0.259	0.451 (0.134, 1.521)	0.199
Pulmonary embolism	0.928 (0.186, 4.621)	0.927	0.461 (0.037, 5.825)	0.550	4.141 (0.264, 65.022)	0.312	0.663 (0.124, 3.547)	0.631
Aortic aneurysm	0.416 (0.077, 2.241)	0.307	16.162 (0.901, 289.931)	0.059	1.939 (0.196, 19.203)	0.571	1.838 (0.371, 9.098)	0.456
Dissection of aorta	1.733 (0.020, 149.196)	0.809	8.244 (0.007, 10011.830)	0.560	0.225 (0.000, 268.333)	0.680	17.242 (0.181, 1643.971)	0.221
Peripheral vascular disease	1.243 (0.060, 25.824)	0.888	191.403 (1.561, 23472.847)	0.032*	0.011 (0.000, 0.467)	0.019*	0.256 (0.014, 4.604)	0.356
Coronary artery disease	1.444 (0.715, 2.914)	0.305	1.585 (0.437, 5.750)	0.483	3.189 (0.862, 11.794)	0.082	1.707 (0.826, 3.527)	0.149

* Estimates with P<0.05 are reported. The P value less than 0.05 means the associations of sleep duration with cardiovascular diseases were completely mediated by the mediator (s).

Table S7 Estimates of depression on cardiovascular diseases mediated by multiple mediators

Cardiovascular diseases	Adjustment for body mass index		Adjustment for smoking initiation		Adjustment for type 2 diabetes		Adjustment for body mass index, smoking initiation and type 2 diabetes	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Heart failure	6.727 (1.010, 44.820)	0.049*	0.023 (0.001, 0.655)	0.027*	1.696 (0.043, 67.168)	0.779	6.991 (1.040, 47.010)	0.045*
Hypertension	0.142 (0.005, 3.905)	0.249	0.282 (0.001, 63.049)	0.646	2.673 (0.022, 326.676)	0.688	1.417 (0.056, 35.599)	0.832
Stroke	1.322 (0.183, 9.565)	0.782	0.205 (0.005, 8.617)	0.406	3.227 (0.172, 60.650)	0.434	0.641 (0.094, 4.359)	0.649
Atrial fibrillation	3.618 (0.699, 18.724)	0.125	0.103 (0.006, 1.845)	0.123	3.389 (0.141, 81.389)	0.452	5.261 (0.983, 28.163)	0.052
Arrhythmia	1.044 (0.996, 1.093)	0.070	1.021 (0.933, 1.118)	0.654	1.097 (1.017, 1.183)	0.017*	1.028 (0.978, 1.080)	0.278
Conduction disorders	41.312 (0.668, 2555.660)	0.077	0.024 (0.000, 36.248)	0.317	158.126 (0.274, 91114.284)	0.118	95.880 (1.478, 6218.371)	0.032*
Coronary atherosclerosis	10.052 (0.799, 126.534)	0.074	2.646 (0.037, 187.654)	0.654	78.841 (0.737, 8438.597)	0.067	20.179 (1.512, 269.360)	0.023*
Myocardial infarction	3.868 (0.401, 37.286)	0.242	0.158 (0.003, 8.753)	0.367	95.233 (1.548, 5858.572)	0.030*	5.085 (0.517, 49.993)	0.163
Non-ischemic cardiomyopathy	1.063 (0.068, 16.571)	0.965	0.124 (0.000, 32.654)	0.463	0.106 (0.001, 16.801)	0.385	1.054 (0.061, 18.171)	0.971
Non-rheumatic valve diseases	1.790 (0.070, 45.892)	0.725	5.145 (0.024, 1123.612)	0.551	20.825 (0.129, 3368.171)	0.242	2.119 (0.073, 61.608)	0.662
Pulmonary embolism	1.761 (0.025, 122.167)	0.794	3.841 (0.003, 4557.096)	0.709	0.213 (0.000, 632.335)	0.705	0.307 (0.003, 32.513)	0.620
Aortic aneurysm	0.866 (0.010, 74.612)	0.949	1.152 (0.000, 3569.913)	0.972	16.890 (0.022, 12852.350)	0.404	0.824 (0.011, 64.204)	0.931
Dissection of aorta	20.983 (0.000, 2929154)	0.615	0.000 (0.000, 507.580)	0.181	0.000 (0.000, 915.198)	0.194	0.003 (0.000, 1123.809)	0.382
Peripheral vascular disease	0.816 (0.000, 2368.681)	0.960	122137.200 (0.158, 94244090000.000)	0.090	0.016 (0.000, 910.938)	0.461	0.144 (0.000, 413.667)	0.634
Coronary artery disease	2.658 (0.415, 17.040)	0.302	0.332 (0.010, 10.792)	0.535	46.522 (0.945, 2290.065)	0.053	1.185 (1.055, 1.332)	0.004*

* Estimates with P<0.05 are reported. The P value less than 0.05 means the associations of depression with cardiovascular diseases were completely mediated by the mediator (s).

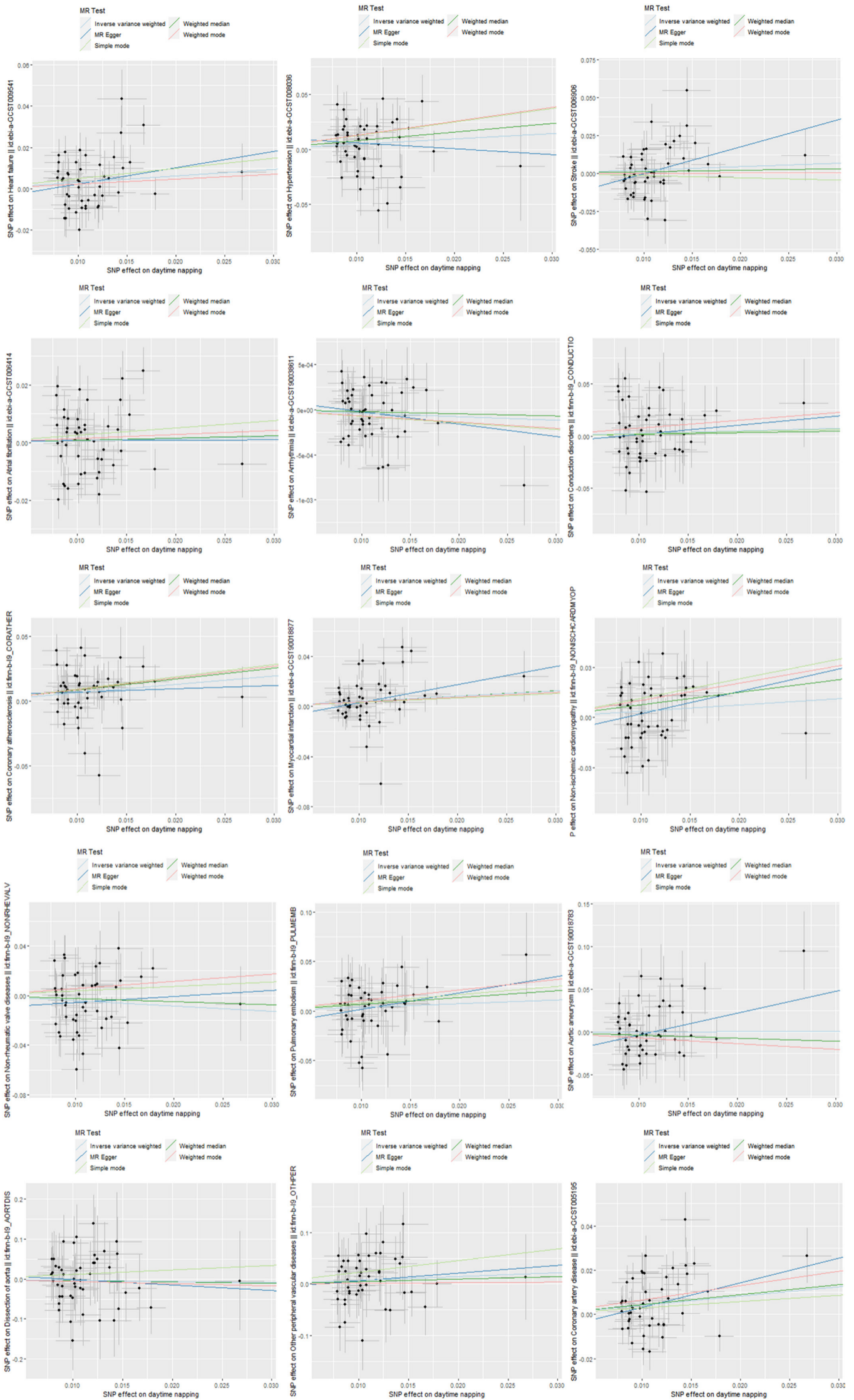


Figure S1 Scatter plots of the association of daytime napping with cardiovascular diseases. MR, Mendelian randomization; SNP, single nucleotide polymorphisms.

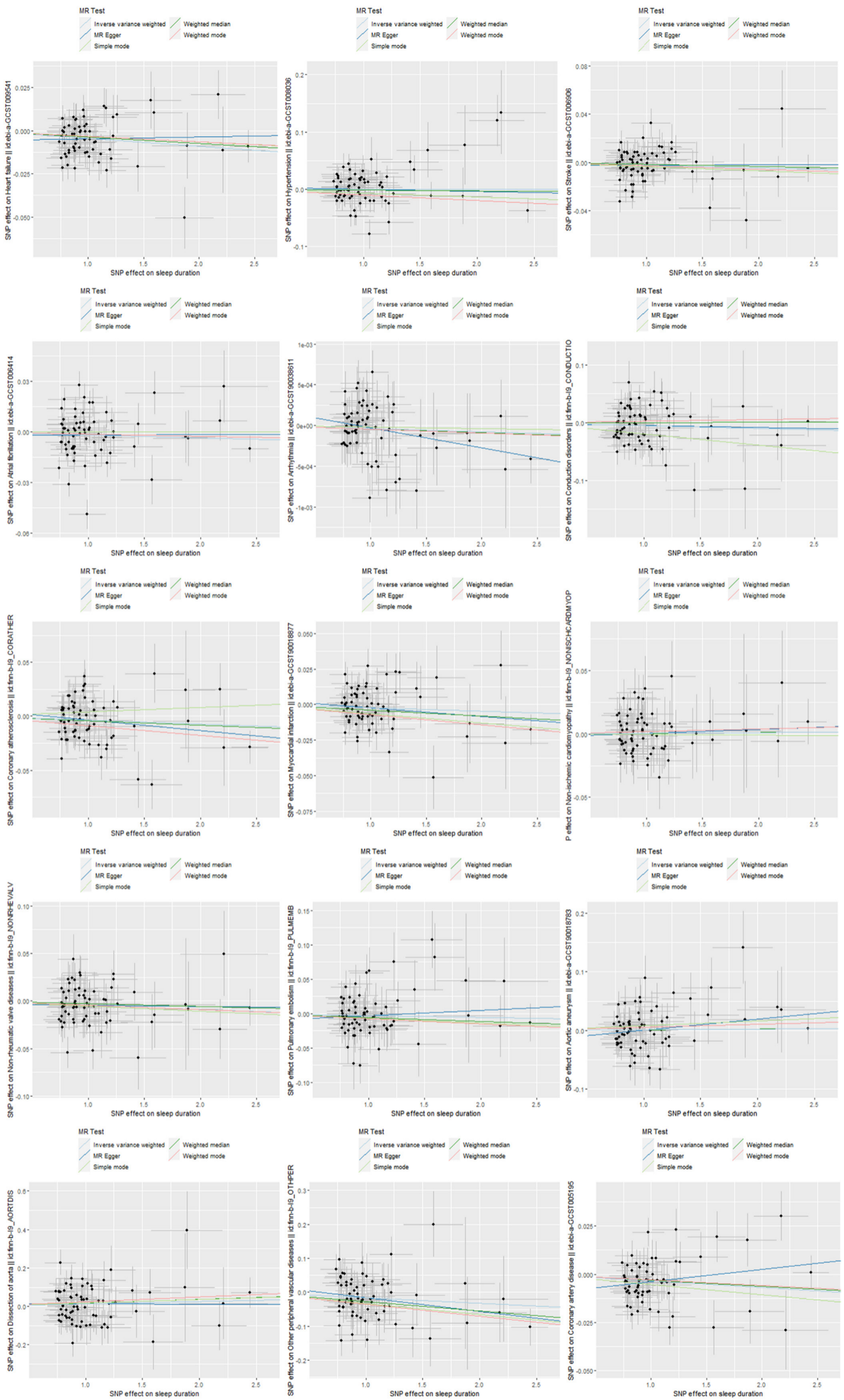


Figure S2 Scatter plots of the association of sleep duration with cardiovascular diseases. MR, Mendelian randomization; SNP, single nucleotide polymorphisms.

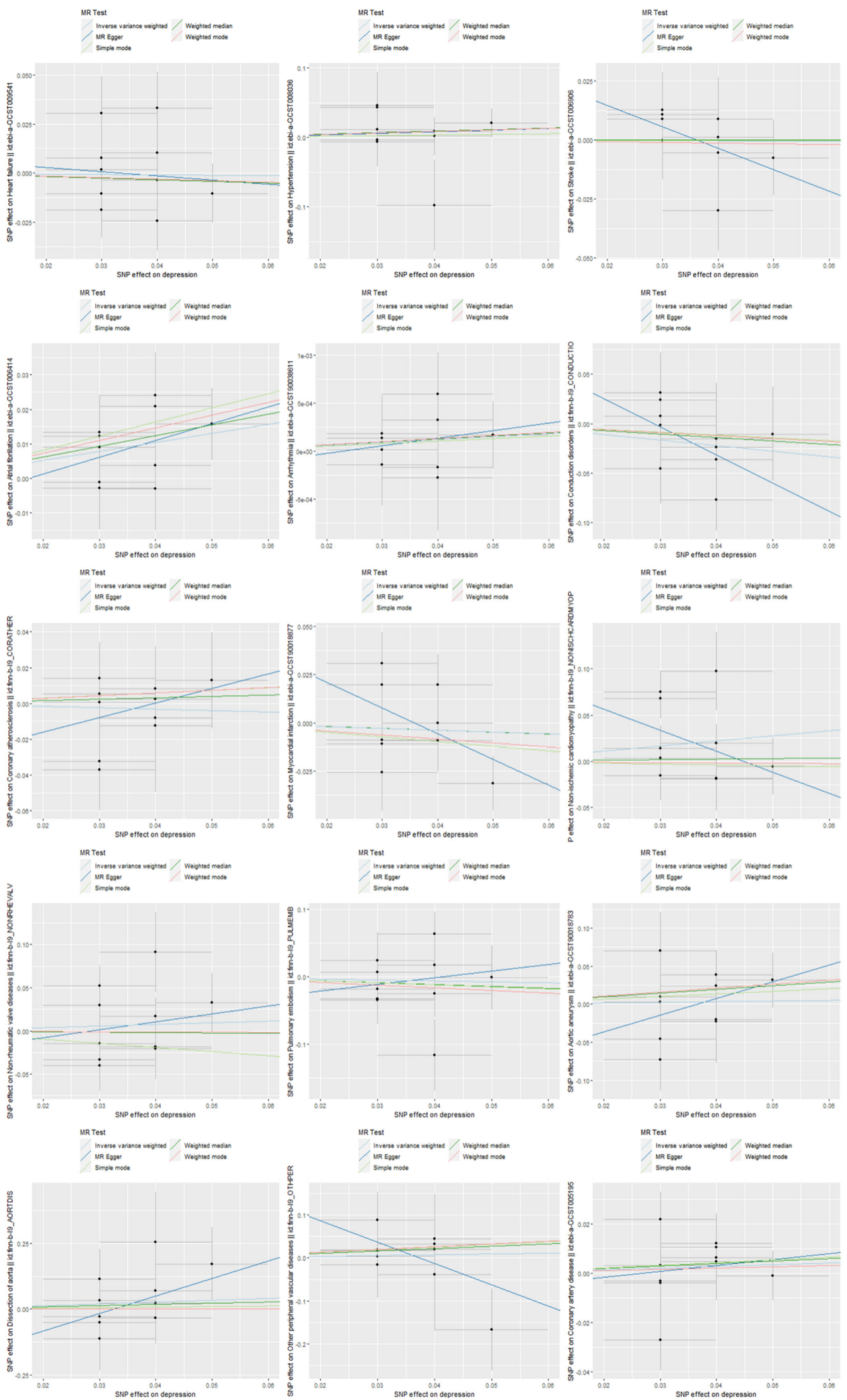


Figure S3 Scatter plots of the association of depression with cardiovascular diseases. MR, Mendelian randomization; SNP, single nucleotide polymorphisms.

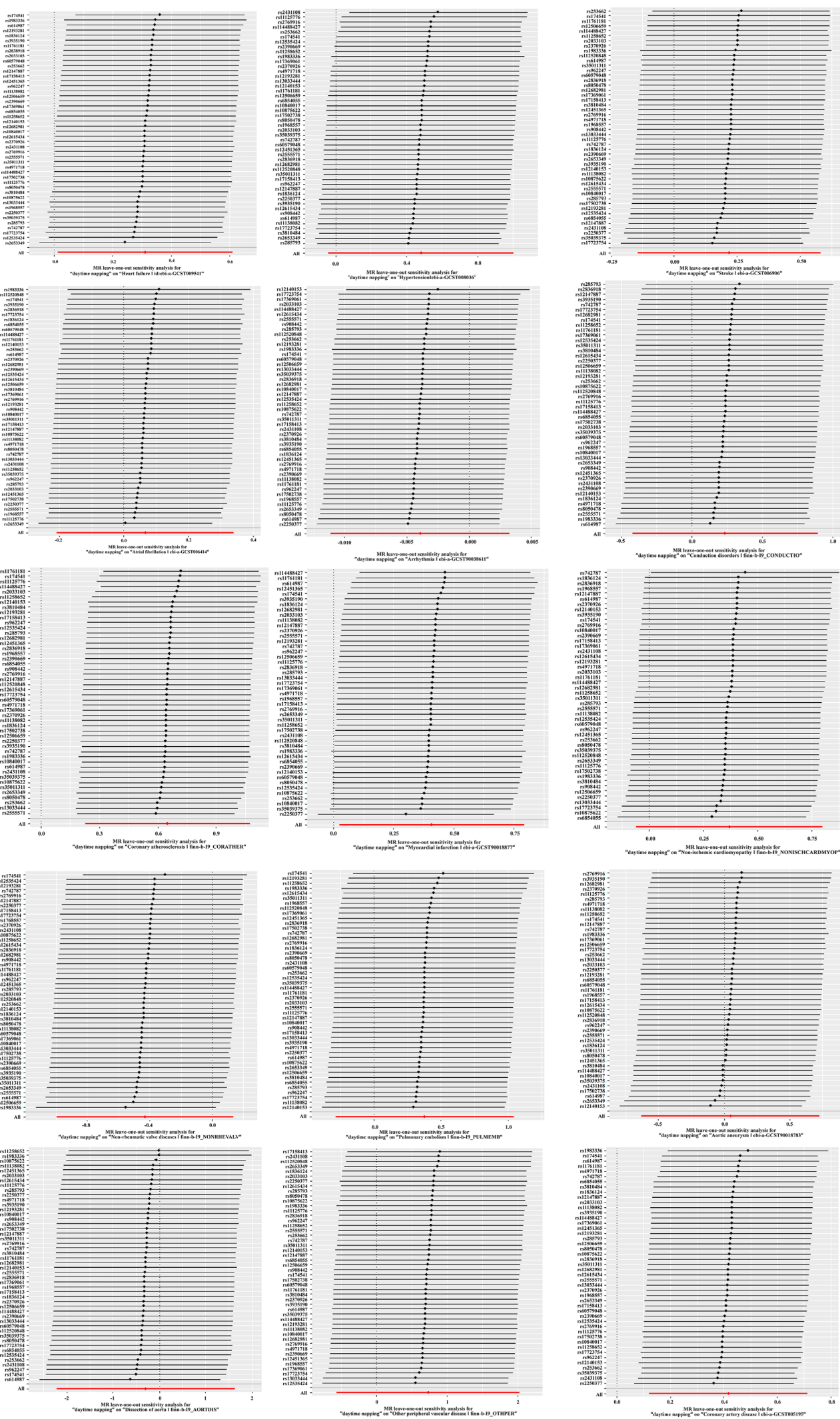


Figure S4 The leave-one-out sensitivity analysis of daytime napping with cardiovascular diseases. MR, Mendelian randomization.

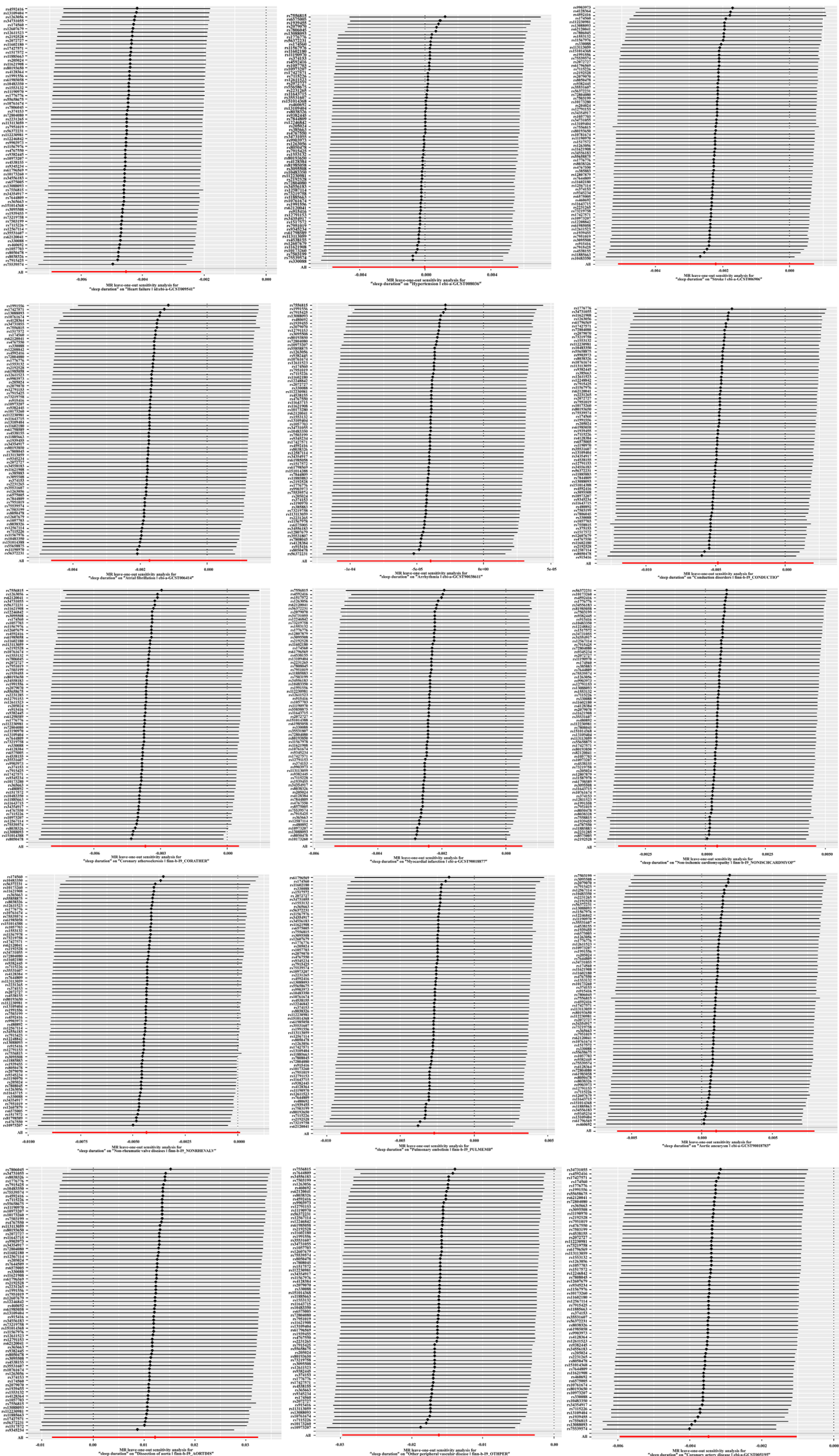


Figure S5 The leave-one-out sensitivity analysis of sleep duration with cardiovascular diseases. MR, Mendelian randomization.

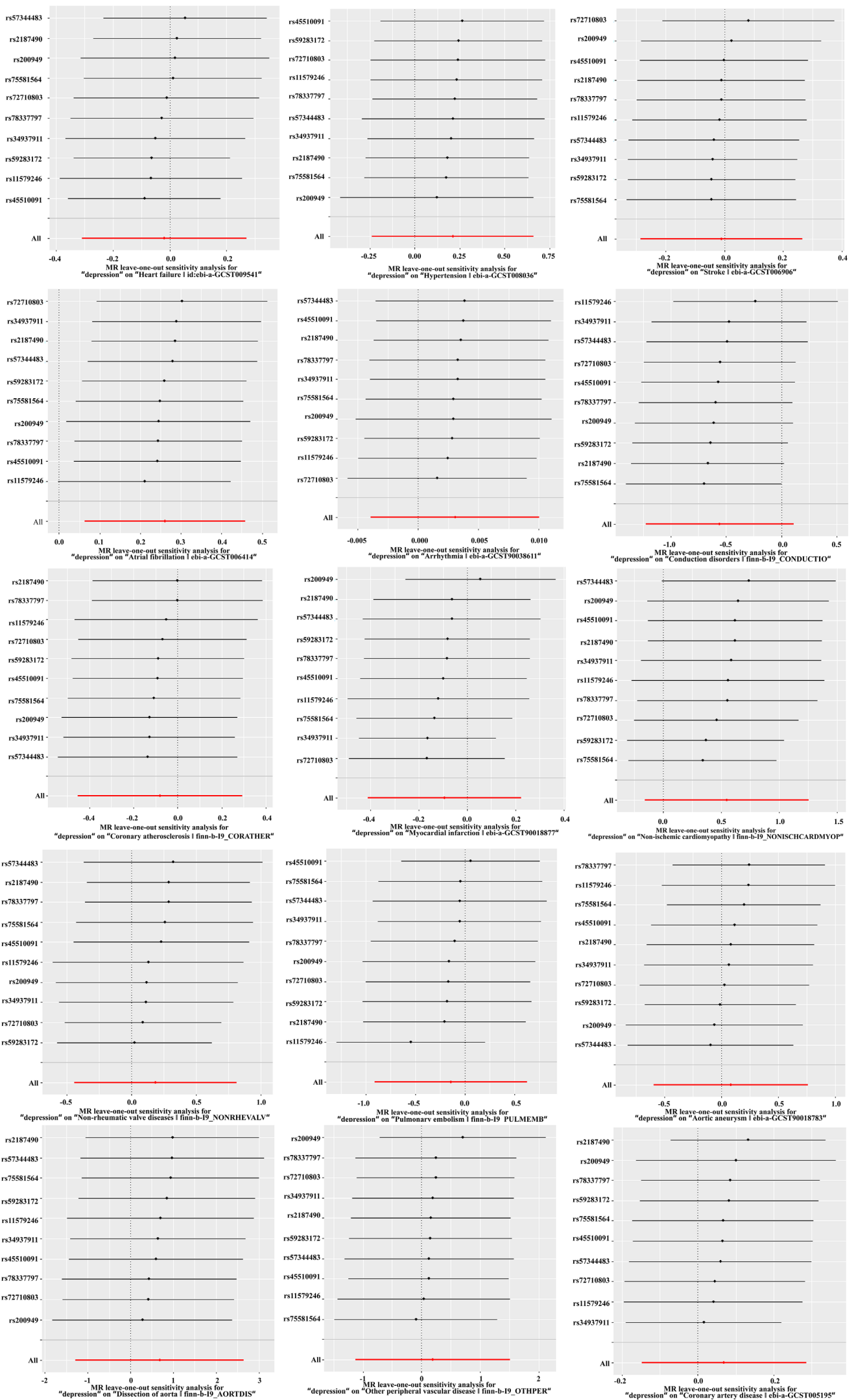


Figure S6 The leave-one-out sensitivity analysis of depression with cardiovascular diseases. MR, Mendelian randomization.

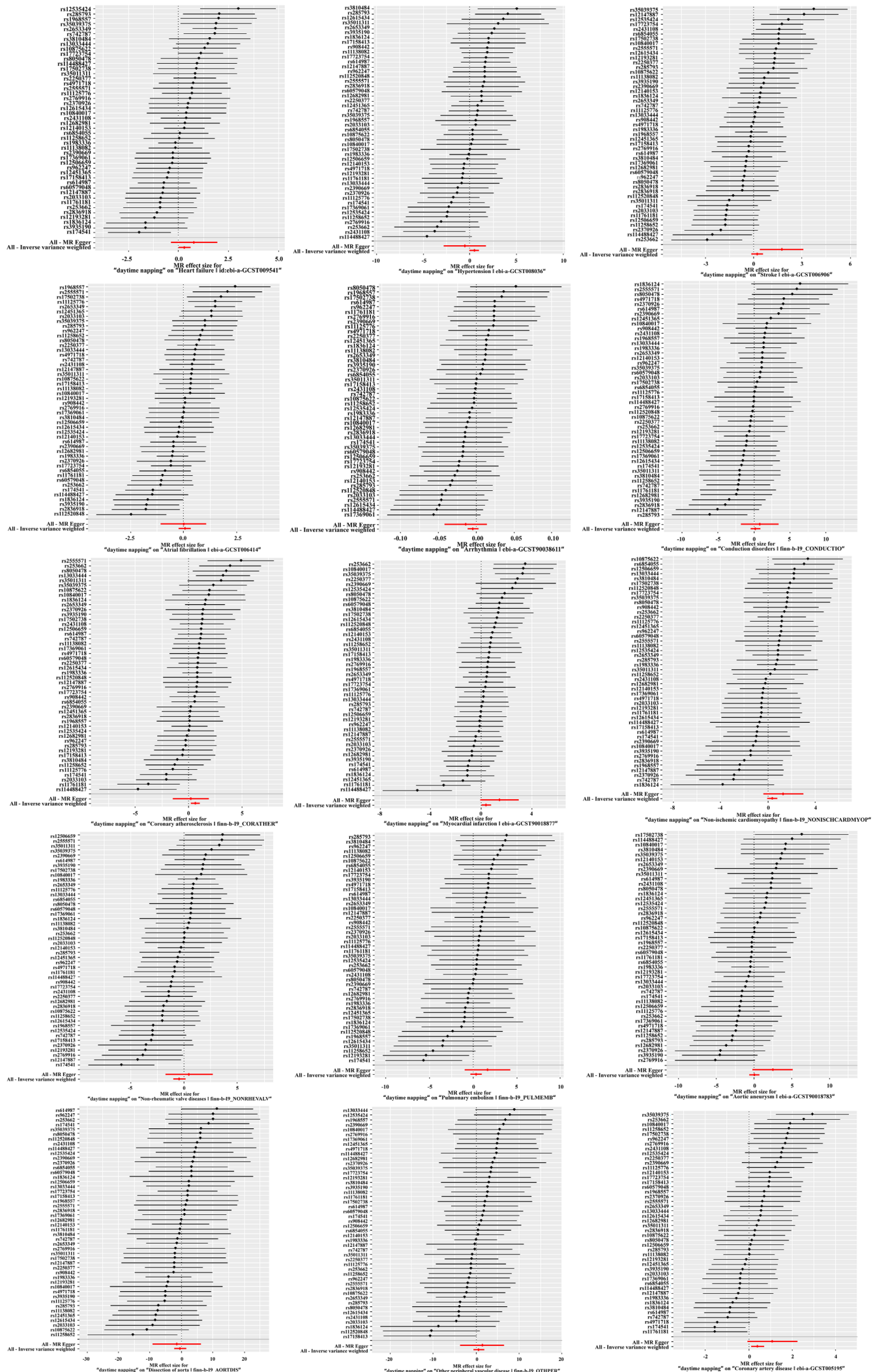


Figure S7 Associations of each variant with daytime napping and risk of cardiovascular diseases. MR, Mendelian randomization.

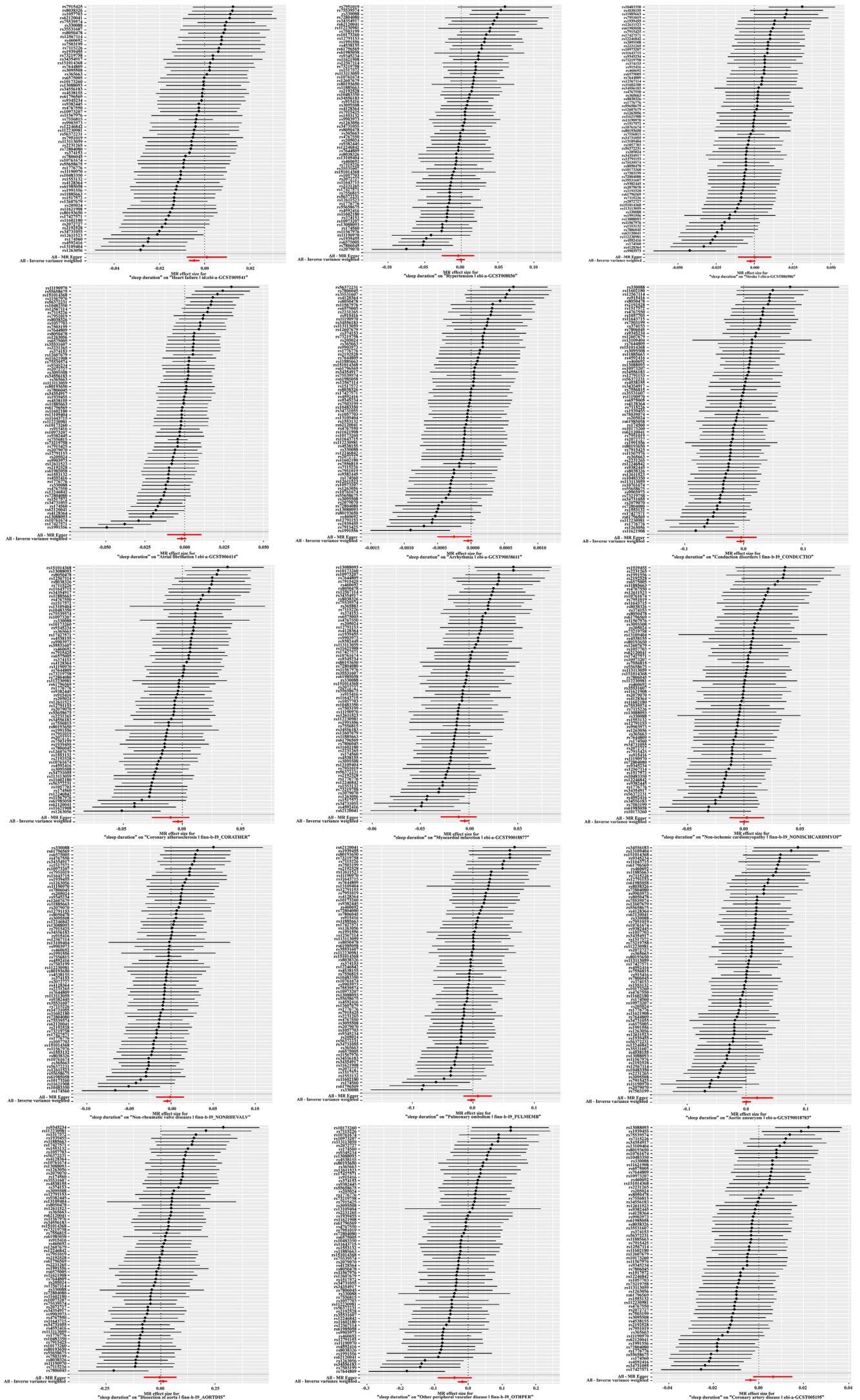


Figure S8 Associations of each variant with sleep duration and risk of cardiovascular diseases. MR, Mendelian randomization.



Figure S9 Associations of each variant with depression and risk of cardiovascular diseases. MR, Mendelian randomization.

Table S8 Estimates of genetical liability to daytime napping on potential mediators

Mediators	IVW		Weighted median		MR-Egger	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Body mass index	1.429 (1.142, 1.787)	0.002*	1.412 (1.204, 1.656)	2.27E-05	3.025 (1.302, 7.025)	0.013
Smoking initiation	1.089 (0.872, 1.359)	0.452	1.137 (0.930, 1.389)	0.211	2.287 (0.995, 5.257)	0.058
Type 2 diabetes	1.409 (0.987, 2.012)	0.059	1.207 (0.857, 1.699)	0.282	4.771 (1.175, 19.370)	0.034

*, estimates with $P < 0.05$ in IVW analysis. OR, odd ratio; CI, confidence interval; IVW, inverse variance weighted; MR, Mendelian randomization.

Table S9 Estimates of genetical liability to sleep duration on potential mediators

Mediators	IVW		Weighted median		MR-Egger	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Body mass index	0.999 (0.997, 1.001)	0.210	0.999 (0.997, 1.000)	0.032	0.997 (0.990, 1.005)	0.494
Smoking initiation	0.999 (0.997, 1.001)	0.581	0.999 (0.997, 1.001)	0.312	1.000 (0.992, 1.007)	0.921
Type 2 diabetes	0.999 (0.996, 1.003)	0.634	0.999 (0.996, 1.002)	0.476	0.999 (0.986, 1.012)	0.882

OR, odd ratio; CI, confidence interval; IVW, inverse variance weighted; MR, Mendelian randomization.

Table S10 Estimates of genetical liability to depression on potential mediators

Mediators	IVW		Weighted median		MR-Egger	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Body mass index	0.973 (0.836, 1.132)	0.724	1.012 (0.897, 1.141)	0.847	0.654 (0.303, 1.413)	0.312
Smoking initiation	1.369 (1.215, 1.542)	2.00E-07*	1.353 (1.158, 1.580)	1.36E-04	2.078 (1.161, 3.719)	0.039
Type 2 diabetes	0.967 (0.686, 1.363)	0.846	1.011 (0.736, 1.389)	0.947	0.436 (0.056, 3.382)	0.450

*, estimates with $P < 0.05$ in IVW analysis. OR, odd ratio; CI, confidence interval; IVW, inverse variance weighted; MR, Mendelian randomization.