

Supplementary Figure S1. Flowchart of the patient inclusion procedure

**Supplementary Table SI.** OR (95% CI) of heart failure risk according to sleep disturbance status

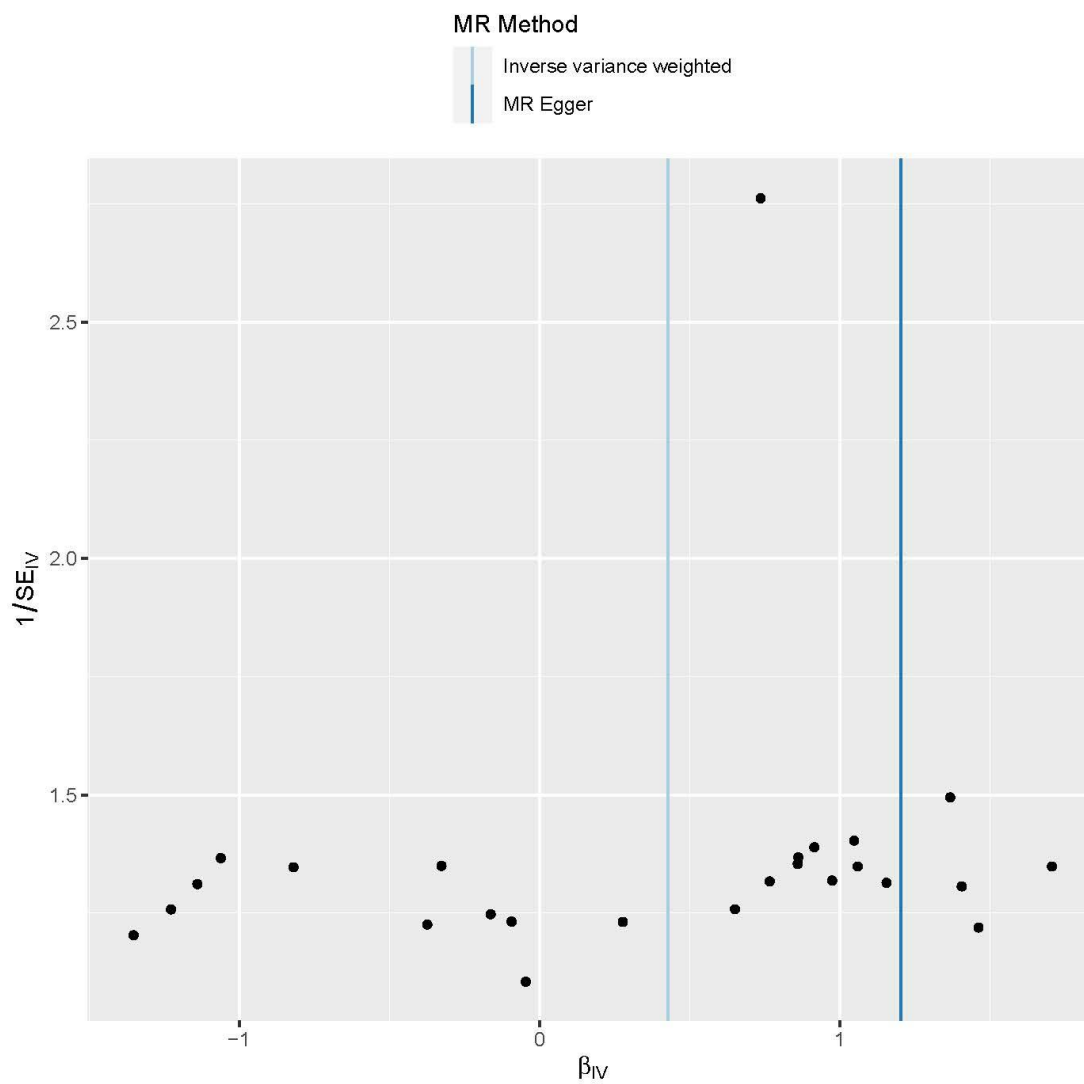
| Variable               | Model 1*          |         | Model 2†          |         | Model 3‡           |         |
|------------------------|-------------------|---------|-------------------|---------|--------------------|---------|
|                        | OR<br>(95% CI)    | P-value | OR<br>(95% CI)    | P-value | OR<br>(95% CI)     | P-value |
| Insomnia               |                   |         |                   |         |                    |         |
| No                     | ref               |         | ref               |         | ref                |         |
| Yes                    | 2.91 (1.58, 5.38) | 0.001   | 3.54 (1.47, 8.51) | 0.01    | 5.10 (1.81, 14.33) | 0.003   |
| Sleep disorder         |                   |         |                   |         |                    |         |
| No                     | ref               |         | ref               |         | ref                |         |
| Yes                    | 3.81 (2.96, 4.90) | <0.001  | 3.81 (2.71, 5.35) | < 0.001 | 3.51 (1.67, 7.39)  | 0.002   |
| Trouble falling asleep |                   |         |                   |         |                    |         |
| No                     | ref               |         | ref               |         | ref                |         |
| Yes                    | 1.51 (1.18, 1.93) | 0.002   | 1.67 (1.29, 2.17) | < 0.001 | 1.55 (1.01, 2.36)  | 0.04    |
| Trouble sleeping       |                   |         |                   |         |                    |         |
| No                     | ref               |         | ref               |         | ref                |         |
| Yes                    | 2.21 (1.77, 2.76) | <0.001  | 2.12 (1.61, 2.80) | < 0.001 | 2.22 (1.49, 3.30)  | < 0.001 |
| Wakeup during night    |                   |         |                   |         |                    |         |
| No                     | ref               |         | ref               |         | ref                |         |
| Yes                    | 1.49 (1.14, 1.95) | 0.005   | 1.51 (1.07, 2.14) | 0.02    | 1.47 (0.99, 2.20)  | 0.06    |

OR and CI determined by logistic regression. \*Model is unadjusted. †Adjusted for age, sex, ethnicity/race, marital status, poverty income ratio level, and education. ‡Model 2 with additional adjustment for hypertension, diabetes mellitus, coronary heart disease, heart attack, stroke, smoking, angina, alcohol consumption, body mass index, Systolic blood pressured, Low-density lipoprotein, High-density lipoprotein, HbA<sub>1c</sub>, creatinine, uric acid, and fasting triglyceride.

**Supplementary Table SII.** Instrumental SNPs from sleeplessness and GWAS of heart failure

| SNP         | Effect allele | Chromosome | Position  | Exposure (sleeplessness) |       |          | Outcome (Heart Failure) |       |         |
|-------------|---------------|------------|-----------|--------------------------|-------|----------|-------------------------|-------|---------|
|             |               |            |           | Beta                     | SE    | P-value  | Beta                    | SE    | P-value |
| rs10087341  | C             | 8          | 10239656  | 0.0147                   | 0.002 | 7.74E-10 | -0.005                  | 0.011 | 0.662   |
| rs10156602  | G             | 9          | 96345328  | -0.0102                  | 0.002 | 2.32E-08 | 0.013                   | 0.008 | 0.121   |
| rs11152363  | A             | 18         | 53057188  | 0.0143                   | 0.002 | 2.54E-10 | 0.015                   | 0.010 | 0.140   |
| rs113851554 | T             | 2          | 66750564  | 0.0478                   | 0.004 | 1.16E-34 | 0.035                   | 0.017 | 0.042   |
| rs11635495  | C             | 15         | 67804682  | 0.0097                   | 0.002 | 2.34E-08 | -0.001                  | 0.008 | 0.908   |
| rs11804386  | A             | 1          | 87738947  | 0.0102                   | 0.002 | 3.59E-08 | -0.004                  | 0.008 | 0.650   |
| rs13186678  | T             | 5          | 135535524 | 0.0110                   | 0.002 | 4.91E-09 | -0.001                  | 0.010 | 0.959   |
| rs1547630   | A             | 13         | 112642528 | 0.0104                   | 0.002 | 1.23E-08 | 0.007                   | 0.008 | 0.415   |
| rs17879819  | T             | 10         | 104662215 | -0.0187                  | 0.003 | 9.83E-09 | -0.032                  | 0.014 | 0.213   |
| rs2132083   | C             | 4          | 14960529  | -0.0101                  | 0.002 | 4.04E-08 | -0.015                  | 0.008 | 0.073   |
| rs224071    | A             | 10         | 64508475  | 0.0097                   | 0.002 | 2.67E-08 | 0.003                   | 0.008 | 0.733   |
| rs2863957   | A             | 2          | 114089551 | -0.0130                  | 0.002 | 6.67E-10 | -0.011                  | 0.010 | 0.241   |
| rs2956278   | G             | 12         | 84698234  | 0.0119                   | 0.002 | 2.03E-08 | -0.016                  | 0.010 | 0.104   |
| rs324017    | C             | 12         | 57487814  | -0.0117                  | 0.002 | 8.83E-10 | 0.010                   | 0.009 | 0.270   |
| rs3808937   | T             | 10         | 104230012 | -0.0143                  | 0.002 | 2.59E-11 | -0.013                  | 0.010 | 0.201   |
| rs3817576   | G             | 7          | 1023191   | -0.0104                  | 0.002 | 2.81E-09 | -0.012                  | 0.008 | 0.129   |
| rs4688760   | T             | 3          | 49980596  | 0.0115                   | 0.002 | 1.06E-09 | 0.010                   | 0.009 | 0.245   |
| rs4886140   | G             | 13         | 59833519  | 0.0111                   | 0.002 | 2.69E-09 | 0.011                   | 0.008 | 0.197   |
| rs4943439   | T             | 13         | 37555770  | 0.0105                   | 0.002 | 4.75E-09 | 0.015                   | 0.008 | 0.067   |
| rs6690017   | G             | 1          | 57842729  | -0.0099                  | 0.002 | 2.66E-08 | 0.002                   | 0.008 | 0.842   |
| rs6744461   | C             | 2          | 145299297 | 0.0109                   | 0.002 | 7.48E-09 | -0.012                  | 0.008 | 0.138   |
| rs71373536  | A             | 17         | 43221808  | 0.0135                   | 0.002 | 1.92E-11 | 0.018                   | 0.009 | 0.041   |
| rs7572387   | C             | 2          | 58866584  | 0.0109                   | 0.002 | 6.21E-10 | -0.012                  | 0.008 | 0.149   |
| rs9815484   | G             | 3          | 117637295 | 0.0132                   | 0.002 | 5.64E-09 | 0.010                   | 0.010 | 0.315   |
| rs9878792   | T             | 3          | 116432671 | -0.0267                  | 0.005 | 9.95E-09 | -0.028                  | 0.020 | 0.153   |

Beta – beta coefficient, SE – standard error.



**Supplementary Figure S2.** Funnel plot to assess heterogeneity. Blue line represents the inverse-variance weighted (IVW) estimate, and dark blue line represents the MR-Egger estimate

SE – standard error, IV – instrumental variable, MR – Mendelian randomization.