

## Appendix 1

### *Removal of abnormal instrumental variables*

#### **Atrial fibrillation**

When resting heart rate (HR) was used as the exposure, no duplicated single-nucleotide polymorphisms (SNPs), after the outliers (rs1015451, rs11153730, rs17287293, rs4489968) were detected and removed by Mendelian randomization pleiotropy residual sum and outlier (MR-PRESSO), a total of 12 SNPs were extracted as instrumental variables.

When heart rate variability\_root mean square of successive differences (HRV\_RMSSD) was used as the exposure, no duplicated SNPs, after the outlier (rs10842383) was detected and removed by MR-PRESSO, a total of 6 SNPs were extracted as instrumental variables.

When heart rate variability\_peak-valley respiratory sinus arrhythmia or high frequency power (HRV\_pvRSA/HF) was used as the exposure, no duplicated SNPs, after the outlier (rs10842383) was detected and removed by MR-PRESSO, a total of 4 SNPs were extracted as instrumental variables.

When heart rate variability\_standard deviation of the normal-to-normal interval (HRV\_SDNN) was used as the exposure, the duplicated SNP (rs1384598) was removed, and after the outliers (rs10842383, rs11922153, rs2349556, rs2680344) were detected and removed by MR-PRESSO, a total of 17 SNPs were extracted as instrumental variables.

When the PR interval was used as the exposure, the following duplicated SNPs were removed (rs10786206, rs12190287, rs2395137, rs2540286, rs2912774, rs6084574, rs6496452, rs7660883).

Detection and removal of outliers were conducted by MR-PRESSO (rs10226357, rs1031262, rs10883908, rs11047497, rs11067104, rs11191116, rs12869776, rs12889267, rs144789148, rs1692144, rs17287293, rs17446418, rs1769758, rs1997571, rs2042995, rs214502, rs2403550, rs2629745, rs28709422, rs287606, rs2970854, rs3176326, rs36034102, rs3922843, rs4245338, rs4390169, rs4655001, rs55734480, rs56049025, rs59212267, rs60632610, rs62521284, rs6682872, rs6900627, rs72690486, rs763076, rs7645178, rs883079).

The outliers were removed by IVW radial regression (rs1037100, rs10516755, rs10784418, rs11153730, rs1124477, rs116757907, rs11689011, rs1173743, rs117845584, rs1188285, rs12228985, rs12443745, rs12513783, rs12751675, rs12961264, rs13032472, rs1337024, rs17496249, rs1986524, rs2072966, rs2137897, rs2163107, rs2243857, rs231276, rs2947080, rs29795, rs35680304, rs35816944, rs3747570, rs3794809, rs3825751, rs41306688, rs4871397, rs55679363, rs56352403, rs565720, rs57214150, rs61824887, rs61928421, rs62008078, rs62472627, rs6435953, rs6599230, rs6599240, rs6791171, rs6824178, rs7552783, rs762032, rs78518764, rs7997798, rs881299), and a total of 156 SNPs were extracted as instrumental variables.

When using P-wave terminal force as the exposure, the duplicated SNP (rs251492) was removed, and after the outliers (rs12144965, rs445754) were detected and removed by MR-PRESSO and the outliers (rs10890369, rs11242779, rs4435363, rs7939513) were detected and removed by IVW radial regression, a total of 22 SNPs were extracted as instrumental variables.

When using P-wave duration as the exposure, the duplicated SNPs (rs41312411, rs6773331, rs6790396) were removed, and after the outliers (rs11894252, rs1467026, rs3807989, rs452036, rs7312625) were detected and removed by MR-PRESSO, a total of 4 SNPs were extracted as instrumental variables.

When T-wave top amplitude\_anterior [electrocardiogram (ECG) lead V3 + V4 + aVL] was used as the exposure, the duplicated SNP (rs6790396) was removed, and after the outliers (rs7633988, rs7638909) were detected and removed by MR-PRESSO and the outliers (rs11134683, rs16928366) were detected and removed by IVW radial regression, a total of 10 SNPs were retained as instrumental variables.

When T-wave top amplitude\_avr (ECG lead aVR) was used as the exposure, the duplicated SNPs (rs12374310, rs4233994) were removed, and after the outliers (rs4076737, rs7638909, rs7846485) were detected and removed by MR-PRESSO and the outliers (rs11134683, rs16928366) were detected and removed by IVW radial regression, a total of 20 SNPs were extracted as instrumental variables.

When T-wave top amplitude\_inferior (ECG lead II + III + aVF) was used as the exposure, the duplicated SNP (rs6790396) was removed, and after the outliers (rs7638909, rs9851710) were detected and removed by MR-PRESSO, a total of 16 SNPs were extracted as instrumental variables.

When T-wave top amplitude\_lateral (ECG lead I + aVL + V5 + V6) was used as the exposure, no duplicated SNPs, after

the outliers (rs6783110, rs7633988) were detected and removed by MR-PRESSO and the outliers (rs17128209, rs7191330, rs728926) were detected and removed by IVW radial regression, a total of 14 SNPs were extracted as instrumental variables.

When T-wave top amplitude\_septal (ECG lead V1 + V2) was used as the exposure, the duplicated SNP (rs12623169) was removed, and after the outliers (rs10111852, rs10850409) were detected and removed by MR-PRESSO, a total of 9 SNPs were extracted as instrumental variables.

### **Bradycardia**

When heart rate was used as the exposure, a total of 10 SNPs were extracted as instrumental variables, no duplicated SNPs, and no outliers were detected by MR-PRESSO.

When HRV\_RMSSD was used as the exposure, a total of 18 SNPs were extracted as instrumental variables, no duplicated SNPs, and no outliers were detected by MR-PRESSO.

When HRV\_pvRSA/HF was used as the exposure, a total of 6 SNPs were extracted as instrumental variables, no duplicated SNPs, and no outliers were detected by MR-PRESSO.

When HRV\_SDNN was used as the exposure, after removing the duplicated SNP: rs1384598, a total of 10 SNPs were extracted as instrumental variables, and no outliers were detected by MR-PRESSO.

When the PR interval was used as the exposure, the duplicated SNPs (rs10786206, rs2540286, rs6084574 and rs6496452) were removed.

Detection and removal of outliers (rs12190287 and rs3746471) were conducted by MR-PRESSO.

The outliers (rs13032472, rs34187723, rs3795063, rs62008078, rs66507060 and rs696) were removed by IVW radial regression and Egger radial regression, and a total of 102 SNPs were extracted as instrumental variables.

When using P-wave terminal force as the exposure, a total of 10 SNPs were extracted as instrumental variables after removing the duplicated SNP (rs251492), and no outliers were detected by MR-PRESSO.

When using P-wave duration as the exposure, the duplicated SNP (rs6790396) was removed, and no outliers were detected by MR-PRESSO, but the heterogeneity test suggested the existence of outliers, so the outliers were removed by IVW radial regression and Egger radial regression (rs1467026 and rs4276421), and a total of 4 SNPs were retained as instrumental variables.

When T-wave top amplitude\_anterior was used as the exposure, the duplicated SNP (rs6790396) was removed, no outliers were detected by MR-PRESSO, but the heterogeneity test suggested the existence of outliers, so the outlier was removed by IVW radial regression and Egger radial regression (rs686930), a total of 7 SNPs were extracted as instrumental variables.

When T-wave top amplitude\_avr was used as the exposure, there were no duplicated SNPs and no outliers were detected by MR-PRESSO, but the heterogeneity test suggested the existence of outliers, so the outlier was removed by IVW radial regression and Egger radial regression (rs10842350), a total of 4 SNPs were extracted as instrumental variables.

When T-wave top amplitude\_inferior was used as the exposure, the duplicated SNP (rs6790396) was removed, and no outliers were detected by MR-PRESSO, a total of 7 SNPs were extracted as instrumental variables.

When T-wave top amplitude\_lateral was used as the exposure, there were no duplicated SNPs, and after the outliers (rs10842350, rs6783110, rs7191330 and rs7633988) were detected and removed by MR-PRESSO a total of 8 SNPs were extracted as instrumental variables.

When T-wave top amplitude\_septal was used as the exposure, the duplicated SNP (rs12623169) was removed. MR-PRESSO did not detect outliers, and a total of 5 SNPs were extracted as instrumental variables.

### **Supraventricular tachycardia**

When heart rate was used as the exposure, a total of 10 SNPs were extracted as instrumental variables, no duplicated SNPs, and no outliers were detected by MR-PRESSO.

When HRV\_RMSSD was used as the exposure, a total of 4 SNPs were extracted as instrumental variables, no duplicated SNPs, and no outliers were detected by MR-PRESSO.

When HRV\_pvRSA/HF was used as the exposure, a total of 4 SNPs were extracted as instrumental variables, no duplicated SNPs, and no outliers were detected by MR-PRESSO.

When HRV\_SDNN was used as the exposure, after removing the duplicated SNP (rs1384598), a total of 10 SNPs were

extracted as instrumental variables, and no outliers were detected by MR-PRESSO.

When the PR interval was used as the exposure, the following duplicated SNPs (rs10786206, rs2540286, rs6084574, rs6496452) were removed. A total of 116 SNPs were extracted as instrumental variables, and no outliers were detected by MR-PRESSO.

When using P-wave terminal force as the exposure, a total of 10 SNPs were extracted as instrumental variables after removing the duplicated SNP (rs251492), and no outliers were detected by MR-PRESSO.

When using P-wave duration as the exposure, after removing the duplicated SNP (rs6790396) and detecting and removing the outlier (rs452036) by MR-PRESSO, the heterogeneity test still suggested that there were potential outliers affecting the results, and after removing the outlier (rs11894252) by IVW radial regression and Egger radial regression, a total of 4 SNPs were extracted as instrumental variables.

When T-wave top amplitude\_anterior was used as the exposure, the duplicated SNP (rs6790396) was removed. After detecting and removing the outlier (rs6807275) by MR-PRESSO, a total of 7 SNPs were retained as instrumental variables.

When T-wave top amplitude\_avr was used as the exposure, there were no duplicated SNPs and no outliers were detected by MR-PRESSO, and a total of 5 SNPs were extracted as instrumental variables.

When T-wave top amplitude\_inferior was used as the exposure, the duplicated SNP (rs6790396) was removed. MR-PRESSO did not detect outliers, and a total of 8 SNPs were extracted as instrumental variables.

When T-wave top amplitude\_lateral was used as the exposure, there were no duplicated SNPs and no outliers were detected by MR-PRESSO, and a total of 4 SNPs were extracted as instrumental variables.

When T-wave top amplitude\_septal was used as the exposure, the duplicated SNP (rs12623169) was removed. MR-PRESSO did not detect outliers, and a total of 6 SNPs were extracted as instrumental variables.

**Table S1** Removal of abnormal instrument variables

Outcome	Exposure	Threshold	Duplicated SNPs	MR-PRESSO	MR-Radial	nSNP
AF	HR	$5 \times 10^{-8}$	√	4	√	12
	HRV_RMSSD	$5 \times 10^{-8}$	√	1	√	6
	HRV_pvRSA/HF	$5 \times 10^{-8}$	√	1	√	4
	HRV_SDNN	$1 \times 10^{-5}$	1	4	√	17
	PR	$5 \times 10^{-8}$	8	38	51	156
	Ptforce	$1 \times 10^{-5}$	1	2	4	22
	Pwave Duration	$5 \times 10^{-8}$	3	5	√	4
	Twave_anterior	$1 \times 10^{-5}$	1	2	2	10
	Twave_avr	$1 \times 10^{-5}$	2	3	4	20
	Twave_inferior	$1 \times 10^{-5}$	1	2	√	16
	Twave_lateral	$1 \times 10^{-5}$	√	2	3	14
	Twave_septal	$1 \times 10^{-5}$	1	2	√	9
	Bradycardia	HR	$5 \times 10^{-8}$	√	√	√
HRV_RMSSD		$1 \times 10^{-5}$	√	√	√	18
HRV_pvRSA/HF		$1 \times 10^{-5}$	√	√	√	6
HRV_SDNN		$1 \times 10^{-5}$	1	√	√	10
PR		$5 \times 10^{-8}$	4	2	6	102
Ptforce		$1 \times 10^{-5}$	1	√	√	10
Pwave Duration		$5 \times 10^{-8}$	1	√	2	4
Twave_anterior		$1 \times 10^{-5}$	1	√	1	7
Twave_avr		$5 \times 10^{-8}$	√	√	1	4
Twave_inferior		$1 \times 10^{-5}$	1	√	√	7
Twave_lateral		$1 \times 10^{-5}$	4	√	√	8
Twave_septal		$1 \times 10^{-5}$	1	√	√	5
Supraventricular tachycardia		HR	$5 \times 10^{-8}$	√	√	√
	HRV_RMSSD	$5 \times 10^{-8}$	√	√	√	4
	HRV_pvRSA/HF	$5 \times 10^{-8}$	√	√	√	4
	HRV_SDNN	$1 \times 10^{-5}$	1	√	√	10
	PR	$5 \times 10^{-8}$	4	√	√	116
	Ptforce	$1 \times 10^{-5}$	1	√	√	10
	Pwave Duration	$5 \times 10^{-8}$	1	1	1	4
	Twave_anterior	$1 \times 10^{-5}$	√	1	√	7
	Twave_avr	$5 \times 10^{-8}$	√	√	√	5
	Twave_inferior	$1 \times 10^{-5}$	1	√	√	8
	Twave_lateral	$5 \times 10^{-8}$	√	√	√	4
	Twave_septal	$1 \times 10^{-5}$	1	√	√	6

SNP, single-nucleotide polymorphism; MR-PRESSO, number of SNPs removed by MR-PRESSO; MR-Radial, number of SNPs removed by IVW radial regression and Egger radial regression; nSNP, number of SNPs used for MR analysis; √, no abnormal SNPs were removed; AF, atrial fibrillation; HR, resting heart rate; Twave, T-wave top amplitude; septal: ECG lead V1 + V2; lateral: ECG lead I + aVL + V5 + V6; inferior, ECG lead II + III + aVF; anterior: ECG lead V3 + V4 + aVL; avr, ECG lead aVR; Ptforce, P-wave terminal force; Pwave duration, P-wave duration; PR, PR interval; HRV, heart rate variability; RMSSD, root mean square of successive differences; pvRSA/HF, peak-valley respiratory sinus arrhythmia or high frequency power; SDNN, standard deviation of the normal-to-normal interval.

**Table S2** Results of univariate Mendelian randomization

Outcome	Exposure	Method	nSNP	P value	OR	or_lci95	or_uci95
AF	HR	Inverse variance weighted	12	0.07	0.981	0.961	1.001
		MR Egger	12	0.68	1.018	0.938	1.104
		Weighted median	12	0.71	0.996	0.974	1.018
		Weighted mode	12	0.89	0.998	0.971	1.026
		Inverse variance weighted (multiplicative random effects)	12	0.07	0.981	0.961	1.001
	HRV_RMSSD	Inverse variance weighted	6	0.02	1.309	1.045	1.640
		MR Egger	6	0.78	0.919	0.525	1.610
		Weighted median	6	0.33	1.154	0.868	1.535
		Weighted mode	6	0.55	1.123	0.786	1.603
		Inverse variance weighted (multiplicative random effects)	6	0.01	1.309	1.067	1.605
	HRV_pvRSA/HF	Inverse variance weighted	4	0.06	1.141	0.995	1.308
		MR Egger	4	0.95	0.990	0.770	1.273
		Weighted median	4	0.33	1.082	0.925	1.267
		Weighted mode	4	0.498	1.068	0.903	1.264
		Inverse variance weighted (multiplicative random effects)	4	0.06	1.141	0.995	1.308
	HRV_SDNN	Inverse variance weighted	17	0.004	1.518	1.140	2.022
		MR Egger	17	0.26	2.092	0.604	7.247
		Weighted median	17	0.12	1.338	0.930	1.926
		Weighted mode	17	0.23	1.406	0.820	2.411
		Inverse variance weighted (multiplicative random effects)	17	0.004	1.518	1.140	2.022
	PR	Inverse variance weighted	156	<0.001	0.994	0.991	0.997
		MR Egger	156	0.19	0.995	0.987	1.003
		Weighted median	156	0.003	0.993	0.988	0.998
		Weighted mode	156	0.07	0.993	0.985	1.001
		Inverse variance weighted (multiplicative random effects)	156	<0.001	0.994	0.991	0.997
	Ptforce	Inverse variance weighted	22	0.46	1.000	1.000	1.000
		MR Egger	22	0.80	1.000	1.000	1.000
		Weighted median	22	0.81	1.000	1.000	1.000
		Weighted mode	22	0.81	1.000	1.000	1.000
		Inverse variance weighted (multiplicative random effects)	22	0.43	1.000	1.000	1.000
	Pwave duration	Inverse variance weighted	4	0.52	0.994	0.976	1.012
		MR Egger	4	0.68	0.985	0.924	1.050
		Weighted median	4	0.54	0.994	0.973	1.014
		Weighted mode	4	0.50	0.989	0.962	1.017
		Inverse variance weighted (multiplicative random effects)	4	0.10	0.994	0.987	1.001
	Twave_anterior	Inverse variance weighted	10	0.17	0.972	0.933	1.012
		MR Egger	10	0.14	0.962	0.918	1.008
		Weighted median	10	0.15	0.965	0.920	1.013
		Weighted mode	10	0.16	0.965	0.921	1.010
		Inverse variance weighted (multiplicative random effects)	10	0.13	0.972	0.937	1.008
	Twave_avr	Inverse variance weighted	20	0.02	1.076	1.012	1.144
		MR Egger	20	0.30	1.099	0.926	1.304
		Weighted median	20	0.07	1.083	0.993	1.181
		Weighted mode	20	0.31	1.069	0.945	1.209
		Inverse variance weighted (multiplicative random effects)	20	0.005	1.076	1.022	1.133
	Twave_inferior	Inverse variance weighted	16	0.41	0.964	0.885	1.050
		MR Egger	16	0.28	0.830	0.600	1.148
		Weighted median	16	0.61	0.969	0.861	1.092
Weighted mode		16	0.76	0.967	0.789	1.186	
Inverse variance weighted (multiplicative random effects)		16	0.41	0.964	0.885	1.050	
Twave_lateral	Inverse variance weighted	14	0.72	0.990	0.935	1.048	
	MR Egger	14	0.99	1.000	0.909	1.101	
	Weighted median	14	0.48	0.971	0.897	1.052	
	Weighted mode	14	0.45	0.952	0.843	1.075	
	Inverse variance weighted (multiplicative random effects)	14	0.69	0.990	0.941	1.041	
Twave_septal	Inverse variance weighted	9	0.10	0.897	0.788	1.021	
	MR Egger	9	0.66	1.100	0.730	1.658	
	Weighted median	9	0.50	0.953	0.829	1.095	
	Weighted mode	9	0.71	0.969	0.828	1.134	
	Inverse variance weighted (multiplicative random effects)	9	0.10	0.897	0.788	1.021	

**Table S2** (continued)

Table S2 (continued)

Outcome	Exposure	Method	nSNP	P value	OR	or_lci95	or_uci95
Bradycardia	HR	Inverse variance weighted	10	<0.001	1.000	0.999	1.000
		MR Egger	10	0.93	1.000	0.999	1.001
		Weighted median	10	0.001	1.000	0.999	1.000
		Weighted mode	10	0.02	0.999	0.999	1.000
		Inverse variance weighted (multiplicative random effects)	10	<0.001	1.000	0.999	1.000
	HRV_RMSSD	Inverse variance weighted	18	0.02	1.002	1.000	1.004
		MR Egger	18	0.59	1.003	0.992	1.014
		Weighted median	18	0.21	1.002	0.999	1.004
		Weighted mode	18	0.85	1.000	0.995	1.004
		Inverse variance weighted (multiplicative random effects)	18	0.01	1.002	1.001	1.004
	HRV_pvRSA/HF	Inverse variance weighted	6	0.26	1.001	0.999	1.003
		MR Egger	6	0.76	1.002	0.992	1.011
		Weighted median	6	0.92	1.000	0.998	1.002
		Weighted mode	6	0.74	0.999	0.996	1.003
		Inverse variance weighted (multiplicative random effects)	6	0.26	1.001	0.999	1.003
	HRV_SDNN	Inverse variance weighted	10	0.03	1.004	1.000	1.007
		MR Egger	10	0.14	1.016	0.997	1.035
		Weighted median	10	0.058	1.004	1.000	1.009
		Weighted mode	10	0.09	1.006	1.000	1.013
		Inverse variance weighted (multiplicative random effects)	10	0.03	1.004	1.000	1.007
	PR	Inverse variance weighted	102	0.12	1.000	1.000	1.000
		MR Egger	102	0.53	1.000	1.000	1.000
		Weighted median	102	0.89	1.000	1.000	1.000
		Weighted mode	102	0.62	1.000	1.000	1.000
		Inverse variance weighted (multiplicative random effects)	102	0.12	1.000	1.000	1.000
	Ptforce	Inverse variance weighted	10	0.98	1.000	1.000	1.000
		MR Egger	10	0.81	1.000	1.000	1.000
		Weighted median	10	0.83	1.000	1.000	1.000
		Weighted mode	10	0.72	1.000	1.000	1.000
		Inverse variance weighted (multiplicative random effects)	10	0.98	1.000	1.000	1.000
	Pwave Duration	Inverse variance weighted	4	0.30	1.000	1.000	1.000
		MR Egger	4	0.70	0.999	0.997	1.002
		Weighted median	4	0.19	1.000	1.000	1.000
		Weighted mode	4	0.36	1.000	1.000	1.000
		Inverse variance weighted (multiplicative random effects)	4	0.15	1.000	1.000	1.000
	Twave_anterior	Inverse variance weighted	7	0.02	1.001	1.000	1.003
		MR Egger	7	0.29	1.002	0.998	1.006
		Weighted median	7	0.01	1.002	1.000	1.003
		Weighted mode	7	0.06	1.002	1.000	1.004
		Inverse variance weighted (multiplicative random effects)	7	0.02	1.001	1.000	1.003
	Twave_avr	Inverse variance weighted	4	<0.001	0.998	0.997	0.999
		MR Egger	4	0.61	0.999	0.996	1.002
		Weighted median	4	<0.001	0.998	0.997	0.999
		Weighted mode	4	0.09	0.998	0.997	1.000
		Inverse variance weighted (multiplicative random effects)	4	<0.001	0.998	0.997	0.998
	Twave_inferior	Inverse variance weighted	7	0.29	1.001	0.999	1.002
		MR Egger	7	0.04	1.004	1.001	1.007
Weighted median		7	0.11	1.001	1.000	1.003	
Weighted mode		7	0.11	1.002	1.000	1.003	
Inverse variance weighted (multiplicative random effects)		7	0.29	1.001	0.999	1.002	
Twave_lateral	Inverse variance weighted	8	0.33	1.000	1.000	1.001	
	MR Egger	8	0.68	1.000	0.998	1.003	
	Weighted median	8	0.35	1.001	0.999	1.002	
	Weighted mode	8	0.42	1.001	0.999	1.002	
	Inverse variance weighted (multiplicative random effects)	8	0.33	1.000	1.000	1.001	
Twave_septal	Inverse variance weighted	5	0.45	1.001	0.999	1.002	
	MR Egger	5	0.16	1.009	0.999	1.018	
	Weighted median	5	0.25	1.001	0.999	1.003	
	Weighted mode	5	0.32	1.001	0.999	1.004	
	Inverse variance weighted (multiplicative random effects)	5	0.42	1.001	0.999	1.002	

Table S2 (continued)

Table S2 (continued)

Outcome	Exposure	Method	nSNP	P value	OR	or_lci95	or_uci95
Supraventricular tachycardia	HR	Inverse variance weighted	10	<0.001	1.000	1.000	1.001
		MR Egger	10	0.73	1.000	0.999	1.001
		Weighted median	10	0.006	1.000	1.000	1.001
		Weighted mode	10	0.10	1.000	1.000	1.001
		Inverse variance weighted (multiplicative random effects)	10	<0.001	1.000	1.000	1.001
	HRV_RMSSD	Inverse variance weighted	4	0.52	0.999	0.995	1.003
		MR Egger	4	0.37	0.984	0.957	1.011
		Weighted median	4	0.13	0.997	0.993	1.001
		Weighted mode	4	0.24	0.997	0.993	1.001
		Inverse variance weighted (multiplicative random effects)	4	0.52	0.999	0.995	1.003
	HRV_pvRSA/HF	Inverse variance weighted	4	0.93	1.000	0.998	1.002
		MR Egger	4	0.64	1.004	0.991	1.017
		Weighted median	4	0.27	0.999	0.997	1.001
		Weighted mode	4	0.47	0.999	0.995	1.002
		Inverse variance weighted (multiplicative random effects)	4	0.93	1.000	0.998	1.002
	HRV_SDNN	Inverse variance weighted	10	0.33	1.002	0.998	1.005
		MR Egger	10	0.82	0.998	0.979	1.017
		Weighted median	10	0.89	1.000	0.995	1.004
		Weighted mode	10	0.60	0.998	0.991	1.005
		Inverse variance weighted (multiplicative random effects)	10	0.33	1.002	0.998	1.005
	PR	Inverse variance weighted	116	0.001	1.000	1.000	1.000
		MR Egger	116	0.02	1.000	1.000	1.000
		Weighted median	116	0.03	1.000	1.000	1.000
		Weighted mode	116	0.03	1.000	1.000	1.000
		Inverse variance weighted (multiplicative random effects)	116	0.001	1.000	1.000	1.000
	Ptforce	Inverse variance weighted	10	0.94	1.000	1.000	1.000
		MR Egger	10	0.36	1.000	1.000	1.000
		Weighted median	10	0.51	1.000	1.000	1.000
		Weighted mode	10	0.52	1.000	1.000	1.000
		Inverse variance weighted (multiplicative random effects)	10	0.92	1.000	1.000	1.000
	Pwave Duration	Inverse variance weighted	4	0.007	1.000	1.000	1.000
		MR Egger	4	0.72	1.001	0.996	1.006
		Weighted median	4	0.02	1.000	0.999	1.000
		Weighted mode	4	0.16	1.000	0.999	1.000
		Inverse variance weighted (multiplicative random effects)	4	<0.001	1.000	1.000	1.000
	Twave_anterior	Inverse variance weighted	7	0.68	1.000	0.998	1.001
		MR Egger	7	0.68	1.001	0.996	1.006
		Weighted median	7	0.75	1.000	0.998	1.001
		Weighted mode	7	0.76	1.000	0.998	1.001
		Inverse variance weighted (multiplicative random effects)	7	0.68	1.000	0.998	1.001
Twave_avr	Inverse variance weighted	5	0.87	1.000	0.999	1.001	
	MR Egger	5	0.77	1.001	0.997	1.004	
	Weighted median	5	0.88	1.000	0.999	1.001	
	Weighted mode	5	0.89	1.000	0.999	1.001	
	Inverse variance weighted (multiplicative random effects)	5	0.87	1.000	0.999	1.001	
Twave_inferior	Inverse variance weighted	8	0.50	1.000	0.998	1.001	
	MR Egger	8	0.14	1.003	1.000	1.006	
	Weighted median	8	0.75	1.000	0.998	1.001	
	Weighted mode	8	0.85	1.000	0.998	1.001	
	Inverse variance weighted (multiplicative random effects)	8	0.50	1.000	0.998	1.001	
Twave_lateral	Inverse variance weighted	4	0.45	1.000	0.998	1.001	
	MR Egger	4	0.93	1.000	0.995	1.006	
	Weighted median	4	0.61	1.000	0.998	1.001	
	Weighted mode	4	0.91	1.000	0.998	1.001	
	Inverse variance weighted (multiplicative random effects)	4	0.33	1.000	0.999	1.000	
Twave_septal	Inverse variance weighted	6	0.40	1.001	0.999	1.002	
	MR Egger	6	0.22	0.998	0.994	1.001	
	Weighted median	6	0.83	1.000	0.998	1.001	
	Weighted mode	6	0.43	0.999	0.998	1.001	
	Inverse variance weighted (multiplicative random effects)	6	0.40	1.001	0.999	1.002	

nSNP, number of SNPs used as instrumental variables; SNP, single-nucleotide polymorphism; OR, odds ratio; or\_lci95, lower limit of the odds ratio; or\_uci95, upper limit of the odds ratio; AF, atrial fibrillation; HR, resting heart rate; Twave, T-wave top amplitude; septal, ECG lead V1 + V2; lateral, ECG lead I + aVL + V5 + V6; inferior, ECG lead II + III + aVF; anterior, ECG lead V3 + V4 + aVL; avr, ECG lead aVR; Ptforce: P-wave terminal force; Pwave duration, P-wave duration; PR, PR interval; HRV, heart rate variability; RMSSD, root mean square of successive differences; pvRSA/HF, peak-valley respiratory sinus arrhythmia or high frequency power; SDNN, standard deviation of the normal-to-normal interval.

**Table S3** Results of heterogeneity test

Outcome	Exposure	Method	Q	Q_df	Q_pval	I <sup>2</sup>
Atrial fibrillation	HR	Inverse variance weighted	17.595	11	0.091	37.482%
		Inverse variance weighted (multiplicative random effects)	17.595	11	0.091	37.482%
	HR	MR Egger	16.237	10	0.093	38.413%
	HRV_RMSSD	MR Egger	2.266	4	0.687	0
	HRV_RMSSD	Inverse variance weighted	4.090	5	0.537	0
	HRV_RMSSD	Inverse variance weighted (multiplicative random effects)	4.090	5	0.537	0
	HRV_pvRSA/HF	MR Egger	1.620	2	0.445	0
	HRV_pvRSA/HF	Inverse variance weighted	3.293	3	0.349	8.893%
	HRV_pvRSA/HF	Inverse variance weighted (multiplicative random effects)	3.293	3	0.349	8.893%
	HRV_SDNN	Inverse variance weighted	23.366	16	0.104	31.526%
	HRV_SDNN	Inverse variance weighted (multiplicative random effects)	23.366	16	0.104	31.526%
	HRV_SDNN	MR Egger	22.952	15	0.085	34.647%
	PR	Inverse variance weighted	142.605	155	0.754	0
	PR	Inverse variance weighted (multiplicative random effects)	142.605	155	0.754	0
	PR	MR Egger	142.487	154	0.737	0
	Ptforce	Inverse variance weighted	18.606	21	0.610	0
	Ptforce	Inverse variance weighted (multiplicative random effects)	18.606	21	0.610	0
	Ptforce	MR Egger	18.407	20	0.561	0
	Pwave Duration	Inverse variance weighted	0.454	3	0.929	0
	Pwave Duration	Inverse variance weighted (multiplicative random effects)	0.454	3	0.929	0
	Pwave Duration	MR Egger	0.365	2	0.833	0
	Pwave Duration	Inverse variance weighted	7.337	9	0.602	0
	Pwave Duration	Inverse variance weighted (multiplicative random effects)	7.337	9	0.602	0
	Pwave Duration	MR Egger	6.573	8	0.583	0
	Twave_anterior	Inverse variance weighted	13.471	19	0.814	0
	Twave_anterior	Inverse variance weighted (multiplicative random effects)	13.471	19	0.814	0
	Twave_anterior	MR Egger	13.405	18	0.767	0
	Twave_avr	Inverse variance weighted	19.693	15	0.184	23.830%
	Twave_avr	Inverse variance weighted (multiplicative random effects)	19.693	15	0.184	23.830%
	Twave_avr	MR Egger	18.524	14	0.184	24.421%
	Twave_inferior	Inverse variance weighted	10.084	13	0.687	0
	Twave_inferior	Inverse variance weighted (multiplicative random effects)	10.084	13	0.687	0
	Twave_inferior	MR Egger	10.011	12	0.615	0
Twave_lateral	MR Egger	12.383	7	0.089	43.473%	
Twave_lateral	Inverse variance weighted	14.258	8	0.075	43.893%	
Twave_lateral	Inverse variance weighted (multiplicative random effects)	14.258	8	0.075	43.893%	
Twave_septal	Inverse variance weighted	17.595	11	0.091	37.482%	
Twave_septal	Inverse variance weighted (multiplicative random effects)	17.595	11	0.091	37.482%	
Twave_septal	MR Egger	16.237	10	0.093	38.413%	
Bradycardia	HR	Inverse variance weighted	9.612	9	0.383	6.367%
		MR Egger	8.506	8	0.386	5.953%
		Inverse variance weighted (multiplicative random effects)	9.612	9	0.383	6.367%
	HRV_RMSSD	Inverse variance weighted	13.940	17	0.671	0
		MR Egger	13.921	16	0.605	0
		Inverse variance weighted (multiplicative random effects)	13.940	17	0.671	0
	HRV_pvRSA/HF	Inverse variance weighted	7.298	5	0.199	31.492%
		MR Egger	7.275	4	0.122	45.019%
		Inverse variance weighted (multiplicative random effects)	7.298	5	0.199	31.492%
	HRV_SDNN	Inverse variance weighted	11.281	9	0.257	20.217%
		MR Egger	9.450	8	0.306	15.347%
		Inverse variance weighted (multiplicative random effects)	11.281	9	0.257	20.217%
	PR	Inverse variance weighted	107.607	101	0.308	6.140%
		MR Egger	107.586	100	0.284	7.051%
		Inverse variance weighted (multiplicative random effects)	107.607	101	0.308	6.140%
Ptforce	Inverse variance weighted	7.320	9	0.604	0	
	MR Egger	7.252	8	0.510	0	
	Inverse variance weighted (multiplicative random effects)	7.320	9	0.604	0	

Table S3 (continued)



Table S3 (continued)

Outcome	Exposure	Method	Q	Q_df	Q_pval	I <sup>2</sup>	
Supraventricular tachycardia	Pwave Duration	Inverse variance weighted	1.576	3	0.665	0	
		MR Egger	1.434	2	0.488	0	
		Inverse variance weighted (multiplicative random effects)	1.576	3	0.665	0	
		MR Egger	1.299	2	0.522	0	
		Inverse variance weighted (multiplicative random effects)	1.353	3	0.717	0	
	Twave_anterior	Inverse variance weighted	7.400	6	0.285	18.917%	
		MR Egger	7.121	5	0.212	29.784%	
		Inverse variance weighted (multiplicative random effects)	7.400	6	0.285	18.917%	
	Twave_avr	Inverse variance weighted	0.884	3	0.829	0	
		MR Egger	0.195	2	0.907	0	
		Inverse variance weighted (multiplicative random effects)	0.884	3	0.829	0	
	Twave_inferior	Inverse variance weighted	9.769	6	0.135	38.583%	
		MR Egger	3.940	5	0.558	0	
		Inverse variance weighted (multiplicative random effects)	9.769	6	0.135	38.583%	
	Twave_lateral	Inverse variance weighted	7.979	7	0.334	12.271%	
		MR Egger	7.979	6	0.240	24.804%	
		Inverse variance weighted (multiplicative random effects)	7.979	7	0.334	12.271%	
	Twave_septal	Inverse variance weighted	3.403	4	0.493	0	
		MR Egger	0.390	3	0.942	0	
		Inverse variance weighted (multiplicative random effects)	3.403	4	0.493	0	
	HR	Inverse variance weighted	Inverse variance weighted	7.357	9	0.600	0
			MR Egger	5.700	8	0.681	0
			Inverse variance weighted (multiplicative random effects)	7.357	9	0.600	0
		HRV_RMSSD	Inverse variance weighted	4.580	3	0.205	34.503%
			MR Egger	2.906	2	0.234	31.176%
			Inverse variance weighted (multiplicative random effects)	4.580	3	0.205	34.503%
		HRV_pvRSA/HF	Inverse variance weighted	3.924	3	0.270	23.552%
			MR Egger	3.369	2	0.186	40.639%
			Inverse variance weighted (multiplicative random effects)	3.924	3	0.270	23.552%
	HRV_SDNN	Inverse variance weighted	9.032	9	0.434	0.359%	
MR Egger		8.845	8	0.356	9.551%		
Inverse variance weighted (multiplicative random effects)		9.032	9	0.434	0.359%		
PR	Inverse variance weighted	113.915	115	0.511	0		
	MR Egger	113.152	114	0.505	0		
	Inverse variance weighted (multiplicative random effects)	113.915	115	0.511	0		
Ptforce	Inverse variance weighted	5.792	9	0.761	0		
	MR Egger	4.813	8	0.777	0		
	Inverse variance weighted (multiplicative random effects)	5.792	9	0.761	0		
Pwave Duration	Inverse variance weighted	0.276	3	0.965	0		
	MR Egger	0.009	2	0.995	0		
	Inverse variance weighted (multiplicative random effects)	0.276	3	0.965	0		
Twave_anterior	Inverse variance weighted	10.546	6	0.103	43.105%		
	MR Egger	9.844	5	0.080	49.208%		
	Inverse variance weighted (multiplicative random effects)	10.546	6	0.103	43.105%		
Twave_avr	Inverse variance weighted	4.522	4	0.340	11.535%		
	MR Egger	4.393	3	0.222	31.711%		
	Inverse variance weighted (multiplicative random effects)	4.522	4	0.340	11.535%		
Twave_inferior	Inverse variance weighted	10.088	7	0.184	30.609%		
	MR Egger	5.881	6	0.437	0		
	Inverse variance weighted (multiplicative random effects)	10.088	7	0.184	30.609%		
Twave_lateral	Inverse variance weighted	1.843	3	0.606	0		
	MR Egger	1.770	2	0.413	0		
	Inverse variance weighted (multiplicative random effects)	1.843	3	0.606	0		
Twave_septal	Inverse variance weighted	5.734	5	0.333	12.807%		
	MR Egger	2.131	4	0.712	0		
	Inverse variance weighted (multiplicative random effects)	5.734	5	0.333	12.807%		

AF, atrial fibrillation; HR, resting heart rate; Twave, T-wave top amplitude; septal, ECG lead V1 + V2; lateral, ECG lead I + aVL + V5 + V6; inferior, ECG lead II + III + aVF; anterior, ECG lead V3 + V4 + aVL; avr, ECG lead aVR; Ptforce, P-wave terminal force; Pwave duration, P-wave duration; PR, PR interval; HRV, heart rate variability; RMSSD, root mean square of successive differences; pvRSA/HF, peak-valley respiratory sinus arrhythmia or high frequency power; SDNN, standard deviation of the normal-to-normal interval.

**Table S4** Results of MR-Egger intercept test

Outcome	Exposure	egger_intercept	se	P value
AF	HR	-0.016	0.017	0.382
	HRV_RMSSD	0.017	0.012	0.248
	HRV_pvRSA/HF	0.015	0.012	0.325
	HRV_SDNN	-0.008	0.016	0.610
	PR	-0.001	0.003	0.732
	Ptforce	0.002	0.004	0.661
	Pwave Duration	0.006	0.021	0.794
	Twave_anterior	0.004	0.004	0.408
	Twave_avr	-0.002	0.008	0.800
	Twave_inferior	0.013	0.013	0.363
	Twave_lateral	-0.002	0.006	0.791
	Twave_septal	-0.017	0.017	0.338
Bradycardia	HR	0.000	0.000	0.338
	HRV_RMSSD	0.000	0.000	0.892
	HRV_pvRSA/HF	0.000	0.000	0.915
	HRV_SDNN	0.000	0.000	0.248
	PR	0.000	0.000	0.889
	Ptforce	0.000	0.000	0.801
	Pwave Duration	0.000	0.001	0.743
	Twave_anterior	0.000	0.000	0.677
	Twave_avr	0.000	0.000	0.494
	Twave_inferior	0.000	0.000	0.061
	Twave_lateral	0.000	0.000	0.998
	Twave_septal	-0.001	0.000	0.181
Supraventricular tachycardia	HR	0.000	0.000	0.234
	HRV_RMSSD	0.001	0.000	0.395
	HRV_pvRSA/HF	0.000	0.000	0.624
	HRV_SDNN	0.000	0.000	0.691
	PR	0.000	0.000	0.384
	Ptforce	0.000	0.000	0.351
	Pwave Duration	-0.001	0.001	0.657
	Twave_anterior	0.000	0.000	0.577
	Twave_avr	0.000	0.000	0.786
	Twave_inferior	0.000	0.000	0.086
	Twave_lateral	0.000	0.000	0.811
	Twave_septal	0.000	0.000	0.130

AF, atrial fibrillation; HR, resting heart rate; Twave, T-wave top amplitude; septal, ECG lead V1 + V2; lateral: ECG lead I + aVL + V5 + V6; inferior, ECG lead II + III + aVF; anterior, ECG lead V3 + V4 + aVL; avr, ECG lead aVR; Ptforce, P-wave terminal force; Pwave duration, P-wave duration; PR, PR interval; HRV, heart rate variability; RMSSD, root mean square of successive differences; pvRSA/HF, peak-valley respiratory sinus arrhythmia or high frequency power; SDNN, standard deviation of the normal-to-normal interval.

Table S5 Results of CAUSE

Outcome	Exposure	Model	Gamma	Eta	Q	P		
AF	HR	Sharing		-0.04 (-0.14, 0.13)	0.08 (0, 0.32)	0.29		
		Causal	-0.02 (-0.03, 0)	0.02 (-0.12, 0.19)	0.05 (0, 0.27)	0.27		
	HRV_RMSSD	Sharing			0.24 (-1.7, 1.79)	0.05 (0, 0.26)	0.93	
		Causal	0.12 (-0.08, 0.32)	-0.15 (-1.85, 1.59)	0.05 (0, 0.27)	0.63		
	HRV_pvRSA/HF	Sharing			0.37 (-0.89, 1.68)	0.05 (0, 0.25)	0.62	
		Causal	0.09 (-0.03, 0.21)	0.12 (-1.06, 1.6)	0.04 (0, 0.24)	0.43		
	HRV_SDNN	Sharing			0.98 (-2.25, 3)	0.07 (0, 0.31)	0.32	
		Causal	0.32 (-0.06, 0.69)	-0.13 (-3.11, 2.68)	0.05 (0, 0.27)	0.31		
	PR	Sharing			0.01 (-0.08, 0.1)	0.03 (0, 0.2)	0.90	
		Causal	0 (0, 0.01)	0.01 (-0.08, 0.08)	0.05 (0, 0.28)	0.96		
	Ptforce	Sharing			0 (0, 0)	0.02 (0, 0.17)	0.95	
		Causal	0 (0, 0)	0 (0, 0)	0 (0, 0)	0.04 (0, 0.26)	0.96	
	Pwave Duration	Sharing			-0.02 (-0.19, 0.1)	0.02 (0, 0.15)	0.87	
		Causal	0 (-0.01, 0.01)	-0.03 (-0.07, 0.06)	0.09 (0, 0.31)	0.56		
	Twave_anterior	Sharing			-0.1 (-1.07, 0.97)	0.06 (0, 0.26)	0.81	
		Causal	-0.04 (-0.24, 0.15)	-0.02 (-1.04, 1.03)	0.06 (0, 0.29)	0.98		
	Twave_avr	Sharing			0.07 (-1.07, 1.22)	0.07 (0, 0.31)	0.30	
		Causal	0.2 (-0.39, 0.79)	0.02 (-1.15, 1.18)	0.07 (0, 0.33)	0.77		
	Twave_inferior	Sharing			-0.02 (-1.03, 0.96)	0.05 (0, 0.26)	1.00	
		Causal	0 (-0.19, 0.18)	-0.02 (-1.03, 0.95)	0.05 (0, 0.28)	1.00		
	Twave_lateral	Sharing			-0.03 (-1.51, 1.4)	0.07 (0, 0.31)	0.43	
		Causal	-0.07 (-0.84, 0.7)	-0.02 (-1.52, 1.45)	0.07 (0, 0.33)	1.00		
	Twave_septal	Sharing			0.14 (-0.73, 0.97)	0.06 (0, 0.29)	0.69	
		Causal	0.1 (-0.1, 0.3)	0.03 (-0.8, 0.91)	0.06 (0, 0.29)	0.70		
	Bradycardia	HR	Sharing		0 (0, 0)	0.27 (0.06, 0.52)	0.01	
			Causal	0 (0, 0)	0 (0, 0)	0.05 (0, 0.26)	0.02	
		HRV_RMSSD	Sharing			0 (-0.01, 0.01)	0.1 (0, 0.35)	0.22
			Causal	0 (0, 0)	0 (-0.01, 0.01)	0.05 (0, 0.28)	0.20	
		HRV_pvRSA/HF	Sharing			0 (-0.01, 0.01)	0.06 (0, 0.26)	0.89
			Causal	0 (0, 0)	0 (-0.01, 0.01)	0.07 (0, 0.31)	1.00	
HRV_SDNN		Sharing			0.01 (-0.02, 0.02)	0.07 (0, 0.32)	0.36	
		Causal	0 (0, 0.01)	0 (-0.02, 0.02)	0.05 (0, 0.28)	0.33		
PR		Sharing			0 (0, 0)	0.05 (0, 0.26)	0.55	
		Causal	0 (0, 0)	0 (0, 0)	0.05 (0, 0.3)	0.57		
Ptforce		Sharing			0 (0, 0)	0.08 (0, 0.31)	0.30	
		Causal	NA	0 (0, 0)	0.05 (0, 0.28)	0.28		
Pwave Duration		Sharing			0 (0, 0)	0.06 (0, 0.24)	0.46	
		Causal	0 (0, 0)	0 (0, 0)	0.07 (0, 0.32)	0.55		
Twave_anterior		Sharing			0 (-0.01, 0.01)	0.06 (0, 0.31)	0.47	
		Causal	0 (0, 0)	0 (-0.01, 0.01)	0.06 (0, 0.29)	0.43		
Twave_avr		Sharing			0 (0, 0.01)	0.05 (0, 0.25)	1.00	
		Causal	0 (0, 0)	0 (0, 0.01)	0.06 (0, 0.3)	1.00		
Twave_inferior		Sharing			0 (0, 0.01)	0.06 (0, 0.3)	0.52	
		Causal	0 (0, 0)	0 (-0.01, 0)	0.06 (0, 0.29)	0.43		
Twave_lateral		Sharing			0 (-0.01, 0.01)	0.06 (0, 0.27)	0.95	
		Causal	0 (0, 0)	0 (-0.01, 0.01)	0.07 (0, 0.32)	0.96		
Twave_septal		Sharing			0 (-0.01, 0.01)	0.06 (0, 0.27)	0.81	
		Causal	0 (0, 0)	0 (-0.01, 0.01)	0.07 (0, 0.3)	0.99		
Supraventricular tachycardia		HR	Sharing		0 (0, 0)	0.05 (0, 0.26)	0.87	
			Causal	0 (0, 0)	0 (0, 0)	0.06 (0, 0.3)	0.79	
		HRV_RMSSD	Sharing			0 (-0.02, 0.01)	0.05 (0, 0.27)	0.56
			Causal	0 (0, 0)	0 (-0.02, 0.01)	0.05 (0, 0.26)	0.52	
		HRV_pvRSA/HF	Sharing			0 (-0.01, 0.01)	0.04 (0, 0.24)	0.98
			Causal	0 (0, 0)	0 (-0.01, 0.01)	0.05 (0, 0.28)	1.00	
	HRV_SDNN	Sharing			0 (-0.02, 0.02)	0.05 (0, 0.26)	0.99	
		Causal	0 (0, 0)	0 (-0.02, 0.02)	0.05 (0, 0.28)	0.98		
	PR	Sharing			0 (0, 0)	0.16 (0.01, 0.43)	0.07	
		Causal	0 (0, 0)	0 (0, 0)	0.03 (0, 0.23)	0.06		
	Ptforce	Sharing			0 (0, 0)	0.09 (0, 0.34)	0.24	
		Causal	0 (0, 0)	0 (0, 0)	0.04 (0, 0.26)	0.20		
	Pwave Duration	Sharing			0 (0, 0)	0.04 (0, 0.22)	0.97	
		Causal	0 (0, 0)	0 (0, 0)	0.05 (0, 0.28)	0.98		
	Twave_anterior	Sharing			0 (-0.01, 0.01)	0.06 (0, 0.29)	0.80	
		Causal	0 (0, 0)	0 (-0.01, 0.01)	0.06 (0, 0.3)	0.69		
	Twave_avr	Sharing			0 (0, 0.01)	0.07 (0, 0.32)	0.38	
		Causal	0 (0, 0)	0 (-0.01, 0)	0.05 (0, 0.27)	0.30		
	Twave_inferior	Sharing			0 (-0.01, 0.01)	0.07 (0, 0.3)	0.37	
		Causal	0 (0, 0)	0 (-0.01, 0.01)	0.07 (0, 0.3)	0.55		
	Twave_lateral	Sharing			0 (-0.01, 0.01)	0.05 (0, 0.27)	0.88	
		Causal	0 (0, 0)	0 (-0.01, 0.01)	0.06 (0, 0.28)	0.60		
	Twave_septal	Sharing			0 (0, 0.01)	0.07 (0, 0.33)	0.36	
		Causal	0 (0, 0)	0 (-0.01, 0.01)	0.06 (0, 0.29)	0.26		

AF, atrial fibrillation; HR, resting heart rate; Twave, T-wave top amplitude; septal, ECG lead V1 + V2; lateral, ECG lead I + aVL + V5 + V6; inferior: ECG lead II + III + aVF; anterior: ECG lead V3 + V4 + aVL; avr, ECG lead aVR; Ptforce, P-wave terminal force; Pwave duration, P-wave duration; PR, PR interval; HRV, heart rate variability; RMSSD, root mean square of successive differences; pvRSA/HF, peak-valley respiratory sinus arrhythmia or high frequency power; SDNN, standard deviation of the normal-to-normal interval; Sharing, means two traits have shared genetics; Causal, means the exposure can causally affect the outcome; Gamma, the effect size of exposure on outcome; Eta: the effect size of correlated pleiotropy; Q, the proportion of variants exhibiting correlated pleiotropy; P, the probability of accepting the model.

**Table S6** Results of multivariable Mendelian randomization

Outcome	Methods	Exposure	nSNP	OR	or_lci95	or_uci95	pval
AF	MVMR-IVW	HRV_RMSSD	98	1.538	0.995	2.379	0.053
	MVMR-Egger	HRV_RMSSD	98	1.576	1.014	2.450	0.04
	MVMR-Lasso	HRV_RMSSD	98	1.538	0.995	2.379	0.053
	MVMR-Median	HRV_RMSSD	98	1.737	1.140	2.646	0.01
	MVMR-PRESSO	HRV_RMSSD	98	1.538	0.997	2.374	0.055
	MVMR-IVW	Twave_avr	98	1.007	0.948	1.069	0.82
	MVMR-Egger	Twave_avr	98	1.007	0.948	1.069	0.82
	MVMR-Lasso	Twave_avr	98	1.007	0.948	1.069	0.82
	MVMR-Median	Twave_avr	98	1.017	0.935	1.106	0.70
	MVMR-PRESSO	Twave_avr	98	1.007	0.949	1.069	0.82
	MVMR-IVW	PR	98	1.000	0.995	1.005	0.95
	MVMR-Egger	PR	98	1.000	0.995	1.005	0.96
	MVMR-Lasso	PR	98	1.000	0.995	1.005	0.95
	MVMR-Median	PR	98	1.001	0.994	1.008	0.81
	MVMR-PRESSO	PR	98	1.000	0.995	1.005	0.95
	MVMR-IVW	HRV_SDNN	98	0.515	0.278	0.954	0.03
	MVMR-Egger	HRV_SDNN	98	0.529	0.284	0.983	0.04
	MVMR-Lasso	HRV_SDNN	98	0.515	0.278	0.954	0.03
	MVMR-Median	HRV_SDNN	98	0.392	0.217	0.705	0.002
	MVMR-PRESSO	HRV_SDNN	98	0.515	0.279	0.951	0.04
Bradycardia	MVMR-IVW	HR	32	1.000	1.000	1.000	0.25
	MVMR-Egger	HR	32	1.000	1.000	1.001	0.13
	MVMR-Lasso	HR	32	1.000	1.000	1.000	0.25
	MVMR-Median	HR	32	1.000	1.000	1.000	0.49
	MVMR-PRESSO	HR	32	1.000	1.000	1.000	0.26
	MVMR-IVW	HRV_RMSSD	32	1.007	1.000	1.015	0.06
	MVMR-Egger	HRV_RMSSD	32	1.007	0.999	1.015	0.09
	MVMR-Lasso	HRV_RMSSD	32	1.007	1.000	1.015	0.06
	MVMR-Median	HRV_RMSSD	32	1.007	0.999	1.014	0.10
	MVMR-PRESSO	HRV_RMSSD	32	1.007	1.000	1.015	0.07
	MVMR-IVW	HRV_SDNN	32	0.988	0.976	1.000	0.045
	MVMR-Egger	HRV_SDNN	32	0.989	0.977	1.001	0.06
	MVMR-Lasso	HRV_SDNN	32	0.988	0.976	1.000	0.045
	MVMR-Median	HRV_SDNN	32	0.992	0.98	1.004	0.19
	MVMR-PRESSO	HRV_SDNN	32	0.988	0.976	1.000	0.055
	MVMR-IVW	Twave_avr	32	0.998	0.996	0.999	<0.001
	MVMR-Egger	Twave_avr	32	0.998	0.997	0.999	0.005
	MVMR-Lasso	Twave_avr	32	0.998	0.996	0.999	<0.001
	MVMR-Median	Twave_avr	32	0.998	0.997	0.999	0.004
	MVMR-PRESSO	Twave_avr	32	0.998	0.996	0.999	0.001
Bradycardia	MVMR-IVW	HR	35	1.000	1.000	1.000	0.08
	MVMR-Egger	HR	35	1.000	1.000	1.001	0.08
	MVMR-Lasso	HR	35	1.000	1.000	1.000	0.08
	MVMR-Median	HR	35	1.000	1.000	1.001	0.17
	MVMR-PRESSO	HR	35	1.000	1.000	1.000	0.09
	MVMR-IVW	HRV_RMSSD	35	1.008	1.000	1.016	0.04
	MVMR-Egger	HRV_RMSSD	35	1.008	1.000	1.016	0.048
	MVMR-Lasso	HRV_RMSSD	35	1.008	1.000	1.016	0.04
	MVMR-Median	HRV_RMSSD	35	1.011	0.999	1.022	0.07
	MVMR-PRESSO	HRV_RMSSD	35	1.008	1.000	1.016	0.049
	MVMR-IVW	HRV_SDNN	35	0.988	0.977	1.000	0.04
	MVMR-Egger	HRV_SDNN	35	0.988	0.977	1.000	0.04
	MVMR-Lasso	HRV_SDNN	35	0.988	0.977	1.000	0.04
	MVMR-Median	HRV_SDNN	35	0.985	0.968	1.002	0.07
	MVMR-PRESSO	HRV_SDNN	35	0.988	0.977	1.000	0.050
	MVMR-IVW	Twave_anterior	35	1.000	0.998	1.001	0.57
	MVMR-Egger	Twave_anterior	35	1.000	0.998	1.001	0.73
	MVMR-Lasso	Twave_anterior	35	1.000	0.998	1.001	0.57
	MVMR-Median	Twave_anterior	35	0.999	0.996	1.002	0.37
	MVMR-PRESSO	Twave_anterior	35	1.000	0.998	1.001	0.58
Supraventricular tachycardia	MVMR-IVW	HR	8	1.000	0.999	1.000	0.19
	MVMR-Egger	HR	8	1.000	0.999	1.001	0.48
	MVMR-Lasso	HR	8	1.000	0.999	1.000	0.19
	MVMR-Median	HR	8	1.000	0.999	1.000	0.19
	MVMR-PRESSO	HR	8	1.000	0.999	1.000	0.24
	MVMR-IVW	Pwave duration	8	1.000	1.000	1.000	0.62
	MVMR-Egger	Pwave duration	8	1.000	0.999	1.000	0.18
	MVMR-Lasso	Pwave duration	8	1.000	1.000	1.000	0.62
	MVMR-Median	Pwave duration	8	1.000	1.000	1.000	0.10
	MVMR-PRESSO	Pwave duration	8	1.000	1.000	1.000	0.63

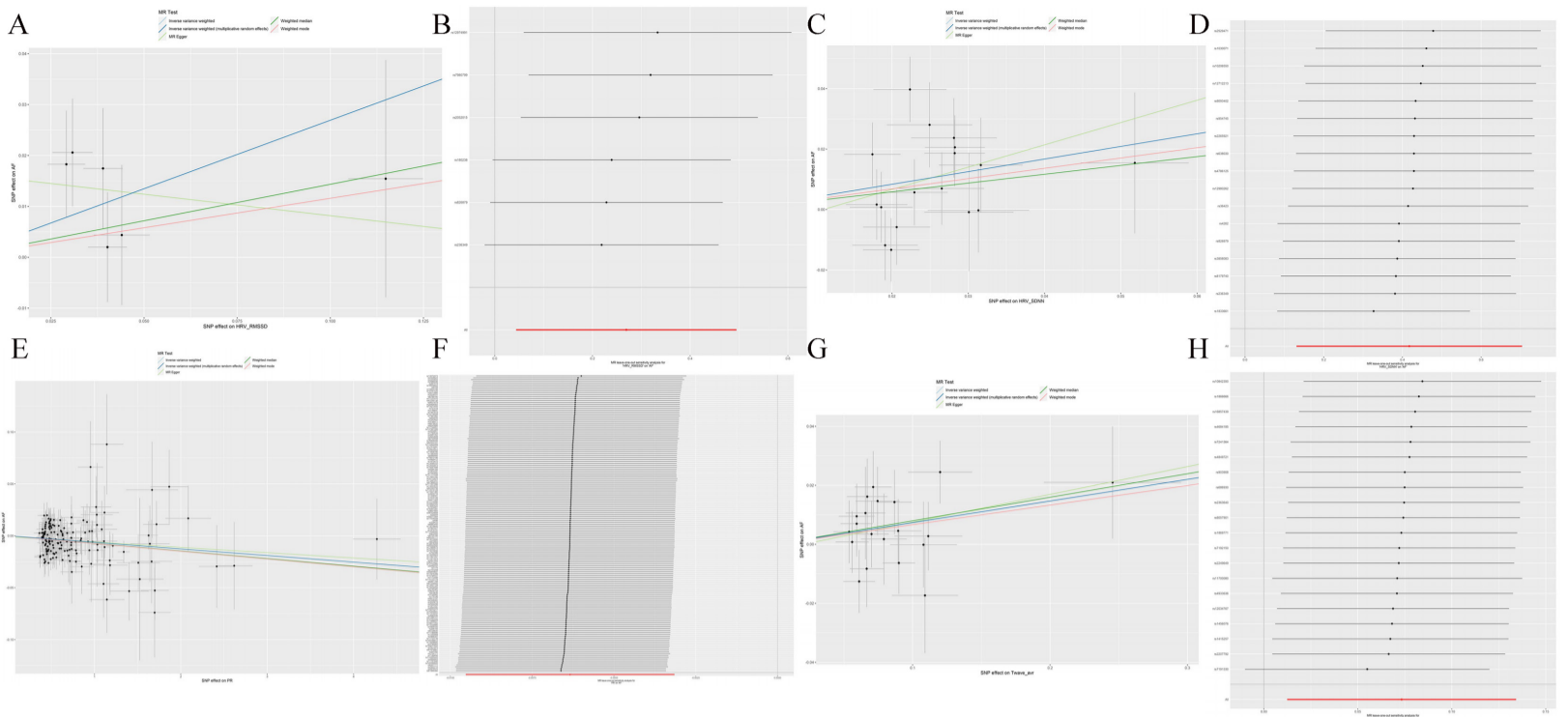
nSNP, number of SNPs used as instrumental variables; pval, P value; or\_lci95, lower limit of the odds ratio; or\_uci95, upper limit of the odds ratio; MVMR, Multivariate Mendel randomization; IVW, inverse-variance weighted; OR, odds ratio; SNP, single-nucleotide polymorphism; AF, atrial fibrillation; HR, resting heart rate; HRV, heart rate variability; RMSSD, root mean square of successive differences; pVRSa/HF, peak-valley respiratory sinus arrhythmia or high frequency power; SDNN, standard deviation of the normal-to-normal interval; Twave, T-wave top amplitude; anterior, ECG lead V3 + V4 + aVL; avr, ECG lead aVR; Pwave duration, P-wave duration.

Table S7 Power for Mendelian randomization

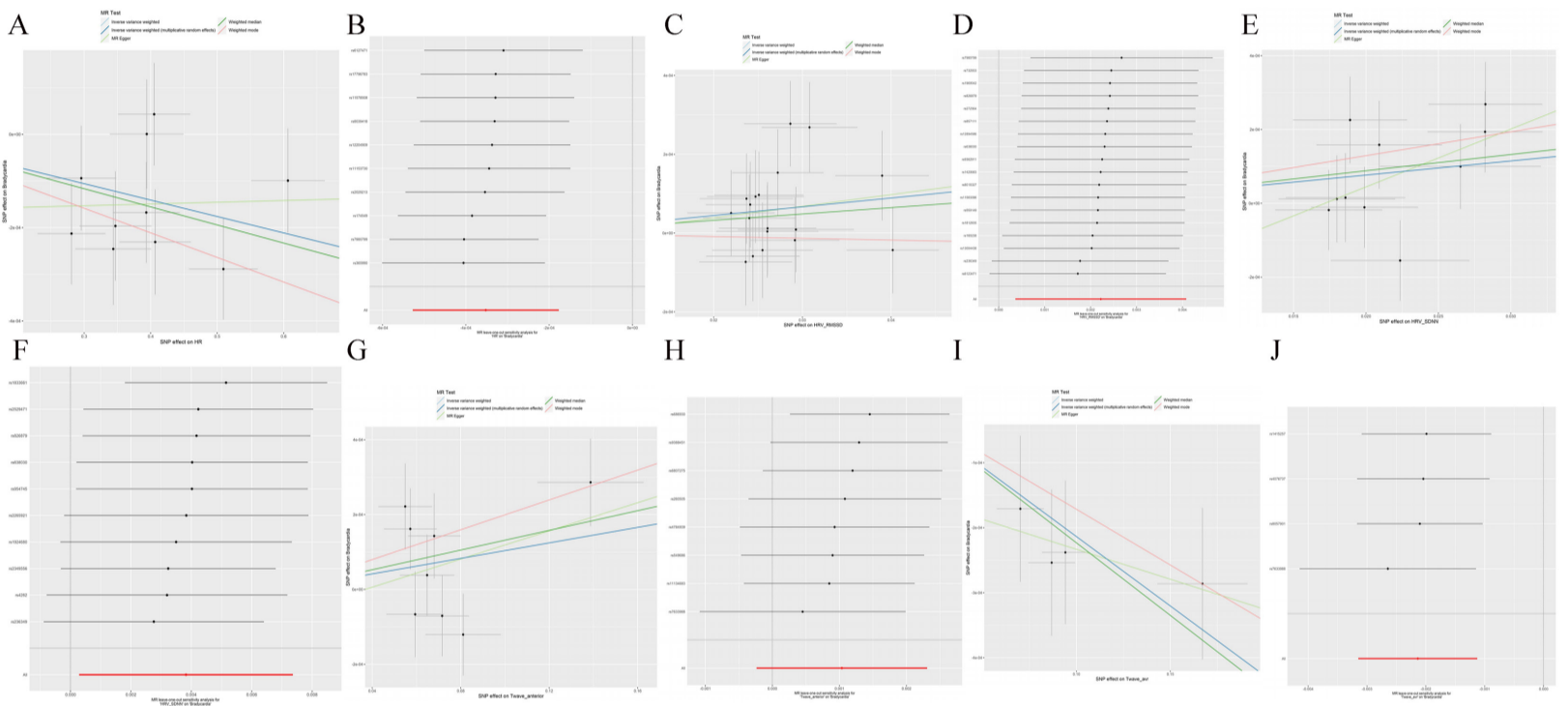
Outcome	Exposures	Power
AF	HR	0.05
	HRV_RMSSD	0.23
	HRV_pvRSAHF	0.07
	HRV_SDNN	0.69
	PR interval	0.05
	P-wave duration	NA
	P-wave terminal force	NA
	Twave_anterior	0.05
	Twave_avr	0.07
	Twave_inferior	0.05
	Twave_lateral	0.05
	Twave_septal	0.07
	Bradycardia	HR
HRV_RMSSD		0.05
HRV_pvRSAHF		0.05
HRV_SDNN		0.05
PR interval		0.05
P-wave duration		NA
P-wave terminal force		NA
Twave_anterior		0.05
Twave_avr		0.05
Twave_inferior		0.05
Twave_lateral		0.05
Twave_septal		0.05
Supraventricular tachycardia		HR
	HRV_RMSSD	0.05
	HRV_pvRSAHF	0.05
	HRV_SDNN	0.05
	PR interval	0.05
	P-wave duration	NA
	P-wave terminal force	NA
	Twave_anterior	0.05
	Twave_avr	0.05
	Twave_inferior	0.05
	Twave_lateral	0.05
	Twave_septal	0.05

Online tools were used to calculate the power of Mendelian randomization (<https://shiny.cnsgenomics.com/mRnd/>). The  $R^2$  used in the calculation is determined by the formula:  $R^2 = 2 \times (1 - \text{MAF}) \times \text{MAF} \times \beta^2 / (\text{se}^2 \times N)$ . Given that the GWAS data for P-wave duration and P-wave terminal force did not provide effect allele frequencies, we did not calculate power for P-wave duration and P-wave terminal force. AF, atrial fibrillation; HR, resting heart rate; Twave, T-wave top amplitude; septal: ECG lead V1 + V2; lateral: ECG lead I + aVL + V5 + V6; inferior: ECG lead II + III + aVF; anterior: ECG lead V3 + V4 + aVL; avr, ECG lead aVR; HRV, heart rate variability; RMSSD, root mean square of successive differences; pvRSA/HF, peak-valley respiratory sinus arrhythmia or high frequency power; SDNN, standard deviation of the normal-to-normal interval.

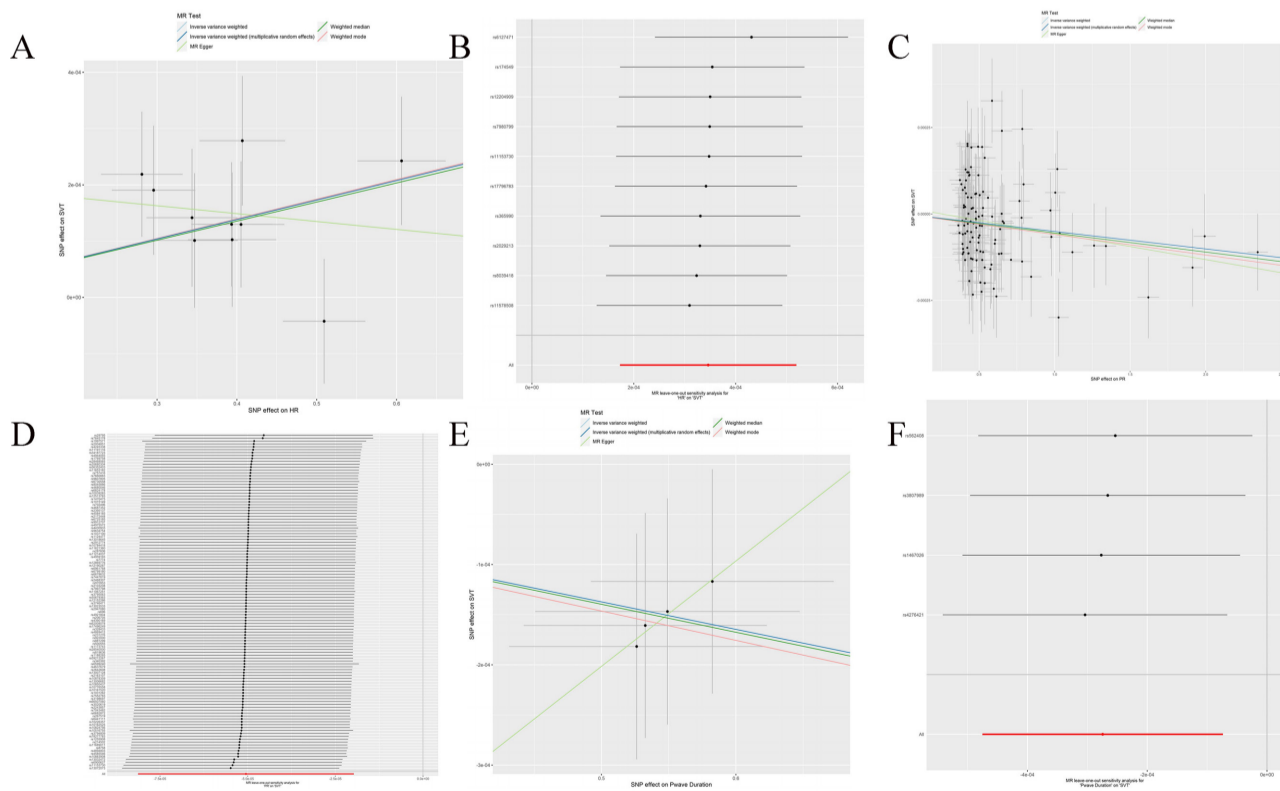
**Appendix 2**



**Figure S1** Visualization of Atrial fibrillation outcomes. (A) Scatter plot of HRV-RMSSD and AF; (B) Leave one out plot of HRV-RMSSD and AF; (C) Scatter plot of HRV-SDNN and AF; (D) Leave one out plot of HRV-SDNN and AF; (E) Scatter plot of PR and AF; (F) Leave one out plot of PR and AF; (G) Scatter plot of Twave\_avr and AF; (H) Leave one out plot of Twave\_avr and AF. Twave, T-wave top amplitude; avr, ECG lead aVR; PR, PR interval; HRV, heart rate variability; RMSSD, root mean square of successive differences; SDNN, standard deviation of the normal-to-normal interval; AF, atrial fibrillation.



**Figure S2** Visualization of bradycardia outcomes. (A) Scatter plot of HR and Bradycardia; (B) Leave one out plot of HR and Bradycardia; (C) Scatter plot of HRV-RMSSD and Bradycardia; (D) Leave one out plot of HRV-RMSSD and Bradycardia; (E) Scatter plot of HRV-SDNN and Bradycardia; (F) Leave one out plot of HRV-SDNN and Bradycardia; (G) Scatter plot of Twave\_anterior and Bradycardia; (H) Leave one out plot of Twave\_anterior and Bradycardia; (I) Scatter plot of Twave\_avr and Bradycardia; (J) Leave one out plot of Twave\_avr and Bradycardia. HR, heart rate (resting); Twave, T-wave top amplitude; anterior, ECG lead V3 + V4 + aVL; avr, ECG lead aVR; HRV, heart rate variability; RMSSD, root mean square of successive differences; SDNN, standard deviation of the normal-to-normal interval.



**Figure S3** Visualization of supraventricular tachycardia outcomes. (A) Scatter plot of HR and SVT; (B) Leave one out plot of HR and SVT; (C) Scatter plot of PR and SVT; (D) Leave one out plot of PR and SVT; (E) Scatter plot of P-wave duration and SVT; (F) Leave one out plot of P-wave duration and SVT. HR, heart rate (resting); PR, PR interval; Pwave duration, P-wave duration; SVT, Supraventricular tachycardia.