Statistics
in Medicine

# Supporting Information for "An evaluation of constrained randomization for the design and analysis of group-randomized trials"

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## Web Tables

**Web Table 1.** Type I error rate for the unadjusted and adjusted tests under simple versus constrained randomization using total balance score (TB) with $g = 7$ and $g = 11$. All four group-level potential confounders were adjusted in constrained randomization ($S = 4$) and in any given adjusted test; candidate set size ($R$) are varied under constrained randomization.

| | | | | Type I error rate | | | |
|---|---|---|---|---|---|---|---|
| | Randomization | ICC | $R$ | Unadj F-test | Unadj P-test | Adj F-test | Adj P-test |
| $g = 7$ | Constrained | 0.01 | 20 | 0.002 | – | 0.050 | – |
| | Constrained | 0.01 | 100 | 0.001 | 0.039 | 0.051 | 0.039 |
| | Constrained | 0.01 | 1000 | 0.002 | 0.051 | 0.048 | 0.047 |
| | Constrained | 0.01 | 2000 | 0.007 | 0.048 | 0.047 | 0.047 |
| | Constrained | 0.01 | 3000 | 0.026 | 0.049 | 0.049 | 0.051 |
| | Simple | 0.01 | – | 0.051 | 0.046 | 0.049 | 0.047 |
| | Constrained | 0.1 | 20 | 0.001 | – | 0.050 | – |
| | Constrained | 0.1 | 100 | 0.002 | 0.041 | 0.051 | 0.037 |
| | Constrained | 0.1 | 1000 | 0.004 | 0.049 | 0.049 | 0.049 |
| | Constrained | 0.1 | 2000 | 0.012 | 0.050 | 0.053 | 0.049 |
| | Constrained | 0.1 | 3000 | 0.027 | 0.051 | 0.052 | 0.048 |
| | Simple | 0.1 | – | 0.058 | 0.048 | 0.048 | 0.049 |
| $g = 11$ | Constrained | 0.01 | 20 | 0.000 | – | 0.049 | – |
| | Constrained | 0.01 | 100 | 0.000 | 0.039 | 0.051 | 0.042 |
| | Constrained | 0.01 | 1000 | 0.000 | 0.050 | 0.056 | 0.054 |
| | Constrained | 0.01 | 5000 | 0.000 | 0.050 | 0.049 | 0.050 |
| | Constrained | 0.01 | 10000 | 0.003 | 0.053 | 0.047 | 0.047 |
| | Simple | 0.01 | – | 0.051 | 0.047 | 0.052 | 0.048 |
| | Constrained | 0.1 | 20 | 0.000 | – | 0.047 | – |
| | Constrained | 0.1 | 100 | 0.000 | 0.037 | 0.049 | 0.040 |
| | Constrained | 0.1 | 1000 | 0.000 | 0.048 | 0.053 | 0.052 |
| | Constrained | 0.1 | 5000 | 0.001 | 0.049 | 0.051 | 0.051 |
| | Constrained | 0.1 | 10000 | 0.007 | 0.052 | 0.049 | 0.048 |
| | Simple | 0.1 | – | 0.047 | 0.047 | 0.048 | 0.051 |




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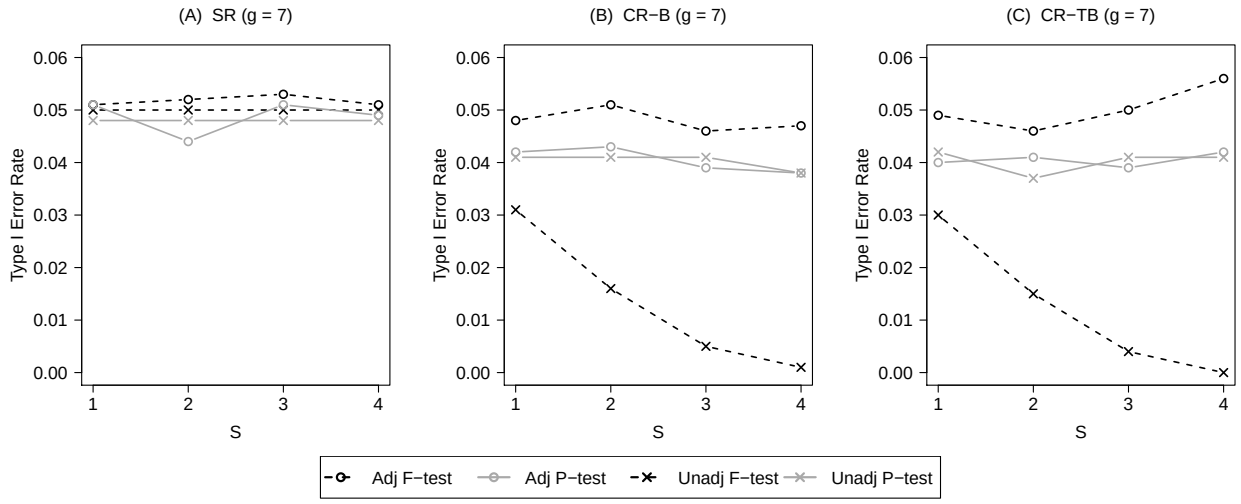
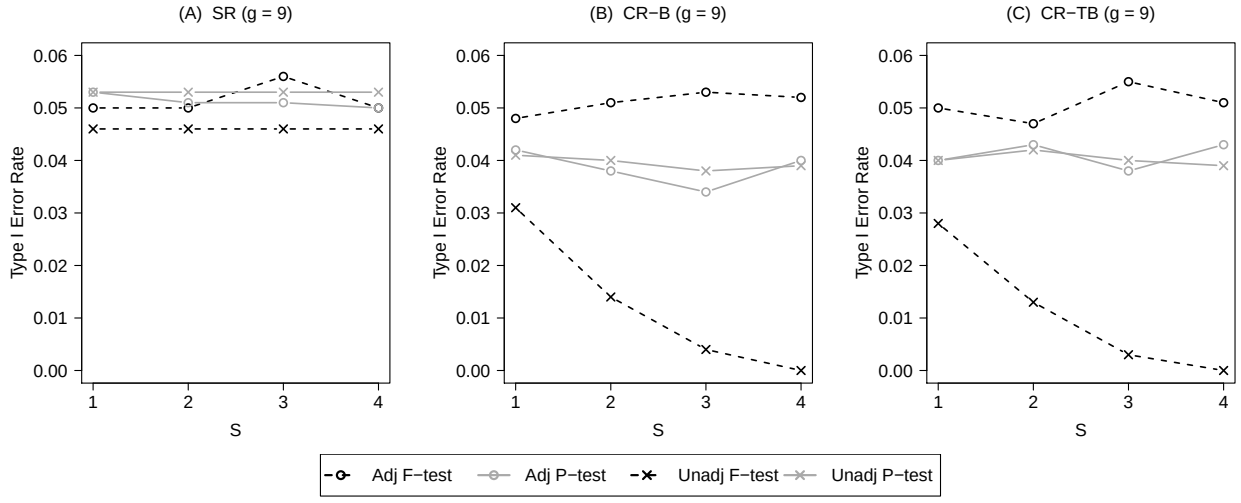
**Web Table 2.** Power for the unadjusted and adjusted tests under simple versus constrained randomization using total balance score (TB) with $g = 7$ and $g = 11$. All four group-level potential confounders were adjusted in constrained randomization ($S = 4$) and in any given adjusted test; candidate set size ($R$) are varied under constrained randomization.

| | | | | Power | | | |
|---|---|---|---|---|---|---|---|
| | Randomization | ICC | $R$ | Unadj F-test | Unadj P-test | Adj F-test | Adj P-test |
| $g = 7$ | Constrained | 0.01 | 20 | 0.002 | – | 1.000 | – |
| | Constrained | 0.01 | 100 | 0.020 | 0.426 | 1.000 | 0.998 |
| | Constrained | 0.01 | 1000 | 0.055 | 0.304 | 1.000 | 0.998 |
| | Constrained | 0.01 | 2000 | 0.094 | 0.227 | 1.000 | 0.993 |
| | Constrained | 0.01 | 3000 | 0.133 | 0.173 | 0.998 | 0.974 |
| | Simple | 0.01 | – | 0.148 | 0.143 | 0.996 | 0.946 |
| | Constrained | 0.1 | 20 | 0.030 | – | 0.644 | – |
| | Constrained | 0.1 | 100 | 0.029 | 0.294 | 0.644 | 0.524 |
| | Constrained | 0.1 | 1000 | 0.059 | 0.234 | 0.595 | 0.561 |
| | Constrained | 0.1 | 2000 | 0.093 | 0.195 | 0.576 | 0.548 |
| | Constrained | 0.1 | 3000 | 0.123 | 0.154 | 0.542 | 0.510 |
| | Simple | 0.1 | – | 0.137 | 0.135 | 0.516 | 0.477 |
| $g = 11$ | Constrained | 0.01 | 20 | 0.030 | – | 1.000 | – |
| | Constrained | 0.01 | 100 | 0.033 | 0.800 | 1.000 | 1.000 |
| | Constrained | 0.01 | 1000 | 0.044 | 0.764 | 1.000 | 1.000 |
| | Constrained | 0.01 | 5000 | 0.112 | 0.499 | 1.000 | 1.000 |
| | Constrained | 0.01 | 10000 | 0.165 | 0.392 | 1.000 | 1.000 |
| | Simple | 0.01 | – | 0.223 | 0.220 | 1.000 | 0.999 |
| | Constrained | 0.1 | 20 | 0.052 | – | 0.891 | – |
| | Constrained | 0.1 | 100 | 0.053 | 0.580 | 0.890 | 0.842 |
| | Constrained | 0.1 | 1000 | 0.060 | 0.576 | 0.886 | 0.879 |
| | Constrained | 0.1 | 5000 | 0.109 | 0.402 | 0.879 | 0.873 |
| | Constrained | 0.1 | 10000 | 0.151 | 0.329 | 0.860 | 0.850 |
| | Simple | 0.1 | – | 0.202 | 0.201 | 0.827 | 0.800 |

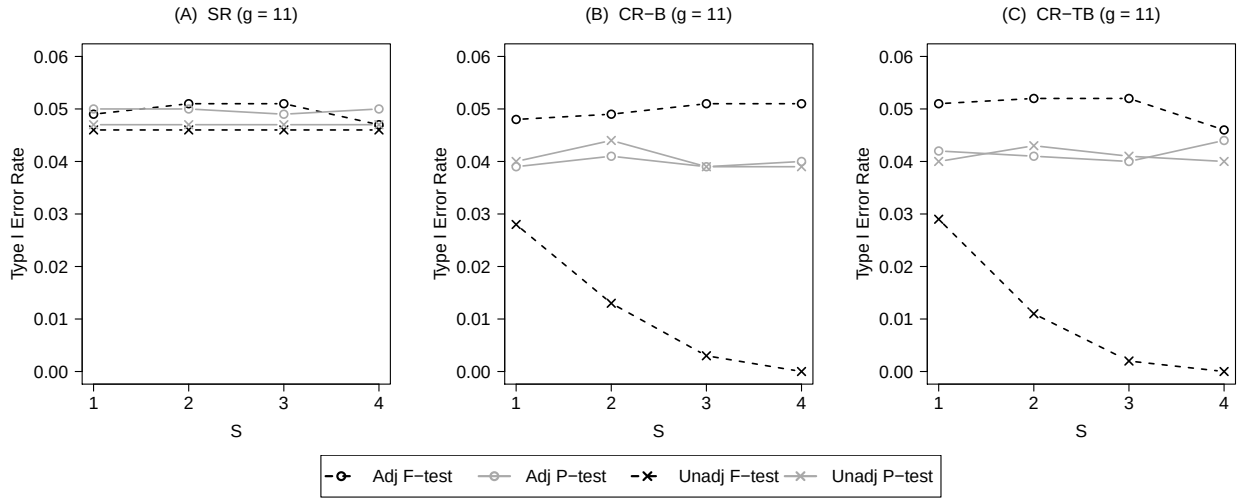
## Web Figures



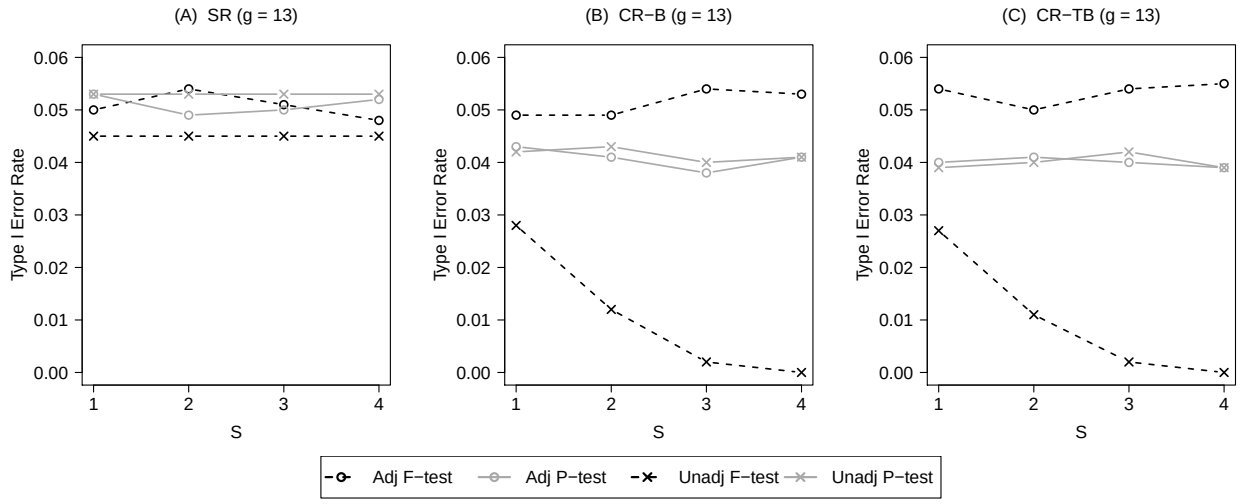

**Web Figure 1.** Type I error rate for F-test and permutation test with different number of group-level potential confounders ($S$) controlled in constrained randomization (CR) versus under simple randomization (SR); B: imbalance score, TB: total balance score, $g = 7$; ICC $= 0.05$, $R = 100$.



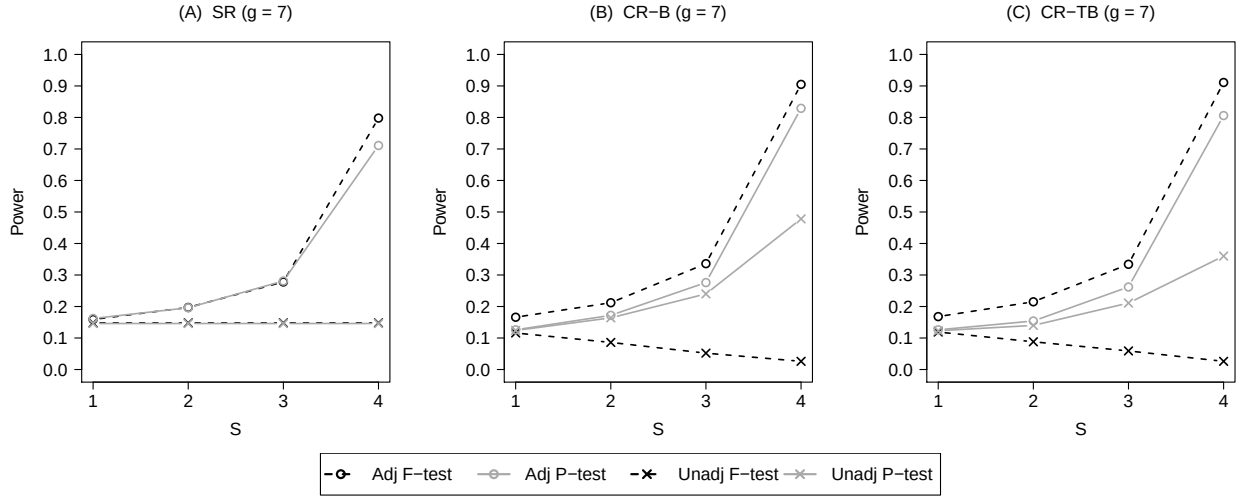

**Web Figure 2.** Type I error rate for F-test and permutation test with different number of group-level potential confounders ($S$) controlled in constrained randomization (CR) versus under simple randomization (SR); B: imbalance score, TB: total balance score, $g = 9$; ICC $= 0.05$, $R = 100$.



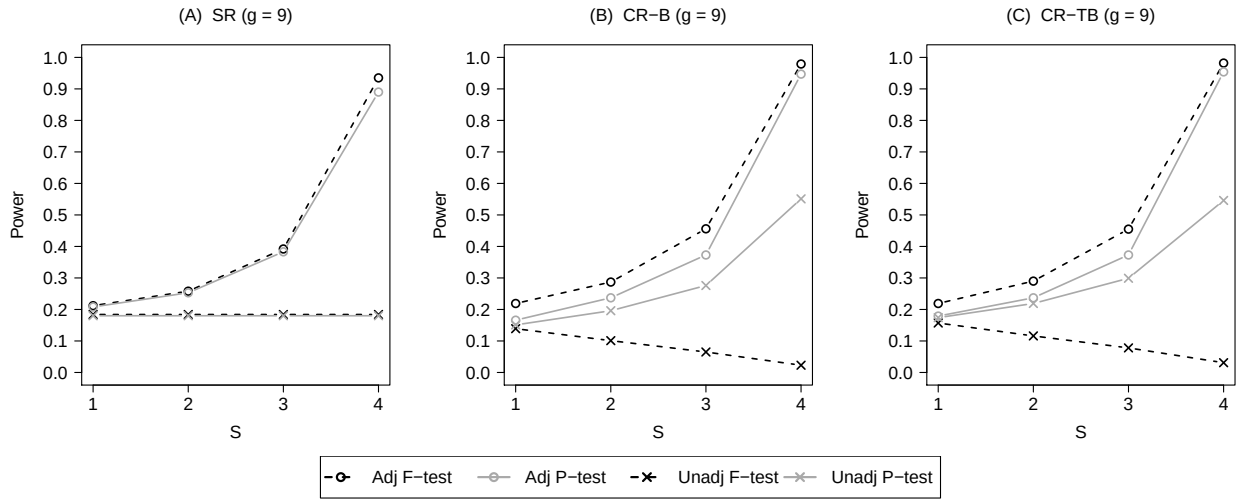

**Web Figure 3.** Type I error rate for F-test and permutation test with different number of group-level potential confounders ($S$) controlled in constrained randomization (CR) versus under simple randomization (SR); B: imbalance score, TB: total balance score, $g = 11$; ICC $= 0.05$, $R = 100$.



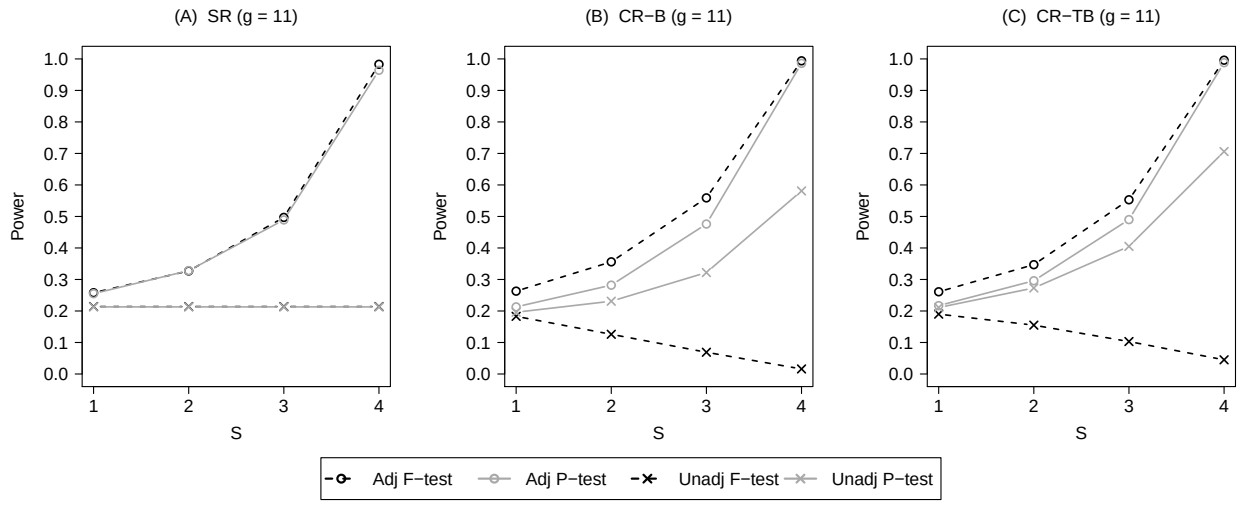

**Web Figure 4.** Type I error rate for F-test and permutation test with different number of group-level potential confounders ($S$) controlled in constrained randomization (CR) versus under simple randomization (SR); B: imbalance score, TB: total balance score, $g = 13$; ICC $= 0.05$, $R = 100$.



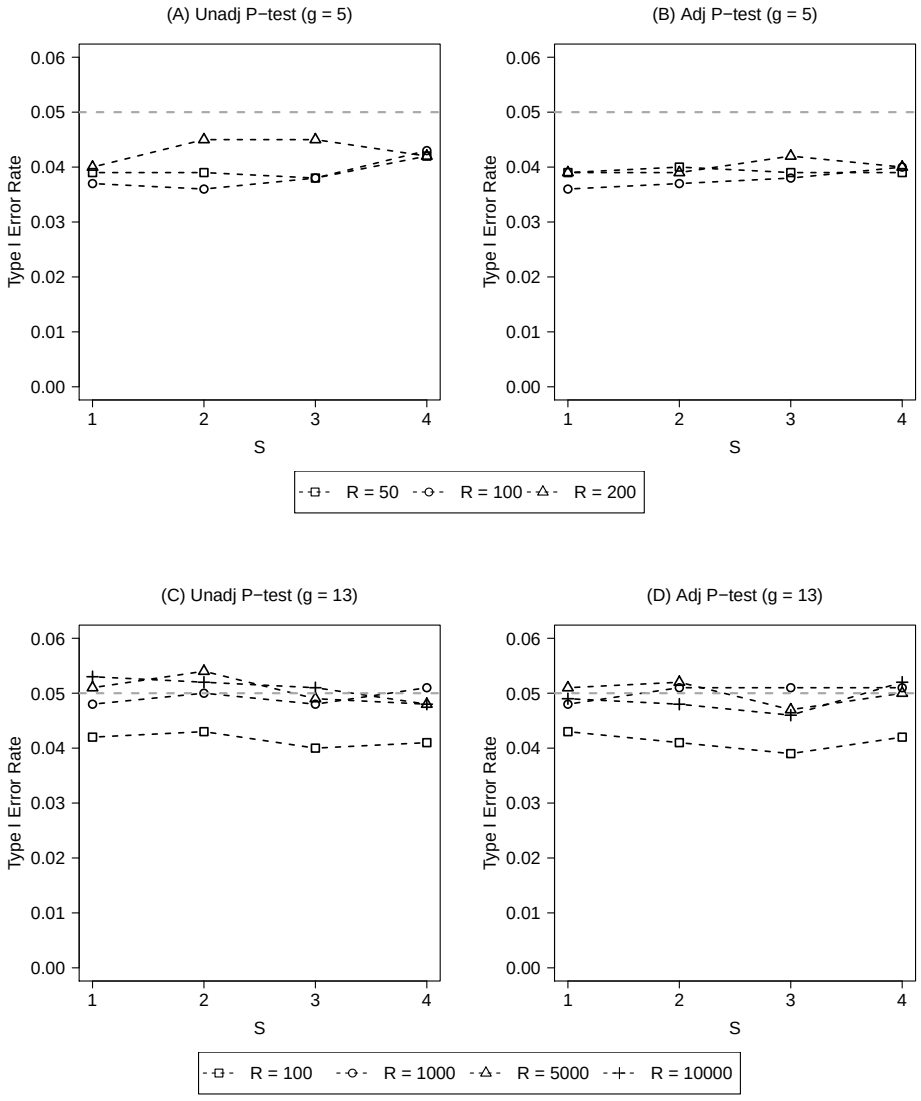

**Web Figure 5.** Power for F-test and permutation test with different number of group-level potential confounders ($S$) controlled in constrained randomization (CR) versus under simple randomization (SR); B: imbalance score, TB: total balance score, $g = 7$; ICC $= 0.05$, $R = 100$.



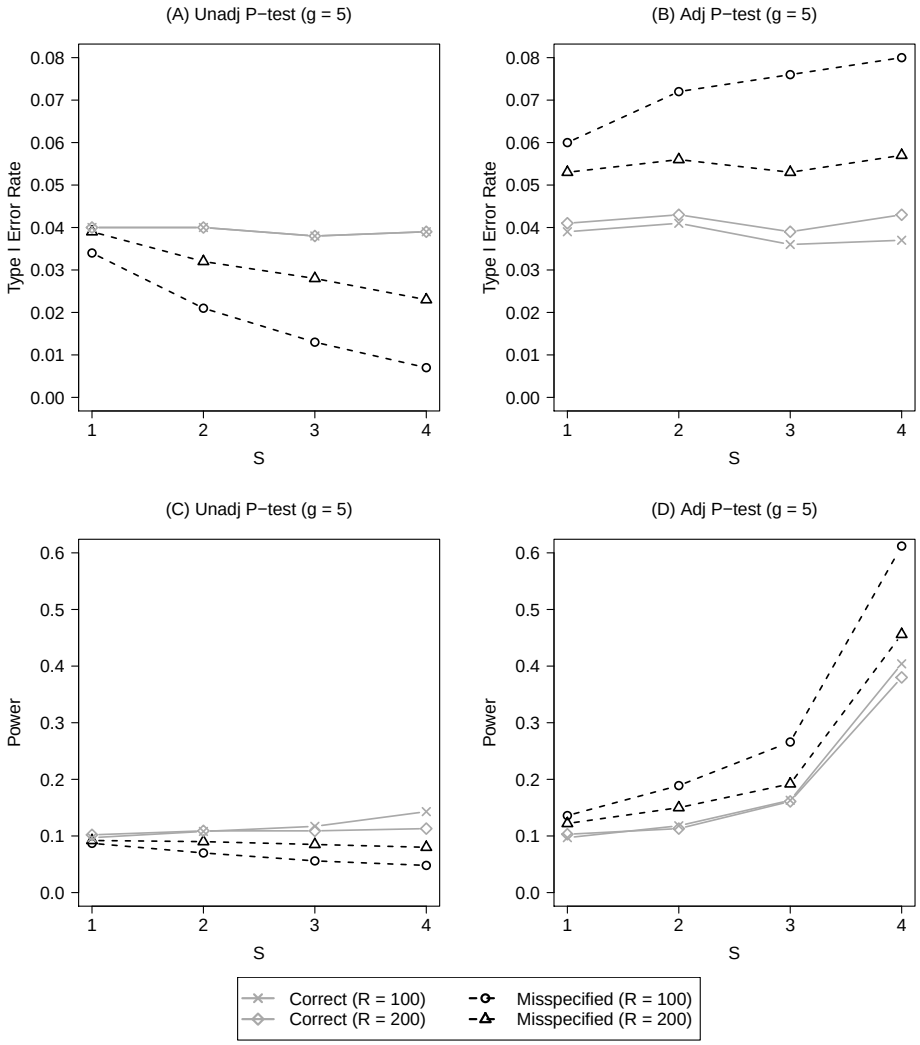

**Web Figure 6.** Power for F-test and permutation test with different number of group-level potential confounders ($S$) controlled in constrained randomization (CR) versus under simple randomization (SR); B: imbalance score, TB: total balance score, $g = 9$; ICC $= 0.05$, $R = 100$.



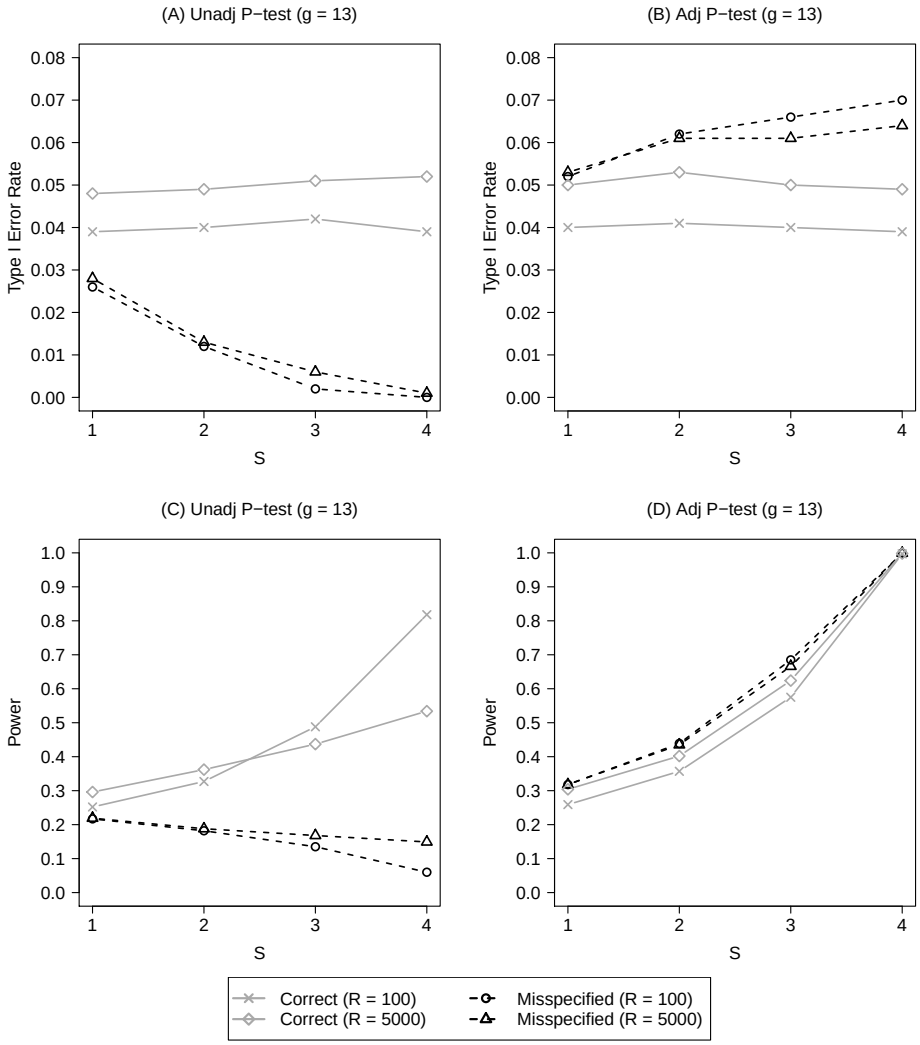

**Web Figure 7.** Power for F-test and permutation test with different number of group-level potential confounders ($S$) controlled in constrained randomization (CR) versus under simple randomization (SR); B: imbalance score, TB: total balance score, $g = 11$; ICC $= 0.05$, $R = 100$.



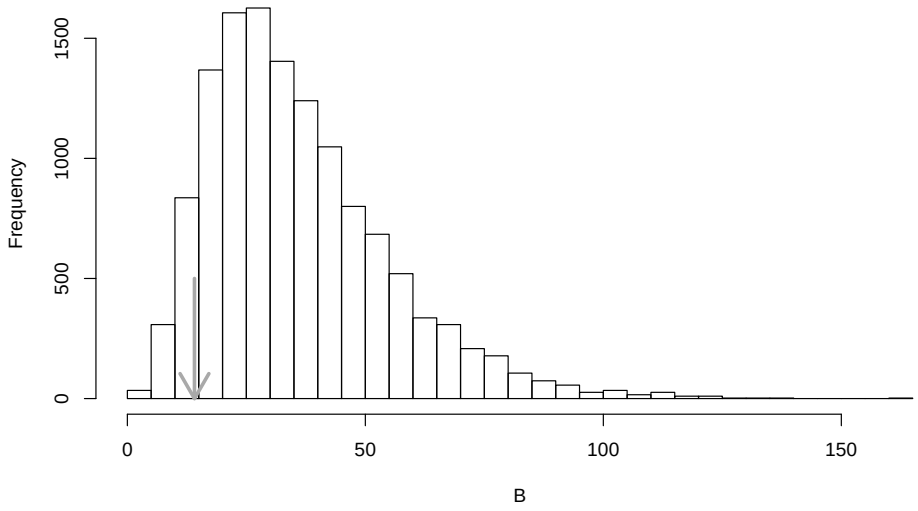

**Web Figure 8.** Type I error rate for the unadjusted and adjusted permutation tests under constrained randomization (B Metric) with different candidate set sizes; $g = 5$ and 13; ICC $= 0.05$. For the unadjusted permutation tests (panels A and C), $S$ represents the number of group-level potential confounders controlled by CR only; for the adjusted permutation tests (panels B and D), $S$ represents the number of group-level potential confounders controlled by both CR and regression modeling. $R$ represents candidate set size and the gray dashed horizontal line indicates the nominal Type I error rate.




**Web Figure 9.** Type I error rate and power for unadjusted and adjusted P-tests under constrained randomization using total balance score (TB) with $g = 5$ and ICC $= 0.05$ when the permutational distribution is misspecified. The results are referenced against the correct permutation analyses from the appropriate distribution. $R$: candidate set size.




**Web Figure 10.** Type I error rate and power for unadjusted and adjusted P-tests under constrained randomization using total balance score (TB) with $g = 13$ and ICC $= 0.05$ when the permutational distribution is misspecified. The results are referenced against the correct permutation analyses from the appropriate distribution. $R$: candidate set size.




**Web Figure 11.** Distribution of imbalance score (B) over all 12870 possible randomization schemes in the R/R for vaccination study. The portion of schemes to the left of the arrow shows the constrained randomization space (candidate set size $R = 1000$).