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**TABLE S1. Number of variants included in computation of the polygenic risk scores**

|                           | MDD       | BD        | SCZ       | ATR       |
|---------------------------|-----------|-----------|-----------|-----------|
| Number of Overlapped SNPs | 4,123,021 | 4,159,913 | 4,374,410 | 4,473,896 |
| Number of Clumped SNPs    | 127,655   | 100,607   | 126,921   | 133,728   |

Number of SNPs in target data: 4,521,262

MDD: Major depressive disorder; BD: Bipolar disorder; SCZ: Schizophrenia;

ATR: Antidepressant treatment response.

**TABLE S2. Association between polygenic risk scores and measures of improvement after ECT**

|                                      | All patients |           |           |                    |                             |                                | Narrow indication (unipolar depression, sensitivity analysis) |           |           |       |                             |                                |
|--------------------------------------|--------------|-----------|-----------|--------------------|-----------------------------|--------------------------------|---|-----------|-----------|-------|-----------------------------|--------------------------------|
|                                      | N            | OR per SD | 95% CI    | P                  | R <sup>2</sup> <sup>c</sup> | P <sub>ALRT</sub> <sup>d</sup> | N   | OR per SD | 95% CI    | P     | R <sup>2</sup> <sup>c</sup> | P <sub>ALRT</sub> <sup>d</sup> |
| <b>CGI-Improvement<sup>a</sup></b>   | 2,320        |           |           |                    |                             |                                | 1,789   |           |           |       |                             |                                |
| PRS-MDD                              |              | 0.89      | 0.82-0.96 | 0.002 <sup>e</sup> | 0.4%                        | 0.758                          |   | 0.87      | 0.79-0.94 | 0.001 | 0.6%                        | 0.880                          |
| PRS-BD                               |              | 1.14      | 1.05-1.23 | 0.001 <sup>e</sup> | 0.5%                        | 0.636                          |   | 1.20      | 1.09-1.30 | 7E-5  | 0.8%                        | 0.558                          |
| PRS-SCZ                              |              | 1.04      | 0.97-1.14 | 0.247              | 0.1%                        | 0.114                          |   | 1.04      | 0.95-1.14 | 0.367 | 0.0%                        | 0.589                          |
| <b>MADRS-S response<sup>b</sup></b>  | 1,207        |           |           |                    |                             |                                | 815   |           |           |       |                             |                                |
| PRS-MDD                              |              | 0.85      | 0.76-0.96 | 0.008              | 0.8%                        | -                              |   | 0.85      | 0.73-0.98 | 0.026 | 0.8%                        | -                              |
| PRS-BD                               |              | 1.13      | 1.00-1.27 | 0.045              | 0.4%                        | -                              |   | 1.13      | 0.98-1.30 | 0.103 | 0.4%                        | -                              |
| PRS-SCZ                              |              | 1.05      | 0.93-1.19 | 0.401              | 0.1%                        |                                |   | 1.01      | 0.87-1.18 | 0.851 | 0.0%                        |                                |
| <b>MADRS-S remission<sup>b</sup></b> | 1,207        |           |           |                    |                             |                                | 815   |           |           |       |                             |                                |
| PRS-MDD                              |              | 0.83      | 0.73-0.94 | 0.002              | 1.0%                        | -                              |   | 0.83      | 0.72-0.96 | 0.014 | 0.9%                        | -                              |
| PRS-BD                               |              | 1.15      | 1.02-1.29 | 0.023              | 0.6%                        | -                              |   | 1.15      | 0.99-1.33 | 0.062 | 0.5%                        | -                              |
| PRS-SCZ                              |              | 1.16      | 1.02-1.31 | 0.020              | 0.6%                        | -                              |   | 1.17      | 1.00-1.37 | 0.045 | 0.6%                        | -                              |

The table shows the results presented in Figure 1 of the manuscript.

Abbreviations: OR: odds ratio; SD: standard deviation; 95% CI: 95% confidence interval; PRS: Polygenic risk score; MDD: Major depressive disorder; BD: Bipolar disorder; SCZ: Schizophrenia; CGI-I: Clinical Global Impressions-Improvement; MADRS-S: Self-rated Montgomery-Åsberg Depression Rating Scale.

<sup>a</sup> An OR >1 represents more improvement with increasing PRS. Estimated from a proportional odds ordinal logistic regression models adjusted for the first five genetic ancestry principal components.

<sup>b</sup> An OR >1 represents higher odds of remission/response with increasing PRS. Estimated from binary logistic regression models adjusted for MADRS-S before ECT, and the first five genetic ancestry principal components.

<sup>c</sup> Difference in Nagelkerke R<sup>2</sup> between model with and without each PRS.

<sup>d</sup> P-value from an approximate likelihood-ratio test of the proportional odds assumption of ordinal logistic regression. A significant p-value indicates violation of the assumption.

<sup>e</sup> Significant after Bonferroni correction (p<0.017, only applied for analysis of the primary outcome among all patients).

**TABLE S3. Associations between quintiles of PRS and CGI improvement after ECT**

|                         | All patients (N=2,320) |           |       |                                | Narrow indication (unipolar depression) (N=1,789) |           |       |                                |
|-------------------------|------------------------|-----------|-------|--------------------------------|---|-----------|-------|--------------------------------|
|                         | OR per SD <sup>a</sup> | 95% CI    | P     | P <sub>ALRT</sub> <sup>b</sup> | OR per SD <sup>a</sup>                            | 95% CI    | P     | P <sub>ALRT</sub> <sup>b</sup> |
| <b>PRS-MDD quintile</b> |                        |           |       |                                |   |           |       |                                |
| 1st                     | Reference              |           |       | 0.048                          |   |           |       | 0.092                          |
| 2nd                     | 1.06                   | 0.83-1.35 | 0.648 |                                | 1.07  | 0.81-1.41 | 0.628 |                                |
| 3rd                     | 0.79                   | 0.62-1.00 | 0.054 |                                | 0.77  | 0.59-1.01 | 0.061 |                                |
| 4th                     | 0.96                   | 0.76-1.22 | 0.736 |                                | 0.90  | 0.69-1.18 | 0.456 |                                |
| 5th                     | 0.69                   | 0.54-0.87 | 0.002 |                                | 0.66  | 0.50-0.86 | 0.002 |                                |
| <b>PRS-BD quintile</b>  |                        |           |       |                                |   |           |       |                                |
| 1st                     | Reference              |           |       | 0.014                          |   |           |       | 3E-8                           |
| 2nd                     | 1.27                   | 1.01-1.61 | 0.044 |                                | 1.33  | 1.02-1.74 | 0.038 |                                |
| 3rd                     | 1.17                   | 0.92-1.49 | 0.210 |                                | 1.35  | 1.02-1.79 | 0.038 |                                |
| 4th                     | 1.49                   | 1.17-1.91 | 0.001 |                                | 1.64  | 1.24-2.17 | 5E-4  |                                |
| 5th                     | 1.44                   | 1.13-1.84 | 0.003 |                                | 1.72  | 1.30-2.27 | 2E-4  |                                |
| <b>PRS-SCZ quintile</b> |                        |           |       |                                |   |           |       |                                |
| 1st                     | Reference              |           |       | 0.210                          |   |           |       | 0.483                          |
| 2nd                     | 1.21                   | 0.95-1.55 | 0.124 |                                | 1.20  | 0.91-1.58 | 0.192 |                                |
| 3rd                     | 1.21                   | 0.96-1.52 | 0.104 |                                | 1.08  | 0.83-1.41 | 0.570 |                                |
| 4th                     | 1.27                   | 1.00-1.61 | 0.052 |                                | 1.20  | 0.92-1.57 | 0.181 |                                |
| 5th                     | 1.11                   | 0.87-1.42 | 0.404 |                                | 1.12  | 0.85-1.48 | 0.426 |                                |

The table shows the results presented in Figure 2 of the manuscript.

Abbreviations: OR: odds ratio; SD: standard deviation; 95% CI: 95% confidence interval; PRS: Polygenic risk score; MDD: Major depressive disorder; BD: Bipolar disorder; SCZ: Schizophrenia.

<sup>a</sup> An OR >1 represents more improvement with increasing PRS. Estimated from a proportional odds ordinal logistic regression models adjusted for the first five genetic ancestry principal components.

<sup>b</sup> P-value from an approximate likelihood-ratio test of the proportional odds assumption of ordinal logistic regression. A significant p-value indicates violation of the assumption.

**TABLE S4. Post hoc analysis of the association between a polygenic risk score for antidepressant treatment response and measures of improvement after ECT**

|                                | All patients |           |           |       |                             |                                | Narrow indication (unipolar depression, sensitivity analysis) |           |           |       |                             |                                |
|--------------------------------|--------------|-----------|-----------|-------|-----------------------------|--------------------------------|---|-----------|-----------|-------|-----------------------------|--------------------------------|
|                                | N            | OR per SD | 95% CI    | P     | R <sup>2</sup> <sup>c</sup> | P <sub>ALRT</sub> <sup>d</sup> | N   | OR per SD | 95% CI    | P     | R <sup>2</sup> <sup>c</sup> | P <sub>ALRT</sub> <sup>d</sup> |
| CGI-Improvement <sup>a</sup>   | 2,320        | 1.03      | 0.95-1.12 | 0.511 | 0.0%                        | 0.676                          | 1,789   | 1.07      | 0.97-1.17 | 0.182 | 0.1%                        | 0.916                          |
| MADRS-S response <sup>b</sup>  | 1,207        | 0.99      | 0.87-1.12 | 0.860 | 0.0%                        | -                              | 815   | 0.95      | 0.82-1.11 | 0.534 | 0.1%                        | -                              |
| MADRS-S remission <sup>b</sup> | 1,207        | 0.96      | 0.85-1.09 | 0.542 | 0.0%                        | -                              | 815   | 0.95      | 0.82-1.11 | 0.516 | 0.1%                        | -                              |

Antidepressant response: Percentage improvement on antidepressants.

Abbreviations: OR: odds ratio; SD: standard deviation; 95% CI: 95% confidence interval; PRS: Polygenic risk score; CGI-I: Clinical Global Impressions-Improvement; MADRS-S: Self-rated Montgomery-Åsberg Depression Rating Scale.

<sup>a</sup> An OR >1 represents more improvement with increasing PRS. Estimated from a proportional odds ordinal logistic regression models adjusted for the first five genetic ancestry principal components.

<sup>b</sup> An OR >1 represents higher odds of remission/response with increasing PRS. Estimated from binary logistic regression models adjusted for MADRS-S before ECT, and the first five genetic ancestry principal components.

<sup>c</sup> Difference in Nagelkerke R<sup>2</sup> between model with and without each PRS.

<sup>d</sup> P-value from an approximate likelihood-ratio test of the proportional odds assumption of ordinal logistic regression. A significant p-value indicates violation of the assumption.

**TABLE S5. Association between polygenic risk scores and measures of improvement after ECT according to electrode placement**

|         | Unilateral (N=2012)    |           |       |                             |                                | Bilateral (N=306)      |           |       |                             |                                |
|---------|------------------------|-----------|-------|-----------------------------|--------------------------------|------------------------|-----------|-------|-----------------------------|--------------------------------|
|         | OR per SD <sup>a</sup> | 95% CI    | P     | R <sup>2</sup> <sup>b</sup> | P <sub>ALRT</sub> <sup>c</sup> | OR per SD <sup>a</sup> | 95% CI    | P     | R <sup>2</sup> <sup>b</sup> | P <sub>ALRT</sub> <sup>c</sup> |
| PRS-MDD | 0.90                   | 0.83-0.98 | 0.014 | 0.3%                        | 0.624                          | 0.79                   | 0.65-0.97 | 0.024 | 1.6%                        | 0.116                          |
| PRS-BD  | 1.15                   | 1.05-1.25 | 0.002 | 0.5%                        | 0.474                          | 1.10                   | 0.92-1.31 | 0.296 | 0.3%                        | 0.178                          |
| PRS-SCZ | 1.03                   | 0.95-1.13 | 0.477 | 0.0%                        | 0.613                          | 1.15                   | 0.93-1.43 | 0.186 | 0.6%                        | 0.322                          |

Data on electrode placement was missing for two participants.

Abbreviations: OR: odds ratio; SD: standard deviation; 95% CI: 95% confidence interval; PRS: Polygenic risk score; MDD: Major depressive disorder; BD: Bipolar disorder; SCZ: Schizophrenia; CGI-I: Clinical Global Impressions-Improvement.

<sup>a</sup> An OR >1 represents more improvement with increasing PRS. Estimated from ordinal logistic regression models adjusted for the first five genetic ancestry principal components.

<sup>b</sup> Difference in Nagelkerke R<sup>2</sup> between model with and without each PRS.

<sup>c</sup> P-value from an approximate likelihood-ratio test of the proportional odds assumption of ordinal logistic regression. A significant p-value indicates violation of the assumption.

**TABLE S6. Association between polygenic risk scores and measures of improvement after ECT according to presence of psychotic features**

|         | Non-psychotic (N=1,972) |           |       |                             |                                | Psychotic (N=348)      |           |       |                             |                                |
|---------|-------------------------|-----------|-------|-----------------------------|--------------------------------|------------------------|-----------|-------|-----------------------------|--------------------------------|
|         | OR per SD <sup>a</sup>  | 95% CI    | P     | R <sup>2</sup> <sup>b</sup> | P <sub>ALRT</sub> <sup>c</sup> | OR per SD <sup>a</sup> | 95% CI    | P     | R <sup>2</sup> <sup>b</sup> | P <sub>ALRT</sub> <sup>c</sup> |
| PRS-MDD | 0.90                    | 0.83-0.97 | 0.010 | 0.4%                        | 0.857                          | 0.90                   | 0.73-1.12 | 0.413 | 0.3%                        | 0.693                          |
| PRS-BD  | 1.11                    | 1.02-1.20 | 0.019 | 0.3%                        | 0.799                          | 1.13                   | 0.91-1.40 | 0.347 | 0.4%                        | 0.584                          |
| PRS-SCZ | 1.02                    | 0.94-1.12 | 0.582 | 0.0%                        | 0.172                          | 1.06                   | 0.84-1.33 | 0.698 | 0.1%                        | 0.678                          |

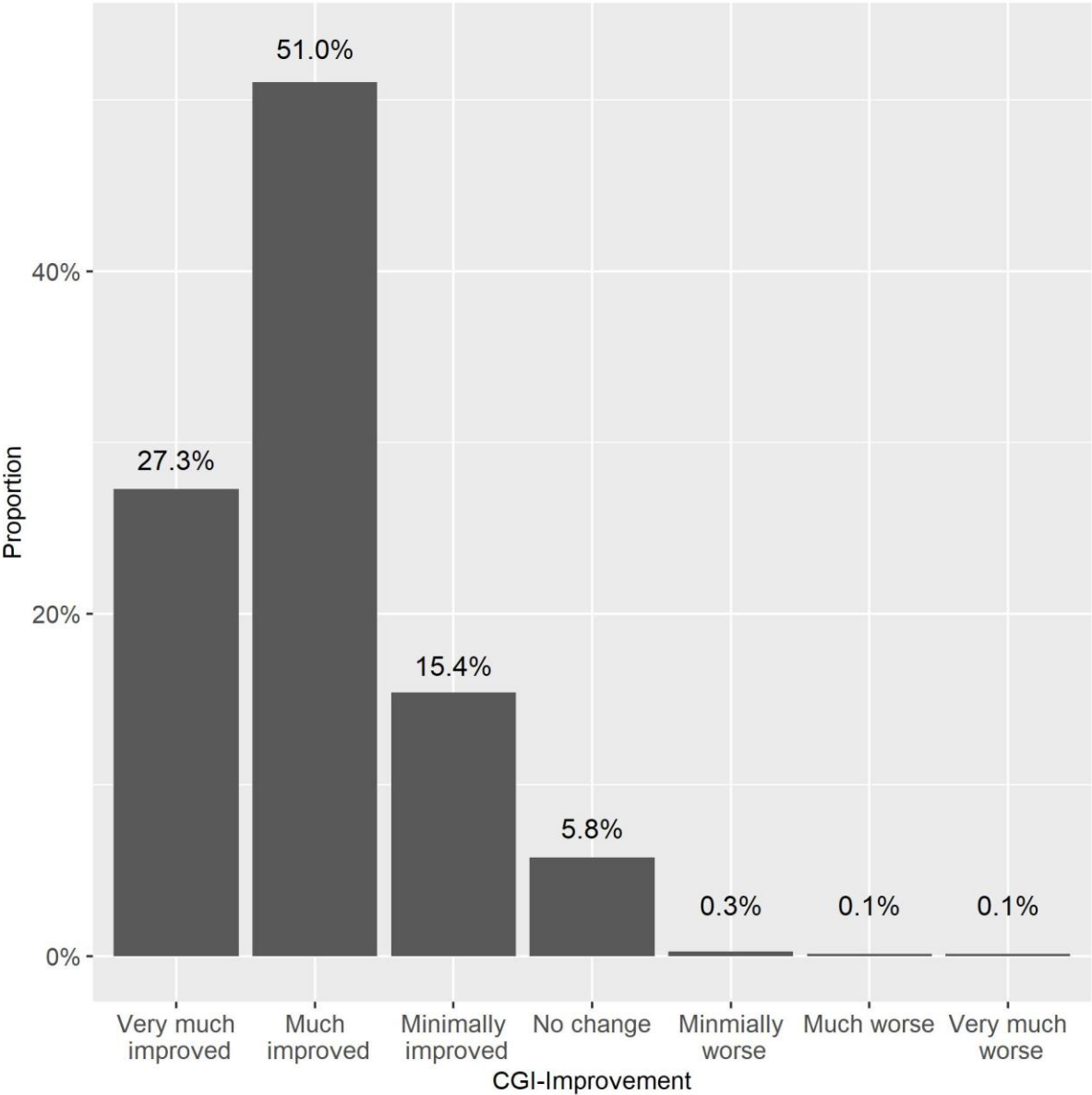
Abbreviations: OR: odds ratio; SD: standard deviation; 95% CI: 95% confidence interval; PRS: Polygenic risk score; MDD: Major depressive disorder; BD: Bipolar disorder; SCZ: Schizophrenia; CGI-I: Clinical Global Impressions-Improvement.

<sup>a</sup> An OR >1 represents more improvement with increasing PRS. Estimated from ordinal logistic regression models adjusted for the first five genetic ancestry principal components.

<sup>b</sup> Difference in Nagelkerke R<sup>2</sup> between model with and without each PRS.

<sup>c</sup> P-value from an approximate likelihood-ratio test of the proportional odds assumption of ordinal logistic regression. A significant p-value indicates violation of the assumption.

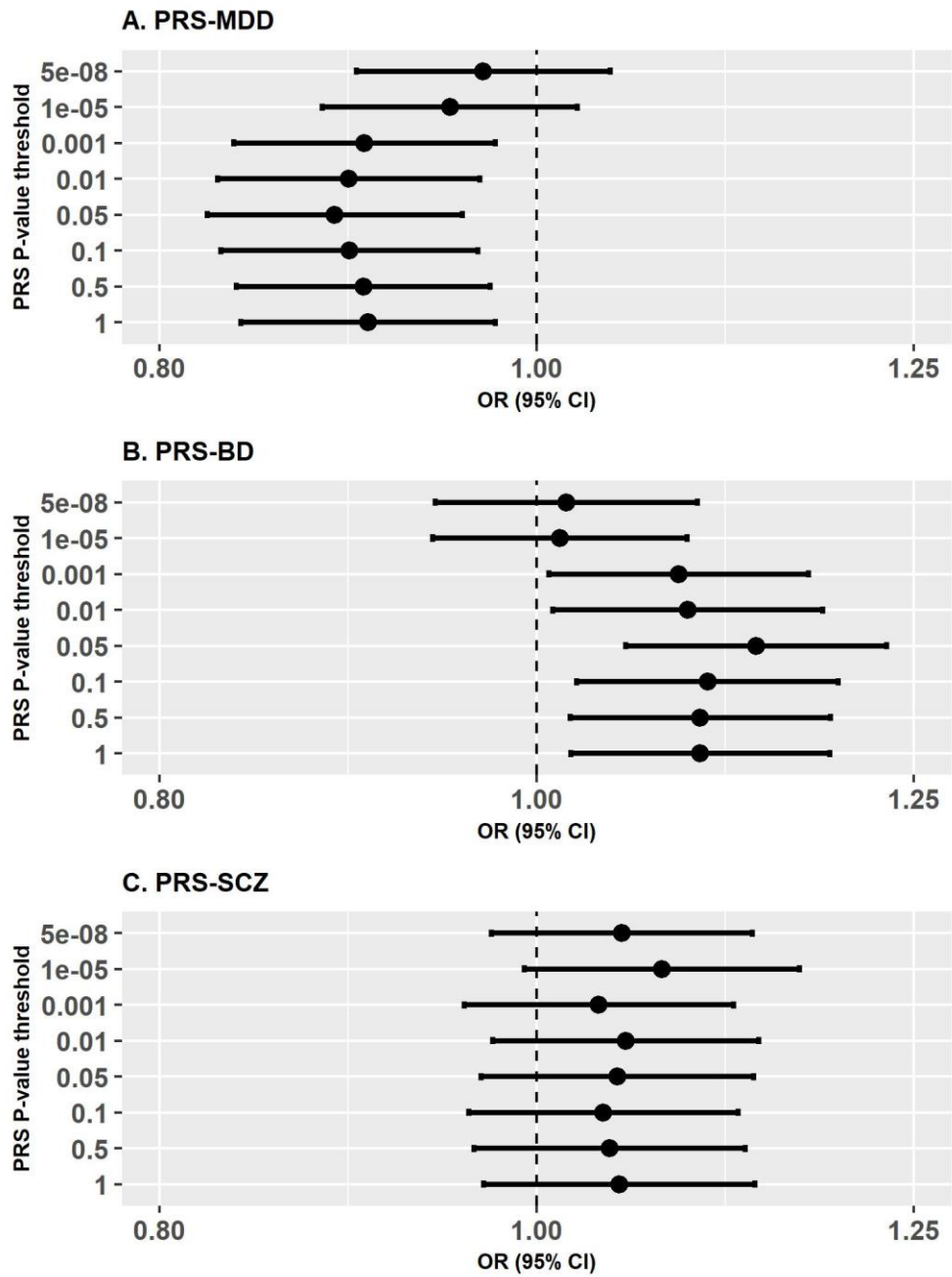
**FIGURE S1. Distribution of CGI improvement scale ratings**



The figure shows the distribution of CGI improvement scale ratings among all patients in the study (N=2,320).



**FIGURE 2. Association between PRS at different p-value thresholds and CGI-Improvement**



The figure shows the odds of a more favorable outcome according to CGI-I (Clinical Global Impressions improvement scale) for PRS (Polygenic risk scores) calculated from different p-value thresholds (N=2,320). The bars represent 95% confidence intervals. Estimated from ordinal logistic regression models adjusted for the first five genetic ancestry principal components. PRS are coded as risk increasing. The x-axis is logarithmic. **Panel A:** PRS-MDD (Major depressive disorder). **Panel B:** PRS-BD (Bipolar disorder). **Panel C:** PRS-SCZ (Schizophrenia)