

| Scenario | Using all rare and common SNVs | | | | Using all rare SNVs | | | |
|----------|--------------------------------|--------|--------|-------|---------------------|--------|--------|-------|
| | SKAT | SKAT-O | Burden | SMT | SKAT | SKAT-O | Burden | SMT |
| 1 | 0.341 | 0.337 | 0.107 | 0.546 | 0.358 | 0.357 | 0.242 | 0.563 |
| 2 | 0.199 | 0.187 | 0.080 | 0.192 | 0.209 | 0.204 | 0.140 | 0.200 |
| 3 | 0.127 | 0.124 | 0.062 | 0.100 | 0.130 | 0.130 | 0.099 | 0.106 |
| 4 | 0.532 | 0.534 | 0.170 | 0.736 | 0.553 | 0.559 | 0.414 | 0.752 |
| 5 | 0.299 | 0.293 | 0.102 | 0.282 | 0.316 | 0.317 | 0.230 | 0.297 |
| 6 | 0.168 | 0.170 | 0.076 | 0.130 | 0.182 | 0.185 | 0.148 | 0.137 |
| 7 | 0.764 | 0.783 | 0.290 | 0.907 | 0.792 | 0.815 | 0.698 | 0.917 |
| 8 | 0.477 | 0.492 | 0.159 | 0.440 | 0.507 | 0.532 | 0.440 | 0.458 |
| 9 | 0.289 | 0.311 | 0.115 | 0.209 | 0.308 | 0.337 | 0.284 | 0.220 |
| 10 | 0.986 | 0.996 | 0.583 | 0.997 | 0.993 | 0.999 | 0.992 | 0.998 |
| 11 | 0.825 | 0.895 | 0.352 | 0.730 | 0.861 | 0.928 | 0.896 | 0.755 |
| 12 | 0.580 | 0.695 | 0.242 | 0.407 | 0.619 | 0.752 | 0.721 | 0.433 |
| 13 | 0.352 | 0.346 | 0.113 | 0.554 | 0.368 | 0.361 | 0.245 | 0.570 |
| 14 | 0.188 | 0.180 | 0.075 | 0.187 | 0.197 | 0.193 | 0.133 | 0.196 |
| 15 | 0.113 | 0.108 | 0.060 | 0.094 | 0.119 | 0.113 | 0.089 | 0.099 |
| 16 | 0.516 | 0.497 | 0.136 | 0.727 | 0.540 | 0.522 | 0.310 | 0.744 |
| 17 | 0.300 | 0.277 | 0.086 | 0.280 | 0.318 | 0.296 | 0.170 | 0.293 |
| 18 | 0.165 | 0.151 | 0.070 | 0.132 | 0.177 | 0.163 | 0.107 | 0.139 |
| 19 | 0.761 | 0.747 | 0.227 | 0.903 | 0.785 | 0.777 | 0.523 | 0.913 |
| 20 | 0.473 | 0.454 | 0.131 | 0.432 | 0.503 | 0.489 | 0.310 | 0.456 |
| 21 | 0.282 | 0.269 | 0.093 | 0.198 | 0.297 | 0.290 | 0.196 | 0.211 |
| 22 | 0.981 | 0.981 | 0.410 | 0.996 | 0.988 | 0.989 | 0.837 | 0.997 |
| 23 | 0.806 | 0.811 | 0.229 | 0.713 | 0.842 | 0.849 | 0.625 | 0.737 |
| 24 | 0.541 | 0.549 | 0.163 | 0.374 | 0.583 | 0.602 | 0.445 | 0.399 |
| 25 | 0.352 | 0.335 | 0.098 | 0.543 | 0.367 | 0.351 | 0.200 | 0.561 |
| 26 | 0.195 | 0.179 | 0.075 | 0.188 | 0.206 | 0.188 | 0.117 | 0.199 |
| 27 | 0.125 | 0.114 | 0.058 | 0.093 | 0.128 | 0.117 | 0.078 | 0.098 |
| 28 | 0.528 | 0.499 | 0.132 | 0.732 | 0.548 | 0.519 | 0.274 | 0.749 |
| 29 | 0.295 | 0.270 | 0.084 | 0.286 | 0.314 | 0.292 | 0.159 | 0.303 |
| 30 | 0.163 | 0.148 | 0.063 | 0.125 | 0.172 | 0.158 | 0.105 | 0.134 |
| 31 | 0.755 | 0.727 | 0.187 | 0.903 | 0.782 | 0.752 | 0.390 | 0.914 |
| 32 | 0.460 | 0.422 | 0.103 | 0.416 | 0.488 | 0.452 | 0.224 | 0.438 |
| 33 | 0.270 | 0.235 | 0.076 | 0.184 | 0.289 | 0.255 | 0.136 | 0.200 |
| 34 | 0.981 | 0.973 | 0.280 | 0.995 | 0.986 | 0.981 | 0.577 | 0.997 |
| 35 | 0.801 | 0.763 | 0.156 | 0.692 | 0.838 | 0.802 | 0.346 | 0.718 |
| 36 | 0.526 | 0.472 | 0.111 | 0.352 | 0.566 | 0.514 | 0.233 | 0.376 |

S3 Table. Power estimates of the SMT and MMTs under the nominal α level of 0.05.

Data was generated under the alternative-hypothesis model described in scenarios 1-36 in Table 1 with size $n = 1,000$ for $m = 10,000$ replicates. The nominal α level was set to 0.05. Adjustments for multiple testing of all SNVs in a gene with the SMT were done using the BH correction. The power results are provided for analyses using all rare and (non-causal) common SNVs in a gene, and for using all rare SNVs in a gene by excluding the common SNVs from the analysis.