Supplementary Table 1. Association of polygenic risk score (PRS) across different training set association thresholds. Parameters are shown from logistic regression models with BD vs. MDD the dependent phenotypic variable and the first 10 principal components, sex and age at interview included as covariates. OR represents the odds ratio of the standardized PRS with a standard deviation as the unit of analysis. Nagelkerke Pseudo R2 represents the overall proportion of variance attributable to the independent variables in the model. Changes in R2 (ΔR2) represent additive increases in the attributable variance compared to a baseline model with first 10 principal components, sex and age at interview included as covariates. BD=PRS derived from Bipolar Disorder GWAS. SCZ=PRS derived from Schizophrenia GWAS.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| GWAS Training Set Threshold (fraction of causal variants) | ***R2*** | *Δ****R2*** | ***OR*** | ***S.E.*** | ***z-score*** | ***p-value*** |
|  |  |  |  |  |  |  |
| Baseline | 0.0610 |  |  |  |  |  |
| BD: 0.0001 | 0.0648 | 0.0038 | 1.12 | 0.0504 | 2.29 | 2.21x10-2 |
| BD: 0.0003 | 0.0617 | 0.0007 | 0.949 | 0.0523 | -1.00 | 3.15x10-1 |
| BD: 0.001 | 0.0622 | 0.0012 | 0.934 | 0.0526 | -1.31 | 1.92x10-1 |
| BD: 0.003 | 0.0963 | 0.0353 | 1.59 | 0.0672 | 6.91 | 4.94x10-12 |
| BD: 0.01 | 0.0942 | 0.0332 | 1.58 | 0.0686 | 6.71 | 1.97x10-11 |
| BD: 0.03 | 0.0917 | 0.0307 | 1.56 | 0.0685 | 6.46 | 1.08x10-10 |
| BD: 0.1 | 0.0907 | 0.0297 | 1.54 | 0.0683 | 6.36 | 2.05x10-10 |
| BD: 0.3 | 0.0903 | 0.0293 | 1.54 | 0.0683 | 6.31 | 2.73x10-10 |
| BD: 1 | 0.0902 | 0.0292 | 1.54 | 0.0682 | 6.30 | 3.01x10-10 |
|  |  |  |  |  |  |  |
|  | ***R2*** | *Δ****R2*** | ***OR*** | ***S.E.*** | ***z-score*** | ***p-value*** |
| SCZ: 0.0001 | 0.0636 | 0.0026 | 1.14 | 0.0693 | 1.89 | 5.87x10-2 |
| SCZ: 0.0003 | 0.0619 | 0.0009 | 1.06 | 0.0488 | 1.13 | 2.59x10-1 |
| SCZ: 0.001 | 0.0612 | 0.0002 | 1.03 | 0.0504 | 0.546 | 5.85x10-1 |
| SCZ: 0.003 | 0.0655 | 0.0045 | 1.14 | 0.0540 | 2.49 | 1.28x10-2 |
| SCZ: 0.01 | 0.0643 | 0.0033 | 1.12 | 0.0541 | 2.15 | 3.16x10-2 |
| SCZ: 0.03 | 0.0850 | 0.024 | 1.38 | 0.0557 | 5.72 | 1.06x10-8 |
| SCZ: 0.1 | 0.0906 | 0.0296 | 1.44 | 0.0571 | 6.34 | 2.29x10-10 |
| SCZ: 0.3 | 0.0926 | 0.0316 | 1.46 | 0.0576 | 6.55 | 5.71x10-11 |
| SCZ: 1 | 0.0918 | 0.0308 | 1.45 | 0.0577 | 6.47 | 9.53x10-11 |

Supplementary Table 2. Incremental predictive ability due to polygenic risk scores (PRS) in models including various clinical symptoms and clinical correlates. C-statistics and their confidence intervals (CI) are shown from each individual model. The reference models represent the effect of baseline covariates (age, sex and 10 principal components). Additional predictors due to PRS are shown as changes in the C-statistic (ΔC). As described in the text, clinical predictors are categorized as depressive symptoms (psychomotor retardation [PMR], incapacitation, delusions and number of mixed symptoms during worst depressive episode) or associated clinical features (length of most severe episode, number of depressive episodes, antidepressant induced “high” feeling).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Model** | ***C-statistic*** | ***CILower*** | ***CIUpper*** | ***ΔC (with PRS)*** |
| Reference | 0.603 | 0.577 | 0.629 | - |
| PRSSCZ | 0.640 | 0.615 | 0.666 | 0.037 |
| PRSBD | 0.640 | 0.615 | 0.666 | 0.038 |
| PRSBD  + PRSSCZ | 0.654 | 0.629 | 0.679 | 0.051 |
|  |  |  |  |  |
| **Symptoms** |  |  |  |  |
| Psychomotor Retardation (PMR) | 0.687 | 0.662 | 0.711 | - |
| PMR + PRSBD  + PRSSCZ | 0.711 | 0.687 | 0.734 | 0.024 |
| Incapacitation | 0.739 | 0.716 | 0.762 | - |
| Incapacitation + PRSBD  + PRSSCZ | 0.760 | 0.738 | 0.782 | 0.021 |
| Delusions | 0.688 | 0.664 | 0.712 | - |
| Delusions + PRSBD  + PRSSCZ | 0.730 | 0.707 | 0.753 | 0.042 |
| Mixed symptoms | 0.635 | 0.609 | 0.661 | - |
| Mixed symptoms + PRSBD  + PRSSCZ | 0.688 | 0.664 | 0.712 | 0.053 |
|  |  |  |  |  |
| **Clinical Features** |  |  |  |  |
| Length of Depressive Episode | 0.670 | 0.645 | 0.695 | - |
| Length + PRSBD  + PRSSCZ | 0.707 | 0.683 | 0.731 | 0.037 |
| Number of Episodes | 0.686 | 0.662 | 0.711 | - |
| Episodes + PRSBD  + PRSSCZ | 0.716 | 0.693 | 0.739 | 0.030 |
| High following antidepressant | 0.717 | 0.693 | 0.741 | - |
| High + PRSBD  + PRSSCZ | 0.748 | 0.726 | 0.771 | 0.031 |
|  |  |  |  |  |
| **Combined** |  |  |  |  |
| All Symptoms | 0.807 | 0.787 | 0.827 |  |
| Symptoms + PRSBD  + PRSSCZ | 0.819 | 0.800 | 0.838 | 0.012 |
| All Clinical Features | 0.774 | 0.752 | 0.795 |  |
| Clinical Features + PRSBD  + PRSSCZ | 0.794 | 0.773 | 0.814 | 0.020 |
| All Clinical (symptoms + features) | 0.855 | 0.837 | 0.872 | - |
| All Clinical + PRSBD | 0.862 | 0.845 | 0.879 | 0.0074 |
| All Clinical + PRSSCZ | 0.861 | 0.845 | 0.879 | 0.0064 |
| All Clinical + PRSBD  + PRSSCZ | 0.865 | 0.848 | 0.881 | 0.011 |