**Supplementary information**

**Genetic assortative mating for schizophrenia and bipolar disorder**

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**Supplementary Results**

|  |  |  |  |
| --- | --- | --- | --- |
|  | *PRSs*  | *PRS residualized by first 20 PCs* | *Difference between correlation coefficients* |
| *PRS* | *Correlation coefficient, r* | *z-score* | *p-value* |
| Educational attainment | 0.193 | 0.189 | -0.16 | 0.877 |
| Bone mineral density | -0.015 | -0.012 | 0.14 | 0.886 |
| Schizophrenia | 0.121 | 0.105 | -0.98 | 0.329 |
| Bipolar disorder | 0.162 | 0.183 | 0.97 | 0.330 |

**Supplementary Table S1.** Correlation coefficients obtained with the PRSs residualized by the first 20 principal components. These estimates are from the total sample, and two-sided z-tests. To test for a significant difference between the correlation coefficients we bootstrapped the difference between the coefficients (with 10,000 repetitions), and calculated z-scores, based on the coefficient difference and the standard deviation of the bootstrap estimate distribution.

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| --- | --- |
| **Total sample** | **Mothers’ PRS** |
|  | r (p-value) | EA | BMD | SZ | BP |
| **Fathers’PRS** | EA |  | 0.056(0.351) | 0.041(0.497) | 0.060(0.321) |
| BMD | 0.034(0.576) |  | 0.057(0.341) | 0.026(0.663) |
| SZ | -0.014(0.813) | 0.007(0.912) |  | 0.007(0.911) |
| BP | 0.059(0.323) | -0.047(0.431) | 0.087(0.149) |  |

**Supplementary Table S2.** Cross-trait between-parent PRS correlation coefficients (and corresponding p-values) calculated in the total sample (n = 279 pairs). EA = educational attainment. BMD = bone mineral density. SZ = schizophrenia. BP = bipolar disorder.

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| --- | --- |
| **Population-based controls** | **Mothers’ PRS** |
|  | r (p-value) | EA | BMD | SZ | BP |
| **Fathers’PRS** | EA |  | 0.218(0.013) | 0.019(0.831) | 0.257(0.003) |
| BMD | 0.042(0.635) |  | 0.110(0.214) | 0.048(0.587) |
| SZ | -0.600(0.500) | 0.161(0.068) |  | 0.044(0.618) |
| BP | 0.079(0.373) | -0.065(0.465) | -0.077(0.382) |  |

**Supplementary Table S3.** Cross-trait between-parent PRS correlation coefficients (and corresponding p-values) calculated in the sample of population-based controls (n = 130 pairs). EA = educational attainment. BMD = bone mineral density. SZ = schizophrenia. BP = bipolar disorder.

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| **Familial high-risk of schizophrenia sample** | **Mothers’ PRS** |
|  | r (p-value) | EA | BMD | SZ | BP |
| **Fathers’PRS** | EA |  | -0.094(0.382) | 0.160(0.136) | -0.077(0.555) |
| BMD | 0.074(0.495) |  | 0.047(0.720) | -0.009(0.944) |
| SZ | -0.002(0.983) | -0.170(0.191) |  | 0.035(0.792) |
| BP | -0.012(0.927) | 0.103(0.429) | 0.037(0.777) |  |

**Supplementary Table S4.** Cross-trait between-parent PRS correlation coefficients (and corresponding p-values) calculated in the sample of familial high-risk of schizophrenia (n = 88 pairs). EA = educational attainment. BMD = bone mineral density. SZ = schizophrenia. BP = bipolar disorder.

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| --- | --- |
| **Familial high-risk of bipolar disorder sample** | **Mothers’ PRS** |
|  | r (p-value) | EA | BMD | SZ | BP |
| **Fathers’PRS** | EA |  | 0.018(0.889) | -0.069(0.599) | -0.163(0.129) |
| BMD | -0.057(0.664) |  | -0.005(0.966) | 0.011(0.916) |
| SZ | 0.113(0.383) | -0.136(0.208) |  | 0.164(0.128) |
| BP | 0.092(0.392) | -0.159(0.140) | 0.104(0.336) |  |

**Supplementary Table S5.** Cross-trait between-parent PRS correlation coefficients (and corresponding p-values) calculated in the sample of familial high-risk of bipolar disorder (n = 61 pairs). EA = educational attainment. BMD = bone mineral density. SZ = schizophrenia. BP = bipolar disorder.



**Supplementary Figure S1.** Correlation coefficients (r) between parents’ polygenic risk scores (PRSs) for schizophrenia (SZ) and bipolar disorder (BP) using different p-value thresholds (pT) in the PRS generation.



**Supplementary Figure S2:** Directed acyclic graph (DAG) illustrating theoretical collider stratification bias in the patient samples. We are interested in the correlation between the PRS in one parent (PRSINDEX) and the PRS in the other parent (PRSNONINDEX) as a measure of genetic assortative mating. Here we assume that PRSINDEX as well as other unknown variables (U1) both affect the risk of illness. When selecting only index-parents with an illness, we condition on illness ([Illness]). In theory, this opens up a biasing path (red arrows) through unknown variables (U1), given that these could cause (or share a common cause, U2, with) PRS in the nonindex-parent (PRSNONINDEX). This could in theory give rise to a negative association between PRSINDEX andPRSNONINDEX if the direction of effect is similar for the U1 → Illness path as for the U1 → PRSNONINDEX path. The collider (illness) stratification bias described by this DAG can only generate a positive association between the two PRSs if U1 has opposite effects on (or association with) Illness and PRSNONINDEX. In other words, there would have to exist a variable (U2) that both increases the risk of illness and at the same time decreases the PRS of the non-index parent – a scenario that we find unlikely.