**Supplementary Material for:**

Shared genetic etiology between alcohol dependence and major depressive disorder

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**Supplementary Text:**

*Effect of Sample Sex Configuration*

To examine whether having a male-only target sample might have had an effect on predictive ability, we also calculated MDD-PRS in the GESGA sample using a PGC-MDD wave 1 leave BoMa out meta-analysis data for males only (male cases, n = 2780; male controls, n =3420) as the discovery sample. Unfortunately, the PGC-MDD wave 2 meta-analysis data were not available in such a format.

We observed only a slight increase in the ability for MDD-PRS to predict AD status. The results of the original analysis were (best p-threshold=0.2, p=0.00023, R2=0.622%) with the PGC-MDD1 base data with both sexes; looking at males only yielded (best p-threshold: 1.0, p = 0.00075, R2= 0.718%). Based on these results, we conclude there is no major influence of sex on our findings.

We also examined whether BoMA MDD-PRS differed across sexes. Comparing MDD1-PRS across sex, no significant differences were observed between males and females (P-threshold =1.0, F(1,1646), p = 0.522). In contrast, the MDD2-PRS were statistically significantly higher in females than in males (P-threshold = 1.0, F(1,1646), p = 0.007). We then calculated the contribution of MDD2-PRS to case-control status of the BoMa sample controlling for sex as a covariate (in addition to using 10 PCs), finding that predictive ability decreased slightly (with sex covariate, P-threshold = 1.0, p = 0.00015, R2= 1.11% vs. without sex covariate, p-threshold=1.0, p=0.000038, R2=1.34%).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
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| **Table S1**. Polygenic Risk Score Model Fit in Alcohol Dependence (*GESGA*) Target Sample in PGC-MDD Wave 2 (n=59 265 cases; n=112 092 controls)  and PGC-MDD Wave 1 (n=8148 cases; n=7955 controls) Discovery Samples   |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | |  | PGC-MDD Wave 2 | | | PGC-MDD Wave 1 | | | | P-Value Threshold | Sig. | R2 | Number of SNPs | Sig. | R2 | Number of SNPs | | 0.000001 | 0.13347659 | 0.00102096 | 15 | 0.47804967 | 0.00022822 | 2 | | 0.0001 | 0.32155953 | 0.00044551 | 144 | 0.82065642 | 2.3291E-05 | 37 | | 0.001 | 0.18089249 | 0.00081203 | 675 | 0.51212083 | 0.00019482 | 300 | | 0.01 | 0.0527535 | 0.00170416 | 3311 | 0.02241567 | 0.00236773 | 2212 | | 0.05 | 0.0172684 | 0.00257727 | 10581 | 0.00533112 | 0.00352963 | 8676 | | 0.1 | 0.00520875 | 0.00355442 | 17081 | 0.00024776 | 0.0061273 | 14961 | | 0.2 | 0.00128255 | 0.00472862 | 27415 | **0.00013907** | **0.00662807** | **25479** | | 0.5 | 0.0011197 | 0.00484634 | 48295 | 0.0006264 | 0.0053353 | 47299 | | 1 | **0.00063271** | **0.00533254** | **66704** | 0.00076019 | 0.00517076 | 66776 | |  |  |

**Table S2.**  Polygenic Risk Score Model Fit in BoMa-MDD Target Sample and PGC-MDD Wave 2 and Wave 1 Discovery Samples

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | MDD wave 2 | | | MDD wave 1 | | |
| P-Value Threshold | Sig. | R2 | Number of SNPs | Sig. | R2 | Number of SNPs |
| 0.00000005 | 0.53729651 | 0.00029731 | 11 | - | - | - |
| 0.000001 | 0.10627467 | 0.0020424 | 25 | 0.66150838 | 0.00014965 | 2 |
| 0.0001 | 0.09775962 | 0.0021459 | 263 | 0.49192544 | 0.00036907 | 73 |
| 0.001 | 0.2499612 | 0.00103494 | 1056 | 0.92116459 | 7.6503E-06 | 482 |
| 0.01 | 0.00740699 | 0.00563384 | 4976 | 0.64673568 | 0.00016407 | 3293 |
| 0.05 | 0.00082112 | 0.00882772 | 14608 | 0.05593942 | 0.00285823 | 11688 |
| 0.1 | 0.00010523 | 0.01188285 | 22806 | 0.00374917 | 0.00659156 | 19478 |
| 0.2 | 0.0001154 | 0.01173739 | 34923 | 0.00185245 | 0.00761328 | 31746 |
| 0.5 | 5.8086E-05 | 0.01277664 | 57552 | 0.00154691 | 0.00787859 | 55657 |
| 1 | **3.7883E-05** | **0.01342009** | **73785** | **0.00134771** | **0.00807912** | **73954** |

**Table S3.** Polygenic Risk Score Model Fit in Non *PREDICT* and *PREDICT* Target Samples in PGC-MDD Wave 2 Discovery Sample

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Non *PREDICT* | | | *PREDICT* | | |
| P-Value Threshold | Sig. | R2 | Number of SNPs | Sig. | R2 | Number of SNPs |
| 0.00000005 | 0.72994128 | 6.203E-05 | 6 | 0.66880659 | 0.00017521 | 6 |
| 0.000001 | 0.2240976 | 0.00076977 | 15 | 0.23904379 | 0.00132976 | 15 |
| 0.0001 | 0.13889156 | 0.00114149 | 144 | 0.54031888 | 0.0003589 | 142 |
| 0.001 | 0.05145778 | 0.00197744 | 679 | 0.39460354 | 0.00069453 | 675 |
| 0.01 | 0.01438127 | 0.00313121 | 3317 | 0.76216026 | 8.7698E-05 | 3310 |
| 0.05 | 0.0085361 | 0.00361859 | 10577 | 0.25076774 | 0.00126568 | 10560 |
| 0.1 | 0.00285797 | 0.00465409 | 17076 | 0.17097427 | 0.00179816 | 17067 |
| 0.2 | 0.00037457 | 0.0066341 | 27422 | 0.19138506 | 0.00163677 | 27378 |
| 0.5 | 0.00045432 | 0.00645131 | 48280 | 0.05908597 | 0.00342508 | 48102 |
| 1 | **0.00028083** | **0.00692785** | **66723** | **0.04209097** | **0.00397614** | **66418** |

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