**Supplement to ‘Mental illness and cardiovascular health: Observational and polygenic risk score analyses in a population-based cohort study’**

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# Supplementary methods

## Anatomical Therapeutic Chemical codes

For antipsychotic use, all Anatomical Therapeutic Chemical (ATC) codes were selected from the category N05A Antipsychotics except for N05AN (Lithium). For lithium, we selected the ATC code N05AN. For antidepressants (including selective serotonin reuptake inhibitors, non-selective serotonin reuptake inhibitors and tricyclic antidepressants) the following ATC codes were selected: N06AA (01 - 23), N06AB (02 - 10), N06AF (01 - 06), N06AG (02, 03) and N06AX (01 - 26). For antihypertensive medication use, ATC codes were selected from the following categories: C09 Agents Acting on the Renin-Angiotensin System, C08 Calcium Channel Blockers, C03 Diuretics, C07 Beta-Blocking Agents, C02 Antiadrenergic Agents, centrally and peripherally acting. The exact ATC codes included were the following: C09AA (01-16), C09BA (01-09, 12, 13, 15), C09BA (02-09, 12, 13, 15), C09BB (02-07, 10, 12, 13), C09BX (01- 05), C09CA (01-04, 06-10), C09DA (01-04, 06-10), C09DB (01, 02, 04-09), C09DX (01-08), C09XA (01, 02, 52-54), C08CA (01-17, 51, 55), C08DB (01), C08DA (01, 02, 51 , C03AA (01-09, 13), C03AB (01-09), C03AH (01, 02), C03AX (01), C03CA (01-05), C03CB (01, 02), C03DA (01), C03EB (01, 02), C07AA (01, 02, 03, 05-07, 12, 14-17, 19, 23, 27), C07AB (01-14), C07AG (01, 02), C07BA (02, 05-07, 12, 68), C07BB (02-04, 06, 07, 12, 52), C07BG (01), C07CA (02, 03, 17, 23), C07CA (23), C07CB (02, 03, 53), C07CG (01), C07DA (06), C07DB (01-03, 07, 12, 13), C07FX (01-06), C02AA (01-07, 52, 53, 57), C02AB (01, 02), C02AC (01, 02, 04-06), C02BA (01), C02BB (01), C02CA (01-06), C02CC (01-07), C02DA (01), C02DB (01-04), C02DC (01), C02DD (01), C02DG (01), C02KA (01), C02KB (01), C02KC (01), C02KD (01), C02KX (01-05), C02KX (52, 54) , C02LA (01-09, 50-52, 71), C02LA (71), C02LB (01), C02LC (01, 05, 51), C02LE (01), C02LF (01), C02LG (01-03), C02LG (51, 73), C02LK (01), C02LL (01), C02LX (01).

## Lifelines genotype data

DNA data of the Lifelines participants were genotyped at three different platforms. The first sample, referred to as GWAS, is based on the Illumina HumanCytoSNP-12 BeadChip v2 array and consists of 15.400 adult Lifelines participants of European ancestry. GWAS includes participants from the age of 18, the average age is 47.8. The GWAS sample contains 58.2% women and 41.8% men. The second sample consists of the UMCG Genetics Lifelines Initiative (UGLI) consortium, including 38,030 Lifelines participants of European ancestry. UGLI also includes children from the age of 8, but most participants are between the age of 18 and 64. The UGLI GWAS sample contains 58,5% men and 41,5% women. The third sample, called UGLI2, was genotyped using the FinnGen Thermo Fisher Axiom Custom array. UGLI2 compromised 28,284 participants of European ancestry. Principal components (PCs) were computed over each sample separately.

After quality control and removing missing data, we ended up with a total sample size of 75,253. There were 937 participants included in both GWAS and UGLI, and 351 participants in both GWAS and UGLI2. There was no overlap between UGLI and UGLI2. After exclusion of overlapping participants (UGLI2 was given priority over UGLI, and UGLI over GWAS), the total genotype sample size was 73,965.

## Summary-level GWAS data

To compute PGSs we used summary level data of the largest publicly available genome-wide association studies (GWASs). These GWAS did not include the Lifelines cohort, which prevents over-estimation of the genetic predisposition of the trait in question.(NR *et al.*, 2013) For depressive disorder we employed a large meta-analysis that included three large GWASs of depression in individuals of European ancestry(Howard *et al.*, 2019), of which we only used the UK Biobank GWAS (52% males and 48% females) and GWAS of the Psychiatric Genomics Consortium (PGC), resulting in a total sample size of 170,756 cases and 329,443 controls. The UK Biobank GWAS used a broad definition of depression that entailed self-reported past help-seeking for problems with nerves, anxiety, tension, or depression. Participants were excluded if they were diagnosed with bipolar disorder, schizophrenia, or personality disorder, or reported using prescriptions for antipsychotic medications. The PCG GWAS used clinically-derived diagnosis of major depressive disorder. SNP associations for bipolar disorder were derived from the largest available GWAS based on 57 cohorts collected in Europe, North America, and Australia (41,917 cases and 371,549 controls)(Mullins *et al.*, 2021). For 52 cohorts, cases were defined following international consensus criteria for lifetime bipolar disorder (DSM-IV, ICD-9, or ICD-10) and in the five additional cohorts most cases were ascertained using International Classification of Diseases (ICD) codes. For schizophrenia, we used European ancestry summary level data from the latest and largest available GWAS (53,386 cases and 77,258 controls) of the Psychiatric Genomics Consortium (PGC).(Trubetskoy *et al.*, 2022) The PGC GWAS included 90 cohorts on schizophrenia and schizoaffective disorder, where cases were identified by clinical diagnosis.

## PGS analyses

All PGS analyses were conducted individually across the three genetic samples (GWAS, UGLI, UGLI2), to ensure precise PC correction. Subsequently, the results were meta-analysed using the inverse-variance weighted method. For separate results of the genetic samples see table S6 – S8. When we encountered fitting issues in one of the subsamples, we performed the analyses in non-related individuals only. This approach allowed us to perform regression analysis while circumventing the complexities introduced by random effects. Sample sizes using only non-related individuals were reduced to 7,527 for GWAS, 7,899 for UGLI and 9,487 for UGLI2.

# Supplementary tables

**Table S1.** Overlap in depressive disorder, bipolar disorder, and schizophrenia diagnoses in the Lifelines cohort sample

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | **Schizophrenia** | |
| **Depressive disorder** | **Bipolar disorder** | No | Yes |
| No | No | 132,366 | 64 |
|  | Yes | 166 | <10\* |
| Yes | No | 14,392 | 51 |
|  | Yes | 283 | <10\* |
| *Total* | | *147,177* | *130* |

\*All results reporting numbers below 10 were not specified for privacy reasons, as this might identify certain participants.

**Table S2.** Regression models with mental health disorder *polygenic risk scores* as independent variable and mental health disorder diagnoses as dependent variable, corrected only for PC’s.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Depressive disorder** | **Bipolar disorder** | **Schizophrenia** |
|  | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) |
| **PGS Depressive disorder** | 1.30, 1.3 to 1.4, <2.0E-16 | 1.30, 1.1 to 1.6, 5.6E-03 | 1.22, 0.9 to 1.7, 0.224 |
| **PGS Bipolar disorder** | 1.17, 1.1 to 1.2, 9.5E-15 | 1.83, 1.5 to 2.2, 1.8E-10 | 1.90, 1.4 to 2.7, 2.3E-04 |
| **PGS Schizophrenia** | 1.16, 1.1 to 1.2, 1.3E-13 | 1.38, 1.4 to 3.2, 2.1E-04 | 2.14, 1.4 to 3.2, 2.1E-04 |

Note: All analyses to confirm the predictive value of the PGS were performed in non-related individuals only (N=69,526), and were performed separately within the three samples (based on chip type) before meta-analysis using the inverse-variance weighted method.

**Table S3.** Regression models with mental health disorder diagnoses as independent variable and cardiovascular disease (risk) factors as dependent variable, uncorrected (model 1a), corrected for psychotropic medication use (model 1b), and corrected for psychotropic medication use + other covariates (model 1c).

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Depressive disorder** | | | **Bipolar disorder** | | | **Schizophrenia** | | |
|  | Model 1a | Model 1b | Model 1c | Model 1a | Model 1b | Model 1c | Model 1a | Model 1b | Model 1c |
| Linear models | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) |
| DBP | -0.04, -0.06 to -0.03,  7.5E-07 | -0.09, -0.11 to -0.08, <2.0E-16 | -0.04, -0.06 to -0.02, 5.1E-05 | 0.08, -0.01 to 0.17,  0.082 | 0.01, -0.08 to 0.10,  0.835 | -0.02, -0.12 to 0.07,  0.637 | 0.08, -0.09 to 0.25,  0.347 | -0.005, -0.18 to 0.17, 0.955 | -0.02, -0.20 to 0.16, 0.827 |
| *DBP – women\** | - | - | *-0.05, -0.07 to -0.03, 2.7E-06* | - | - | - | - | - | - |
| *DBP – men\** | - | - | *-1.5E-03, -0.04 to 0.03, 0.933* | - | - | - | - | - | - |
| SBP | -0.1, -0.12 to -0.08, <2.0E-16 | -0.15, -0.16 to -0.13, <2.0E-16 | -0.09, -0.11 to -0.08,  <2.0E-16 | -0.04, -0.13 to 0.05,  0.384 | -0.09, -0.18 to -0.01,  0.068 | -0.19, -0.28 to -0.1,  4.0E-05 | -0.07, -0.24 to 0.10, 0.412 | -0.13, -0.30 to 0.05, 0.152 | -0.24, -0.41 to -0.06, 0.008 |
| *SBP – women\** | - | - | *-0.10, -0.12 to -0.08, <2.0E-16* | - | - | - | - | - | - |
| *SBP – men\** | - | - | *-0.06, -0.09 to -0.03,*  *1.2E-04* | - | - | - | - | - | - |
| HRV | -0.08, -0.1 to -0.06,  <2.0E-16 | -0.006, -0.03 to 0.02, 0.626 | -0.05, -0.07 to -0.02, 1.3E-04 | -0.11, -0.23 to 0.01, 0.063 | 0.05, -0.08 to 0.17,  0.464 | 0.05, -0.08 to 0.18,  0.440 | -0.31, -0.53 to -0.08, 0.007 | -0.13, -0.35 to 0.09, 0.257 | -0.09, -0.34 to 0.16, 0.480 |
| QRS duration | -0.13, -0.14 to -0.11,  <2.0E-16 | -0.11, -0.13 to -0.10, <2.0E-16 | -0.02, -0.04 to -0.0004, 0.018 | 0.09, -2.1E-03 to 0.18, 0.051 | 0.15, 0.06 to 0.24,  0.001 | 0.12, 0.02 to 0.21,  0.017 | 0.13, -0.04 to 0.31,  0.133 | 0.2, 0.03 to 0.38,  0.022 | -0.13, -0.32 to 0.06, 0.187 |
| QTc interval | 0.03, 0.02 to 0.05,  7.1E-05 | 0.009, -0.01 to 0.03, 0.342 | -0.02, -0.04 to -0.0004, 0.098 | 0.11, 0.02 to 0.2,  0.018 | 0.06, -0.03 to 0.15,  0.210 | 0.08, -0.02 to 0.18,  0.107 | 8.9E-04, -0.17 to 0.17, 0.992 | -0.06, -0.24 to 0.11, 0.473 | 0.03, -0.17 to 0.23, 0.780 |
| *QTc – women\** | - | - | *-4.0E-03, -0.03 to 0.02, 0.733* | - | - | - | - | - | - |
| *QTc – men\** | - | - | *-0.06, -0.09 to -0.02,*  *0.004* | - | - | - | - | - | - |
| Logistic models | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) |
| Hypertension | 0.96, 0.92 to 1.5,  0.027 | 0.83, 0.79 to 0.87,  4.6E-16 | 0.88, 0.84 to 0.94,  1.7E-05 | 1.12, 0.91 to 1.39,  0.281 | 0.92, 0.74 to 1.13,  0.423 | 0.74, 0.57 to 0.98,  0.032 | 0.73, 0.47 to 1.14,  0.166 | 0.57, 0.37 to 0.89,  0.013 | 0.42, 0.21 to 0.86,  0.017\* |
| Arrhythmia | 1.66, 1.56 to 1.76,  <2.0E-16 | 1.52, 1.42 to 1.62,  <2.0E-16 | 1.54, 1.43 to 1.66,  <2.0E-16 | 1.72, 1.26 to 2.33,  5.3E-04 | 1.28, 0.94 to 1.74,  0.122 | 1.04, 0.72 to 1.51,  0.821 | 1.32, 0.71 to 2.45,  0.383 | 0.91, 0.49 to 1.7,  0.78 | 0.60, 0.21 to 1.67,  0.327\* |
| *Arrh – women\** | - | - | *n.a.* | - | - | - | - | - | - |
| *Arrh – men\** | - | - | *n.a.* | - | - | - | - | - | - |
| Atherosclerosis | 1.28, 1.22 to 1.34,  <2.0E-16 | 1.09, 1.03 to 1.15,  2.3E-03 | 1.23, 1.15 to 1.31,  1.6E-09 | 1.78, 1.40 to 2.26,  2.3E-06 | 1.28, 0.94 to 1.74,  0.122 | 1.15, 0.85 to 1.55,  0.377 | 1.99, 1.28 to 3.08,  0.002 | 1.36, 0.87 to 2.11,  0.174 | 1.47, 0.84 to 2.59,  0.18 |
| Heart failure | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* |
| BBB | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* |
| ECG-LVH | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* |

\*Evidence for an interaction is presented table S5. N.a. : models could not converge and results were unreliable due to low numbers in some cells.

**Table S4.** Estimates of all covariates included in the regression models with mental health disorder diagnoses as independent variable and cardiovascular disease (risk) factors as dependent variable.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **CVD** | **Coviarate** | **Depressive disorder** | | | **Bipolar disorder** | | | **Schizophrenia** | | |
| *Linear models* |  | Beta | SE | p-value | Beta | SE | p-value | Beta | SE | p-value |
| SBP | Medication | 0.03 | 0.01 | 0.003 | -5.8E-03 | 0.01 | 0.595 | -9.6E-03 | 0.01 | 0.373 |
|  | Sex | -0.45 | 5.0E-03 | < 2e-16 | -0.46 | 5.0E-03 | < 2e-16 | -0.46 | 5.0E-03 | < 2e-16 |
|  | Age | 0.28 | 2.9E-03 | < 2e-16 | 0.28 | 2.9E-03 | < 2e-16 | 0.28 | 2.9E-03 | < 2e-16 |
|  | Education | -0.07 | 6.2E-03 | < 2e-16 | -7.4E-02 | 6.2E-03 | < 2e-16 | -0.07 | 6.2E-03 | < 2e-16 |
|  | Employment | -0.16 | 6.8E-03 | < 2e-16 | -0.16 | 6.8E-03 | < 2e-16 | -0.16 | 6.8E-03 | < 2e-16 |
|  | Physical activity | 7.1E-03 | 2.6E-03 | 0.006 | 7.3E-03 | 2.6E-03 | 0.005 | 7.3E-03 | 2.6E-03 | 0.004 |
|  | BMI | 0.24 | 2.6E-03 | < 2e-16 | 0.24 | 2.6E-03 | < 2e-16 | 0.24 | 2.6E-03 | < 2e-16 |
|  | Smoking | -4.6E-03 | 2.6E-03 | 0.080 | -6.3E-03 | 2.6E-03 | 0.016 | -6.4E-03 | 2.6E-03 | 0.015 |
|  | Diabetes | 0.30 | 0.02 | < 2e-16 | 0.30 | 0.02 | < 2e-16 | 0.30 | 0.02 | < 2e-16 |
| DBP | Medication | 0.09 | 0.01 | 2.5E-13 | 0.07 | 0.01 | 4.3E-10 | 0.07 | 0.01 | 4.6E-10 |
|  | Sex | -0.44 | 5.3E-03 | < 2e-16 | -0.44 | 0.005 | < 2e-16 | -0.44 | 5.3E-03 | < 2e-16 |
|  | Age | 0.30 | 3.0E-03 | < 2e-16 | 0.30 | 3.0E-03 | < 2e-16 | 0.30 | 3.0E-03 | < 2e-16 |
|  | Education | -0.04 | 6.5E-03 | 2.6E-09 | -0.04 | 6.5E-03 | 2.0E-09 | -0.04 | 6.5E-03 | 2.0E-09 |
|  | Employment | 0.09 | 7.1E-03 | < 2e-16 | 0.09 | 7.1E-03 | < 2e-16 | 0.09 | 7.1E-03 | < 2e-16 |
|  | Physical activity | -0.03 | 2.7E-03 | < 2e-16 | -0.03 | 2.7E-03 | < 2e-16 | -0.03 | 2.7E-03 | < 2e-16 |
|  | BMI | 0.20 | 2.7E-03 | < 2e-16 | 0.20 | 2.7E-03 | < 2e-16 | 0.20 | 2.7E-03 | < 2e-16 |
|  | Smoking | 0.01 | 2.7E-03 | 1.3E-05 | 0.01 | 2.7E-03 | 4.2E-05 | 0.01 | 2.7E-03 | 4.3E-05 |
|  | Diabetes | 0.08 | 0.02 | 4.3E-06 | 0.08 | 0.02 | 4.3E-06 | 0.08 | 0.02 | 4.3E-06 |
| HRV | Medication | -0.21 | 0.02 | < 2e-16 | -0.24 | 0.02 | < 2e-16 | -0.24 | 0.01 | < 2e-16 |
|  | Sex | 0.21 | 7.0E-03 | < 2e-16 | 0.21 | 7.0E-03 | < 2e-16 | 0.21 | 7.0E-03 | < 2e-16 |
|  | Age | -0.34 | 4.2E-03 | < 2e-16 | -0.34 | 4.2E-03 | < 2e-16 | -0.34 | 4.2E-03 | < 2e-16 |
|  | Education | 4.0E-03 | 8.6E-03 | 0.642 | 3.6E-03 | 8.6E-03 | 0.674 | 3.7E-03 | 8.6E-03 | 6.7E-01 |
|  | Employment | -0.13 | 9.4E-03 | < 2e-16 | -0.13 | 9.4E-03 | < 2e-16 | -0.13 | 9.4E-03 | < 2e-16 |
|  | Physical activity | 0.03 | 3.4E-03 | < 2e-16 | 0.03 | 3.4E-03 | < 2e-16 | 0.03 | 3.4E-03 | < 2e-16 |
|  | BMI | -9.1E-03 | 3.6E-03 | 0.011 | -9.2E-03 | 3.6E-03 | 0.010 | -9.2E-03 | 3.6E-03 | 0.010 |
|  | Smoking | -1.7E-03 | 3.7E-03 | 0.650 | -2.7E-03 | 3.7E-03 | 0.458 | -2.6E-03 | 3.7E-03 | 0.473 |
|  | Diabetes | -0.04 | 0.02 | 0.121 | -0.04 | 0.02 | 0.118 | -0.04 | 0.02 | 0.117 |
| QRS duration | Medication | 4.3E-03 | 0.01 | 0.729 | -0.01 | 0.01 | 0.345 | -5.7E-03 | 0.01 | 0.625 |
|  | Sex | -0.74 | 5.5E-03 | < 2e-16 | -0.74 | 5.4E-03 | < 2e-16 | -0.74 | 5.4E-03 | < 2e-16 |
|  | Age | 0.08 | 3.1E-03 | < 2e-16 | 0.08 | 3.1E-03 | < 2e-16 | 0.08 | 3.1E-03 | < 2e-16 |
|  | Education | 0.01 | 6.7E-03 | 0.132 | 9.9E-03 | 6.7E-03 | 0.142 | 1.0E-02 | 6.7E-03 | 0.138 |
|  | Employment | -9.5E-03 | 7.3E-03 | 0.193 | -8.2E-03 | 7.3E-03 | 0.261 | -8.9E-03 | 7.3E-03 | 0.224 |
|  | Physical activity | 2.2E-03 | 2.8E-03 | 0.435 | 2.3E-03 | 2.8E-03 | 0.416 | 2.2E-03 | 2.8E-03 | 0.423 |
|  | BMI | 0.10 | 2.7E-03 | < 2e-16 | 0.10 | 2.7E-03 | < 2e-16 | 0.10 | 2.7E-03 | < 2e-16 |
|  | Smoking | -3.5E-03 | 2.8E-03 | 0.211 | -4.1E-03 | 2.8E-03 | 0.143 | -3.9E-03 | 2.8E-03 | 0.161 |
|  | Diabetes | 0.07 | 0.02 | 1.4E-04 | 0.07 | 0.02 | 1.4E-04 | 0.07 | 0.02 | 1.4E-04 |
| QTc interval | Medication | 3.8E-03 | 0.01 | 0.771 | -7.3E-03 | 0.01 | 0.550 | -4.8E-03 | 0.01 | 0.694 |
|  | Sex | 0.30 | 5.7E-03 | < 2e-16 | 0.30 | 5.7E-03 | < 2e-16 | 0.30 | 5.7E-03 | < 2e-16 |
|  | Age | 0.21 | 3.3E-03 | < 2e-16 | 0.21 | 3.3E-03 | < 2e-16 | 0.21 | 3.3E-03 | < 2e-16 |
|  | Education | 0.06 | 7.0E-03 | < 2e-16 | 0.06 | 7.0E-03 | < 2e-16 | 0.06 | 7.0E-03 | < 2e-16 |
|  | Employment | -7.9E-03 | 7.6E-03 | 0.301 | -7.0E-03 | 7.6E-03 | 0.361 | -7.2E-03 | 7.6E-03 | 0.344 |
|  | Physical activity | 0.01 | 2.9E-03 | 5.3E-06 | 0.01 | 2.9E-03 | 4.7E-06 | 0.01 | 2.9E-03 | 4.9E-06 |
|  | BMI | 0.06 | 2.9E-03 | < 2e-16 | 0.06 | 2.9E-03 | < 2e-16 | 0.06 | 2.9E-03 | < 2e-16 |
|  | Smoking | -0.02 | 3.0E-03 | 4.0E-11 | -0.02 | 2.9E-03 | 1.3E-11 | -0.02 | 2.9E-03 | 1.6E-11 |
|  | Diabetes | 0.04 | 0.02 | 0.017 | 0.04 | 0.02 | 0.017 | 0.04 | 0.02 | 0.017 |
| *Logistic models* | | OR | SE | p-value | OR | SE | p-value | OR | SE | p-value |
| Hypertension | Medication | 1.22 | 1.04 | 9.5E-09 | 1.16 | 1.03 | 3.7E-06 | 1.05 | 1.04 | 0.203 |
|  | Sex | 0.53 | 1.02 | < 2e-16 | 0.53 | 1.02 | < 2e-16 | 0.54 | 1.02 | < 2e-16 |
|  | Age | 2.47 | 1.01 | < 2e-16 | 2.48 | 1.01 | < 2e-16 | 2.56 | 1.02 | < 2e-16 |
|  | Education | 0.89 | 1.02 | 1.9E-09 | 0.89 | 1.02 | 1.5E-09 | 0.86 | 1.03 | 5.0E-09 |
|  | Employment | 0.83 | 1.02 | < 2e-16 | 0.84 | 1.02 | < 2e-16 | 0.92 | 1.03 | 0.005 |
|  | Physical activity | 0.97 | 1.01 | 0.001 | 0.97 | 1.01 | 0.001 | 0.98 | 1.01 | 0.087 |
|  | BMI | 1.69 | 1.01 | < 2e-16 | 1.69 | 1.01 | < 2e-16 | 1.64 | 1.01 | < 2e-16 |
|  | Smoking | 1.02 | 1.01 | 0.001 | 1.02 | 1.01 | 0.003 | 1.01 | 1.01 | 0.455 |
|  | Diabetes | 2.66 | 1.05 | < 2e-16 | 2.66 | 1.05 | < 2e-16 | 2.30 | 1.06 | < 2e-16 |
|  |  |  |  |  |  |  |  |  |  |  |
| Arrhythmia | Medication | 1.10 | 1.05 | 0.058 | 1.37 | 1.05 | 6.3E-12 | 1.31 | 1.06 | 3.7E-07 |
|  | Sex | 1.16 | 1.03 | 3.1E-09 | 1.18 | 1.03 | 4.5E-11 | 1.06 | 1.03 | 0.067 |
|  | Age | 1.71 | 1.02 | < 2e-16 | 1.69 | 1.02 | < 2e-16 | 1.65 | 1.02 | < 2e-16 |
|  | Education | 1.03 | 1.03 | 0.339 | 1.03 | 1.03 | 0.267 | 0.98 | 1.04 | 0.685 |
|  | Employment | 0.79 | 1.03 | 6.8E-15 | 0.77 | 1.03 | < 2e-16 | 0.80 | 1.04 | 4.5E-08 |
|  | Physical activity | 1.00 | 1.01 | 0.977 | 1.00 | 1.01 | 0.987 | 1.00 | 1.02 | 0.977 |
|  | BMI | 1.07 | 1.01 | 7.4E-09 | 1.07 | 1.01 | 5.9E-09 | 1.05 | 1.02 | 4.6E-04 |
|  | Smoking | 1.06 | 1.01 | 5.9E-08 | 1.07 | 1.01 | 5.4E-10 | 1.05 | 1.01 | 1.4E-04 |
|  | Diabetes | 1.29 | 1.06 | 3.0E-05 | 1.29 | 1.06 | 3.2E-05 | 1.16 | 1.08 | 0.060 |
| Atherosclerosis | Medication | 1.37 | 1.04 | 4.0E-14 | 1.51 | 1.04 | < 2e-16 | 1.51 | 1.04 | < 2e-16 |
|  | Sex | 0.58 | 1.02 | < 2e-16 | 0.58 | 1.02 | < 2e-16 | 0.58 | 1.02 | < 2e-16 |
|  | Age | 2.48 | 1.01 | < 2e-16 | 2.47 | 1.01 | < 2e-16 | 2.47 | 1.01 | < 2e-16 |
|  | Education | 0.90 | 1.02 | 3.5E-06 | 0.90 | 1.02 | 5.2E-06 | 0.90 | 1.02 | 5.2E-06 |
|  | Employment | 1.02 | 1.03 | 0.341 | 1.02 | 1.03 | 0.494 | 1.02 | 1.03 | 0.479 |
|  | Physical activity | 0.96 | 1.01 | 5.0E-06 | 0.96 | 1.01 | 4.6E-06 | 0.96 | 1.01 | 4.5E-06 |
|  | BMI | 1.25 | 1.01 | < 2e-16 | 1.25 | 1.01 | < 2e-16 | 1.25 | 1.01 | < 2e-16 |
|  | Smoking | 1.14 | 1.01 | < 2e-16 | 1.15 | 1.01 | < 2e-16 | 1.15 | 1.01 | < 2e-16 |
|  | Diabetes | 5.69 | 1.05 | < 2e-16 | 5.70 | 1.05 | < 2e-16 | 5.71 | 1.05 | < 2e-16 |

**Table S5.** Regression models with mental health disorder *polygenic scores* as independent variable and cardiovascular disease (risk) factors as dependent variable, corrected only for PCs (model 2a), corrected for PCs and psychotropic medication use (model 2b), and corrected for PCs, psychotropic medication use + other covariates (model 2c).

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **PGS Depressive disorder** | | | **PGS Bipolar disorder** | | | **PGS Schizophrenia** | | |
|  | Model 2a | Model 2b | Model 2c | Model 2a | Model 2b | Model 2c | Model 2a | Model 2b | Model 2c |
| Linear models | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) |
| DBP | 0.01, 0.003 to 0.02,  0.005 | 0.01, 0.001 to 0.02, 0.024 | 2.7E-03, -0.004 to 0.01,  0.455 | -5.1E-04, -0.01 to 0.01, 0.891 | -1.7E-04, -0.01 to 0.01, 0.643 | 1.7E-03, -0.01 to 0.01, 0.640 | 0.01, -0.002 to 0.01,  0.148 | 0.01, -0.001 to 0.01, 0.103 | 0.01, -0.001 to 0.01,  0.113 |
| SBP | 0.01, -0.0004 to 0.02,  0.064 | 0.01, -.001 to 0.01,  0.117 | -3.2E-03, -0.01 to 0.004, 0.359 | -2.4E-03, -0.01 to 0.01, 0.532 | -3.0E-03, -0.01 to 0.004, 0.427 | 3.4E-03, -0.003 to 0.01,  0.326 | 1.5E-03, -0.01 to 0.01, 0.684 | 9.6E-04, -0.01 to 0.01, 0.800 | 0.01, -0.001 to 0.01,  0.105 |
| HRV | 2.3E-03, -0.007 to 0.01, 0.614 | 0.01, -0.003 to 0.02,  0.194 | 0.01, -0.002 to 0.02, 0.109\* | -1.0E-03, -0.01 to 0.01, 0.823 | 1.3E-03, -0.01 to 0.01, 0.780 | 1.5E-03, -0.01 to 0.01, 0.782\* | -0.01, -0.02 to -0.01,  0.001 | -0.01, -0.02 to -0.004,  0.005 | -0.01, -0.02 to -0.003, 0.013\* |
| QRS duration | -1.9E-03, -0.01 to 0.01, 0.634\* | -6.9E-04, -0.01 to 0.01, 0.859\* | -3.9E-03, -0.01 to 0.004, 0.315\* | -3.9E-05, -0.01 to 0.01, 0.992\* | 6.4E-04, -0.01 to 0.01, 0.871\* | 3.0E-03, -0.005 to 0.01, 0.439\* | 2.1E-03, -0.01 to 0.01, 0.591\* | 2.7E-03, -0.005 to 0.01, 0.489\* | 4.1E-03, -0.004 to 0.01, 0.289\* |
| QTc interval | -0.01, -0.02 to -0.001, 0.021 | -0.01, -0.02 to -0.003, 0.008 | -0.01, -0.01 to 0.002, 0.151 | 3.9E-03, -0.004 to 0.01, 0.308 | 3.2E-03, -0.004 to 0.01,  0.404 | 2.6E-03, -0.01 to 0.01, 0.507 | 1.4E-03, -0.01 to 0.01, 0.724 | 7.0E-04, -0.01 to 0.01, 0.855 | 0.003, -0.004 to 0.01, 0.396 |
| Logistic models | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) |
| Hypertension | 1.02, 1.004 to 1.04,  0.017 | 1.01, 0.99 to 1.03,  0.333 | 1.00005, 0.98 to 1.02,  0.996 | 0.997, 0.98 to 1.01,  0.730 | 0.99, 0.98 to 1.01,  0.498 | 1.01, 0.99 to 1.03,  0.383 | 1.01, 0.99 to 1.03,  0.260 | 1.02, 0.998 to 1.03,  0.088 | 1.02, 0.995 to 1.04,  0.119 |
| Arrhythmia | 1.17, 1.13 to 1.22,  1.3E-18\* | 1.17, 1.12 to 1.21,  3.7E-17\* | 1.16, 1.12 to 1.21,  6.0E-14\* | 1.03, 0.99 to 1.06,  0.162\* | 1.02, 0.98 to 1.06,  0.263\* | 1.01, 0.97 to 1.05,  0.529\* | 1.08, 1.04 to 1.12,  1.6E-05\* | 1.08, 1.04 to 1.12,  4.4E-05\* | 1.08, 1.03 to 1.12,  3.3E-04\* |
| Atherosclerosis | 1.08, 1.05 to 1.1,  7.3E-08 | 1.06, 1.04 to 1.09,  3.9E-06 | 1.07, 1.04 to 1.11,  3.6E-05\* | 1.04, 1.01 to 1.06,  0.010 | 1.03, 1.002 to 1.06,  0.033 | 1.02, 0.982 to 1.05,  0.370\* | 1.04, 1.01 to 1.07,  0.004 | 1.04, 1.01 to 1.06,  0.012 | 1.02, 0.99 to 1.05,  0.280\* |
| Heart failure | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* |
| BBB | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* |
| ECG-LVH | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* |

Note: Analyses marked with (\*) were performed in non-related individuals only. N.a. : models could not converge and results were unreliable due to low numbers in some cells.

**Table S5.** Estimates of the interaction terms with sex of the regression models with mental health disorder *diagnosis* and *polygenic risk scores* as independent variable and cardiovascular disease (risk) factors as dependent variable, corrected for PCs and psychotropic medication use + other covariates (model 1d and 2d).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Depressive disorder** | | **Bipolar disorder** | | **Schizophrenia** | |
|  | *Diagnosis* | *PGS* | *Diagnosis* | *PGS* | *Diagnosis* | *PGS* |
| Linear models | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) | (beta, CIs, *p-*value) |
| DBP | **-0.06, -0.1 to -0.03, 0.001** | -3.3E-03, -0.02 to 0.01, 0.617\* | 0.08, -0.11 to 0.27,  0.415 | -0.01, -0.02 to 0.01, 0.405\* | 0.26, -0.11 to 0.64, 0.170 | -0.01, -0.03 to 0.001, 0.067\* |
| SBP | **-0.05, -0.08 to -0.01,**  **0.010** | -3.3E-03, -0.02 to 0.01, 0.617\* | 0.04, -0.14 to 0.23, 0.632 | -0.01, -0.02 to 0.004, 0.182\* | 0.29, -0.07 to 0.66, 0.111 | -0.01, -0.03 to 0.001, 0.067\* |
| HRV | -0.02, -0.08 to 0.04, 0.513 | -0.01, -0.03 to 0.01, 0.421\* | -0.05, -0.3 to 0.2,  0.693 | 4.5E-03, -0.1 to 0.02, 0.615\* | -0.04, -0.55 to 0.47, 0.867 | 1.6E-03, -0.02 to 0.02,  0.877\* |
| QRS duration | -0.03, -0.07 to 0.01, 0.181 | -0.01, -0.02 to 0.01, 0.359\* | 0.07, -0.13 to 0.27, 0.472 | -3.2E-03, -0.02 to 0.01, 0.646\* | -0.34, -0.73 to 0.05, 0.093 | -3.7E-03, -0.02 to 0.01, 0.592\* |
| QTc interval | **0.05, 0.01 to 0.09, 0.016** | 0.01, -0.01 to 0.02, 0.317\* | 0.14, -0.08 to 0.36, 0.176 | -3.3E-03, -0.02 to 0.01, 0.617\* | -0.15, -0.56 to 0.26, 0.465 | -0.01, -0.02 to 0.01, 0.317\* |
| Logistic models | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) | (OR, CIs, *p-*value) |
| Hypertension | 1.0004, 0.90 to 1.11,  0.994 | 0.98, 0.94 to 1.02,  0.385\* | 0.95, 0.55 to 1.64, 0.860 | 0.98, 0.94 to 1.02, 0.355\* | *n.a.* | 0.98, 0.94 to 1.02, 0.396\* |
| Arrhythmia | **0.86, 0.74 to 0.99,**  **0.040** | 0.97, 0.90 to 1.04, 0.354\* | 0.76, 0.35 to 1.65, 0.483 | 0.99, 0.91 to 1.07, 0.760\* | *n.a.* | 1.06, 0.98 to 1.15, 0.142\* |
| Atherosclerosis | 1.09, 0.96 to 1.23, 0.189 | 0.96, 0.92 to 1.01, 0.160\* | 0.81, 0.44 to 1.48, 0.495 | 1.004, 0.96 to 1.05,  0.851\* | *n.a.* | 1.02, 0.96 to 1.17, 0.560\* |
| Heart failure | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* |
| Bundle Branch Block | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* |
| ECG-voltages LVH | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* | *n.a.* |

Note: Both the main effect of sex and the interaction term of sex\*PGS are included in the analyses. Analyses marked with (\*) were performed in non-related individuals only. Outcomes in **bold** show evidence for an interaction with sex, thus we also performed stratified analyses on sex of model 1c, results can be found in table S2. N.a. : models could not converge and results were unreliable due to low numbers in some cells.

**Table S6.** Regression models with mental health disorder *polygenic scores* as independent variable and cardiovascular disease (risk) factors as dependent variable (model 2a), corrected for PCs, stratified in subsamples based on chip type (GWAS, UGLI, UGLI2).

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | Depressive disorder | | | Bipolar disorder | | | Schizophrenia | | |  |
| CVD | Chip | Model | Beta | SE | p-value | Beta | SE | p-value | Beta | SE | p-value | N |
| Arrhythmia | GWAS | 2a | 0.15 | 0.04 | 2.5E-04 | -0.02 | 0.04 | 0.603 | 0.09 | 0.04 | 0.027 | 13750 |
| Atherosclerosis | GWAS | 2a | 0.10 | 0.06 | 0.112 | 0.07 | 0.06 | 0.272 | 0.09 | 0.06 | 0.127 | 13750 |
| SBP | GWAS | 2a | 0.01 | 0.01 | 0.357 | -1.6E-03 | 0.01 | 0.853 | 4.2E-03 | 0.01 | 0.631 | 13750 |
| DBP | GWAS | 2a | 0.01 | 0.01 | 0.129 | -3.0E-03 | 0.01 | 0.721 | 1.2E-03 | 0.01 | 0.886 | 13750 |
| HRV | GWAS | 2a | 0.01 | 0.01 | 0.402 | -2.0E-03 | 0.01 | 0.819 | -0.02 | 0.01 | 0.040 | 13750 |
| Hypertension | GWAS | 2a | 0.02 | 0.02 | 0.298 | -0.02 | 0.02 | 0.375 | -0.02 | 0.02 | 0.383 | 13750 |
| QRS | GWAS | 2a | 0.01 | 0.01 | 0.332 | -0.01 | 0.01 | 0.604 | -0.01 | 0.01 | 0.645 | 13750 |
| QTc | GWAS | 2a | 0.00 | 0.01 | 0.795 | 2.6E-03 | 0.01 | 0.764 | -0.01 | 0.01 | 0.243 | 13750 |
| Arrhythmia | UGLI | 2a | 0.16 | 0.02 | 3.6E-11 | 0.02 | 0.02 | 0.319 | 0.05 | 0.02 | 0.031 | 32298 |
| Atherosclerosis | UGLI | 2a | 0.07 | 0.02 | 2.5E-04 | 0.04 | 0.02 | 0.047 | 0.05 | 0.02 | 0.009 | 32298 |
| SBP | UGLI | 2a | 0.01 | 0.01 | 0.044 | -4.1E-03 | 0.01 | 0.471 | 0.00 | 0.01 | 0.564 | 32298 |
| DBP | UGLI | 2a | 0.02 | 0.01 | 0.003 | -9.2E-04 | 0.01 | 0.870 | 0.01 | 0.01 | 0.305 | 32298 |
| HRV | UGLI | 2a | 0.01 | 0.01 | 0.370 | -1.0E-03 | 0.01 | 0.882 | -0.01 | 0.01 | 0.066 | 32298 |
| Hypertension | UGLI | 2a | 0.03 | 0.01 | 0.027 | -3.9E-03 | 0.01 | 0.779 | 0.02 | 0.01 | 0.177 | 32298 |
| QRS | UGLI | 2a | 0.00 | 0.01 | 0.901 | 1.6E-03 | 0.01 | 0.777 | 3.5E-03 | 0.01 | 0.531 | 32298 |
| QTc | UGLI | 2a | -0.01 | 0.01 | 0.088 | 3.3E-03 | 0.01 | 0.568 | 1.3E-04 | 0.01 | 0.982 | 32298 |
| Arrhythmia | UGLI2 | 2a | 0.17 | 0.04 | 6.1E-06 | 0.07 | 0.04 | 0.076 | 0.13 | 0.04 | 4.6E-04 | 26845 |
| Atherosclerosis | UGLI2 | 2a | 0.08 | 0.02 | 2.3E-04 | 0.03 | 0.02 | 0.171 | 0.02 | 0.02 | 0.390 | 26845 |
| SBP | UGLI2 | 2a | 0.00 | 0.01 | 0.854 | -6.6E-04 | 0.01 | 0.915 | -1.9E-03 | 0.01 | 0.760 | 26845 |
| DBP | UGLI2 | 2a | 0.00 | 0.01 | 0.778 | 1.3E-03 | 0.01 | 0.830 | 0.01 | 0.01 | 0.243 | 26845 |
| HRV | UGLI2 | 2a | -0.01 | 0.01 | 0.351 | -1.3E-04 | 0.01 | 0.988 | -0.01 | 0.01 | 0.085 | 26845 |
| Hypertension | UGLI2 | 2a | 0.01 | 0.02 | 0.446 | 0.01 | 0.02 | 0.671 | 0.02 | 0.02 | 0.271 | 26845 |
| QRS | UGLI2 | 2a | -0.01 | 0.01 | 0.263 | -3.8E-04 | 0.01 | 0.951 | 2.5E-03 | 0.01 | 0.692 | 26845 |
| QTc | UGLI2 | 2a | -0.01 | 0.01 | 0.079 | 0.01 | 0.01 | 0.400 | 0.01 | 0.01 | 0.158 | 26845 |

**Table S7.** Regression models with mental health disorder *polygenic scores* as independent variable and cardiovascular disease (risk) factors as dependent variable, corrected for PCs and psychotropic medication use (model 2b), stratified in subsamples based on chip type (GWAS, UGLI, UGLI2).

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | Depressive disorder | | | Bipolar disorder | | | Schizophrenia | | |  |
| CVD | Chip | Model | Beta | SE | p-value | Beta | SE | p-value | Beta | SE | p-value | N |
| Arrhythmia | GWAS | 2b | 0.14 | 0.04 | 0.001 | -0.03 | 0.04 | 0.409 | 0.08 | 0.04 | 0.044 | 13750 |
| Atherosclerosis | GWAS | 2b | 0.09 | 0.06 | 0.133 | 0.06 | 0.06 | 0.310 | 0.12 | 0.07 | 0.068 | 13750 |
| SBP | GWAS | 2b | 0.01 | 0.01 | 0.176 | -4.1E-03 | 0.01 | 0.623 | 4.5E-04 | 0.01 | 0.957 | 13750 |
| DBP | GWAS | 2b | 0.01 | 0.01 | 0.287 | -4.0E-04 | 0.01 | 0.964 | -0.02 | 0.01 | 0.053 | 13750 |
| HRV | GWAS | 2b | -0.02 | 0.02 | 0.349 | -0.02 | 0.02 | 0.325 | 0.02 | 0.02 | 0.358 | 13750 |
| Hypertension | GWAS | 2b | 0.01 | 0.01 | 0.283 | -0.01 | 0.01 | 0.659 | -4.9E-03 | 0.01 | 0.683 | 13750 |
| QRS | GWAS | 2b | -2.6E-03 | 0.01 | 0.767 | 2.4E-03 | 0.01 | 0.784 | -0.01 | 0.01 | 0.235 | 13750 |
| QTc | GWAS | 2b | 0.01 | 0.01 | 0.366 | -1.8E-03 | 0.01 | 0.840 | 4.1E-03 | 0.01 | 0.639 | 13750 |
| Arrhythmia | UGLI | 2b | 0.16 | 0.02 | 0.000 | 0.02 | 0.02 | 0.380 | 0.05 | 0.02 | 0.041 | 32298 |
| Atherosclerosis | UGLI | 2b | 0.06 | 0.02 | 0.002 | 0.03 | 0.02 | 0.091 | 0.04 | 0.02 | 0.020 | 32298 |
| SBP | UGLI | 2b | 0.01 | 0.01 | 0.010 | -2.2E-03 | 0.01 | 0.695 | 4.6E-03 | 0.01 | 0.415 | 32298 |
| DBP | UGLI | 2b | 0.01 | 0.01 | 0.144 | 1.1E-03 | 0.01 | 0.869 | -0.01 | 0.01 | 0.124 | 32298 |
| HRV | UGLI | 2b | 0.03 | 0.01 | 0.068 | -0.01 | 0.01 | 0.601 | 0.02 | 0.01 | 0.258 | 32298 |
| Hypertension | UGLI | 2b | 4.1E-04 | 0.01 | 0.941 | 2.3E-03 | 0.01 | 0.687 | 4.2E-03 | 0.01 | 0.460 | 32298 |
| QRS | UGLI | 2b | -0.01 | 0.01 | 0.060 | 2.7E-03 | 0.01 | 0.641 | -4.4E-04 | 0.01 | 0.939 | 32298 |
| QTc | UGLI | 2b | 0.01 | 0.01 | 0.076 | -4.9E-03 | 0.01 | 0.385 | 2.5E-03 | 0.01 | 0.661 | 32298 |
| Arrhythmia | UGLI2 | 2b | 0.16 | 0.04 | 0.000 | 0.06 | 0.04 | 0.099 | 0.13 | 0.04 | 0.001 | 26845 |
| Atherosclerosis | UGLI2 | 2b | 0.07 | 0.02 | 0.002 | 0.02 | 0.02 | 0.307 | 0.01 | 0.02 | 0.571 | 26845 |
| SBP | UGLI2 | 2b | -5.1E-04 | 0.01 | 0.935 | 1.6E-04 | 0.01 | 0.980 | 0.01 | 0.01 | 0.081 | 26845 |
| DBP | UGLI2 | 2b | -3.1E-03 | 0.01 | 0.706 | 2.9E-03 | 0.01 | 0.724 | -0.01 | 0.01 | 0.152 | 26845 |
| HRV | UGLI2 | 2b | 0.01 | 0.02 | 0.724 | 3.2E-03 | 0.02 | 0.833 | 0.01 | 0.02 | 0.365 | 26845 |
| Hypertension | UGLI2 | 2b | -0.01 | 0.01 | 0.355 | 2.4E-04 | 0.01 | 0.970 | 3.1E-03 | 0.01 | 0.625 | 26845 |
| QRS | UGLI2 | 2b | -0.01 | 0.01 | 0.035 | 4.2E-03 | 0.01 | 0.505 | 0.01 | 0.01 | 0.210 | 26845 |
| QTc | UGLI2 | 2b | -6.7E-05 | 0.01 | 0.991 | -1.3E-03 | 0.01 | 0.835 | -2.5E-03 | 0.01 | 0.692 | 26845 |

**Table S8.** Regression models with mental health disorder *polygenic scores* as independent variable and cardiovascular disease (risk) factors as dependent variable, corrected for PCs, psychotropic medication use + other covariates (model 2c), stratified in subsamples based on chip type (GWAS, UGLI, UGLI2).

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | Depressive disorder | | | Bipolar disorder | | | Schizophrenia | | |  |
| CVD | Chip | Model | Beta | SE | p-value | Beta | SE | p-value | Beta | SE | p-value | N |
| Arrhythmia | GWAS | 2c | 0.16 | 0.05 | 0.002 | -0.07 | 0.05 | 0.179 | 0.11 | 0.05 | 0.026 | 15375 |
| Atherosclerosis | GWAS | 2c | 0.06 | 0.04 | 0.113 | -0.06 | 0.04 | 0.180 | 0.02 | 0.04 | 0.677 | 15375 |
| SBP | GWAS | 2c | 0.01 | 0.01 | 0.271 | 0.01 | 0.01 | 0.407 | 3.0E-03 | 0.01 | 0.737 | 15375 |
| DBP | GWAS | 2c | 0.03 | 0.01 | 0.034 | 0.01 | 0.01 | 0.658 | -0.03 | 0.01 | 0.028 | 15375 |
| HRV | GWAS | 2c | 0.01 | 0.02 | 0.552 | -2.2E-03 | 0.02 | 0.929 | -4.5E-03 | 0.02 | 0.854 | 15375 |
| Hypertension | GWAS | 2c | 4.5E-04 | 0.01 | 0.973 | -3.1E-03 | 0.01 | 0.819 | -0.02 | 0.01 | 0.216 | 15375 |
| QRS | GWAS | 2c | 0.01 | 0.01 | 0.379 | -1.1E-04 | 0.01 | 0.991 | -1.8E-03 | 0.01 | 0.859 | 15375 |
| QTc | GWAS | 2c | 3.4E-03 | 0.01 | 0.707 | 0.01 | 0.01 | 0.346 | 0.01 | 0.01 | 0.149 | 15375 |
| Arrhythmia | UGLI | 2c | 0.15 | 0.03 | 8.3E-09 | 0.01 | 0.03 | 0.619 | 0.03 | 0.03 | 0.213 | 32298 |
| Atherosclerosis | UGLI | 2c | 0.08 | 0.02 | 3.8E-04 | 0.04 | 0.02 | 0.077 | 0.02 | 0.02 | 0.329 | 32298 |
| SBP | UGLI | 2c | 0.01 | 0.01 | 0.136 | -1.2E-04 | 0.01 | 0.982 | 3.0E-03 | 0.01 | 0.568 | 32298 |
| DBP | UGLI | 2c | 0.01 | 0.01 | 0.382 | 5.6E-04 | 0.01 | 0.935 | -0.01 | 0.01 | 0.065 | 32298 |
| HRV | UGLI | 2c | 0.02 | 0.02 | 0.249 | 0.01 | 0.02 | 0.527 | 0.01 | 0.02 | 0.441 | 32298 |
| Hypertension | UGLI | 2c | -4.2E-03 | 0.01 | 0.438 | 3.2E-03 | 0.01 | 0.556 | 2.4E-03 | 0.01 | 0.667 | 32298 |
| QRS | UGLI | 2c | -4.8E-03 | 0.01 | 0.403 | 3.6E-03 | 0.01 | 0.543 | -1.1E-03 | 0.01 | 0.852 | 32298 |
| QTc | UGLI | 2c | 2.5E-04 | 0.01 | 0.960 | 2.0E-03 | 0.01 | 0.690 | 3.8E-03 | 0.01 | 0.463 | 32298 |
| Arrhythmia | UGLI2 | 2c | 0.15 | 0.04 | 2.9E-04 | 0.06 | 0.04 | 0.116 | 0.14 | 0.04 | 0.001 | 26845 |
| Atherosclerosis | UGLI2 | 2c | 0.05 | 0.04 | 0.134 | 3.3E-03 | 0.03 | 0.926 | 0.01 | 0.04 | 0.759 | 26845 |
| SBP | UGLI2 | 2c | -0.01 | 0.01 | 0.240 | 1.5E-03 | 0.01 | 0.806 | 0.01 | 0.01 | 0.081 | 26845 |
| DBP | UGLI2 | 2c | 1.8E-03 | 0.01 | 0.888 | 1.2E-03 | 0.01 | 0.925 | -3.7E-03 | 0.01 | 0.783 | 26845 |
| HRV | UGLI2 | 2c | -0.03 | 0.02 | 0.080 | 0.02 | 0.02 | 0.405 | 0.04 | 0.02 | 0.056 | 26845 |
| Hypertension | UGLI2 | 2c | -4.4E-03 | 0.01 | 0.468 | 4.0E-03 | 0.01 | 0.508 | 0.01 | 0.01 | 0.079 | 26845 |
| QRS | UGLI2 | 2c | -0.01 | 0.01 | 0.047 | 2.7E-03 | 0.01 | 0.677 | 0.01 | 0.01 | 0.087 | 26845 |
| QTc | UGLI2 | 2c | -0.01 | 0.01 | 0.076 | 3.1E-03 | 0.01 | 0.579 | 0.01 | 0.01 | 0.368 | 26845 |

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