**Table S1.** Empirical power to detect causal variants in simulated test sets

|  |  |  |
| --- | --- | --- |
| Traita | P-value Threshold | Average # causal variants discovered |
| HDL (ntest=19,840 ntruth=188,577) | 5×10-8 | 11.7 |
| 5×10-7 | 15.2 |
| 5×10-6 | 20.2 |
| LDL (ntest=19,840 ntruth=188,577) | 5×10-8 | 14.8 |
| 5×10-7 | 17.9 |
| 5×10-6 | 22.2 |
| TG (ntest=19,840 ntruth=188,577) | 5×10-8 | 11.2 |
| 5×10-7 | 12.9 |
| 5×10-6 | 15.4 |
| Height (ntest=133,653 ntruth=693,529) | 5×10-8 | 215 |
| 5×10-7 | 259 |
| 5×10-6 | 319 |
| BMI (ntest=123,865 ntruth=681,275) | 5×10-8 | 46.4 |
| 5×10-7 | 66.7 |
| 5×10-6 | 99.9 |

*Note*: a Number of loci in truth set for HDL: 89, LDL: 72, TG: 60, height: 1100, BMI: 724

**Table S2.** Benjamini-Yekutieli results for extreme thresholds

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Trait | Threshold (FDR) | Empirical | | |  | Simulation | | |
| Positives | | eFDRb |  | Positives | | eFDR |
| False | Truea |  | False | True |
| HDL (ntest=19,840 ntruth=188,577) | 1% | 0 | 14 | 0% |  | 0.08 | 7.0 | 1.1% |
| 3% | 0 | 14 | 0% |  | 0.13 | 7.9 | 1.6% |
| 20% | 1 | 16 | 5.9% |  | 0.34 | 10 | 3.3% |
| 25% | 1 | 17 | 5.6% |  | 0.35 | 10 | 3.3% |
| LDL (ntest=19,840 ntruth=188,577) | 1% | 0 | 14 | 0% |  | 0.06 | 10 | 0.59% |
| 3% | 0 | 14 | 0% |  | 0.08 | 11 | 0.72% |
| 20% | 0 | 15 | 0% |  | 0.27 | 14 | 1.9% |
| 25% | 0 | 15 | 0% |  | 0.30 | 14 | 2.1% |
| TG (ntest=19,840 ntruth=188,577) | 1% | 0 | 8 | 0% |  | 0.02 | 7.8 | 0.26% |
| 3% | 0 | 8 | 0% |  | 0.03 | 8.3 | 0.36% |
| 20% | 1 | 8 | 11% |  | 0.13 | 9.1 | 1.4% |
| 25% | 2 | 8 | 20% |  | 0.14 | 9.2 | 1.5% |
| Height (ntest=133,653 ntruth693,529) | 1% | 0 | 157 | 0% |  | 1.8 | 185 | 0.95% |
| 3% | 0 | 180 | 0% |  | 3.3 | 206 | 1.6% |
| 20% | 1 | 272 | 0.37% |  | 9.3 | 254 | 3.5% |
| 25% | 1 | 281 | 0.35% |  | 11 | 261 | 4.0% |
| BMI (ntest=123,865 ntruth=681,275) | 1% | 0 | 19 | 0% |  | 0.22 | 31 | 0.71% |
| 3% | 0 | 20 | 0% |  | 0.51 | 37 | 1.4% |
| 20% | 0 | 29 | 0% |  | 2.2 | 55 | 3.9% |
| 25% | 0 | 32 | 0% |  | 2.7 | 58 | 4.4% |

*Note:* a Number of loci in truth set for HDL: 89, LDL: 72, TG: 60, height: 1100, BMI: 724.

b eFDR is calculated as number of false positives divided by sum of true and false positives.

**Table S3.** Benjamini-Hochberg results for extreme thresholds

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Trait | Threshold (FDR) | Empirical | | |  | Simulation | | |
| Positives | | eFDRb |  | Positives | | eFDR |
| False | Truea |  | False | True |
| HDL (ntest=19,840 ntruth=188,577) | 1% | 1 | 16 | 5.9% |  | 0.31 | 9.6 | 3.1% |
| 3% | 1 | 17 | 5.6% |  | 0.50 | 11 | 4.3% |
| 20% | 7 | 20 | 26% |  | 2.2 | 15 | 13% |
| 25% | 7 | 20 | 26% |  | 2.7 | 16 | 15% |
| LDL (ntest=19,840 ntruth=188,577) | 1% | 0 | 15 | 0% |  | 0.26 | 13 | 1.9% |
| 3% | 0 | 15 | 0% |  | 0.45 | 15 | 2.9% |
| 20% | 7 | 18 | 28% |  | 2.2 | 19 | 10% |
| 25% | 7 | 18 | 28% |  | 2.8 | 20 | 12% |
| TG (ntest=19,840 ntruth=188,577) | 1% | 1 | 8 | 11% |  | 0.11 | 9.0 | 1.2% |
| 3% | 2 | 8 | 20% |  | 0.24 | 9.6 | 2.5% |
| 20% | 5 | 10 | 33% |  | 1.3 | 12 | 10% |
| 25% | 5 | 10 | 33% |  | 1.6 | 12 | 12% |
| Height (ntest=133,653 ntruth693,529) | 1% | 1 | 249 | 0.40% |  | 7.90 | 246 | 3.1% |
| 3% | 2 | 309 | 0.64% |  | 15 | 281 | 5.2% |
| 20% | 10 | 496 | 2.0% |  | 63 | 368 | 15% |
| 25% | 16 | 540 | 2.9% |  | 76 | 382 | 17% |
| BMI (ntest=123,865 ntruth=681,275) | 1% | 0 | 26 | 0% |  | 1.8 | 52 | 3.4% |
| 3% | 0 | 37 | 0% |  | 4.3 | 68 | 6.0% |
| 20% | 3 | 61 | 4.7% |  | 22 | 111 | 16% |
| 25% | 3 | 66 | 4.3% |  | 27 | 118 | 19% |

*Note:* a Number of loci in truth set for HDL: 89, LDL: 72, TG: 60, height: 1100, BMI: 724.

b eFDR is calculated as number of false positives divided by sum of true and false positives.

**Table S4.** Equivalent P-value thresholds for FDR thresholds in simulation

|  |  |  |  |
| --- | --- | --- | --- |
| Procedure | Trait | FDR threshold | Equivalent P-value threshold |
| B-H | HDLa | 5% | 3.3×10-7 |
| 10% | 6.8×10-7 |
| 15% | 1.2×10-6 |
| Height | 5% | 6.5×10-6 |
| 10% | 1.4×10-5 |
| 15% | 2.3×10-5 |
| BMI | 5% | 1.9×10-6 |
| 10% | 4.7×10-6 |
| 15% | 8.2×10-6 |
| B-Y | HDL | 5% | 8.8×10-9 |
| 10% | 2.9×10-8 |
| 15% | 4.5×10-8 |
| Height | 5% | 3.2×10-7 |
| 10% | 7.2×10-7 |
| 15% | 1.1×10-6 |
| BMI | 5% | 6.2×10-8 |
| 10% | 1.3×10-7 |
| 15% | 2.3×10-7 |

*Note*: a Similar results observed for LDL and TG.

**Table S5.** Simulation results for P-value thresholds under relaxed definition of true positives

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Threshold  P-value | FDR | P-value threshold | | |  | B-H | | |  | BFDP | | |
|  | Positives | | eFDR |  | Positives | | eFDR |  | Positives | | eFDR |
| False | Truea |  | False | True |  | False | True |
| HDL (ntest = 19,840 ntruth = 188,577) | 5×10-8 | 5% | 0.13 | 9.6 | 1.3% |  | 0.42 | 12 | 3.3% |  | 0.16 | 10 | 1.5% |
| 5×10-7 | 10% | 0.58 | 13 | 4.4% |  | 0.92 | 14 | 6.3% |  | 0.44 | 12 | 3.6% |
| 5×10-6 | 15% | 3.6 | 18 | 17% |  | 1.3 | 15 | 8.0% |  | 0.80 | 13 | 5.7% |
| LDL (ntest = 19,840 ntruth = 188,577) | 5×10-8 | 5% | 0.11 | 13 | 0.84% |  | 0.51 | 16 | 3.1% |  | 0.27 | 14 | 1.8% |
| 5×10-7 | 10% | 0.55 | 16 | 3.2% |  | 0.93 | 18 | 5.0% |  | 0.67 | 16 | 3.9% |
| 5×10-6 | 15% | 4.0 | 22 | 15% |  | 1.5 | 19 | 7.2% |  | 1.1 | 18 | 5.9% |
| TG (ntest = 19,840 ntruth = 188,577) | 5×10-8 | 5% | 0.06 | 9.2 | 0.66% |  | 0.23 | 10 | 2.2% |  | 0.25 | 9.9 | 2.5% |
| 5×10-7 | 10% | 0.43 | 11 | 3.9% |  | 0.50 | 11 | 4.5% |  | 0.79 | 11 | 6.6% |
| 5×10-6 | 15% | 3.4 | 14 | 20% |  | 0.80 | 11 | 6.7% |  | 1.4 | 12 | 10% |
| Height (ntest = 133,653 ntruth = 693,529) | 5×10-8 | 5% | 1.1 | 181 | 0.62% |  | 18 | 306 | 5.5% |  | 23 | 322 | 6.6% |
| 5×10-7 | 10% | 3.7 | 225 | 1.6% |  | 30 | 337 | 8.3% |  | 43 | 364 | 10% |
| 5×10-6 | 15% | 13 | 289 | 4.3% |  | 42 | 360 | 11% |  | 65 | 396 | 14% |
| BMI (ntest = 123,865 ntruth = 681,275) | 5×10-8 | 5% | 0.37 | 39 | 0.94% |  | 4.3 | 79 | 5.2% |  | 2.4 | 69 | 3.4% |
| 5×10-7 | 10% | 1.5 | 59 | 2.5% |  | 8.2 | 94 | 8.0% |  | 4.7 | 84 | 5.3% |
| 5×10-6 | 15% | 8.0 | 93 | 7.9% |  | 12 | 106 | 10% |  | 7.6 | 96 | 7.3% |

*Note:* a True positive defined as a locus whose lead variant had r2 > 0.60 with a variant in the truth set with P-value < 5×10-7.

**Table S6.** Effect of sample size on simulation results for Benjamini-Yekutieli

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Trait | Threshold (FDR) | n=8,816 | | |  | n=19,840 | | |  | n=133,653 or 123,865 | | |
| Positives | | eFDRb |  | Positives | | eFDR |  | Positives | | eFDR |
| False | Truea |  | False | True |  | False | True |
| Height | 5% | 0 | 0.22 | 0% |  | 0.01 | 9.0 | 0.11% |  | 4.3 | 217 | 2.0% |
| 10% | 0 | 0.30 | 0% |  | 0.01 | 11 | 0.10% |  | 6.3 | 235 | 2.6% |
| 15% | 0 | 0.35 | 0% |  | 0.06 | 12 | 0.51% |  | 7.9 | 246 | 3.1% |
| BMI | 5% | 0.01 | 0.05 | 17% |  | 0.01 | 0.99 | 1.0% |  | 0.83 | 41 | 2.0% |
| 10% | 0.01 | 0.07 | 13% |  | 0.01 | 1.1 | 0.88% |  | 1.4 | 47 | 2.9% |
| 15% | 0.01 | 0.08 | 11% |  | 0.01 | 1.2 | 0.81% |  | 1.8 | 52 | 3.4% |

*Note:* a Number of loci in truth set for HDL: 89, LDL: 72, TG: 60, height: 1100, BMI: 724.

b eFDR is calculated as number of false positives divided by sum of true and false positives.

**Table S7.** Effect of sample size on simulation results for Benjamini-Hochberg

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Trait | Threshold (FDR) | n=8,816 | | |  | n=19,840 | | |  | n=133,653 or 123,865 | | | |
| Positives | | eFDRb |  | Positives | | eFDR |  | Positives | | eFDR |
| False | Truea |  | False | True |  | False | True |
| Height | 5% | 0.05 | 0.87 | 5.4% |  | 0.27 | 18 | 1.5% |  | 22 | 301 | 6.8% |
| 10% | 0.12 | 1.2 | 9.0% |  | 0.85 | 22 | 3.7% |  | 37 | 331 | 10% |
| 15% | 0.18 | 1.5 | 11% |  | 1.5 | 25 | 5.6% |  | 50 | 351 | 13% |
| BMI | 5% | 0.01 | 0.17 | 5.6% |  | 0.11 | 1.5 | 6.7% |  | 6.6 | 77 | 7.9% |
| 10% | 0.05 | 0.22 | 19% |  | 0.23 | 1.8 | 11% |  | 11 | 91 | 11% |
| 15% | 0.08 | 0.25 | 24% |  | 0.33 | 2.1 | 14% |  | 16 | 102 | 14% |

*Note:* a Number of loci in truth set for HDL: 89, LDL: 72, TG: 60, height: 1100, BMI: 724.

b eFDR is calculated as number of false positives divided by sum of true and false positives.

**Table S8.** BFDP results for extreme thresholds

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Trait | Threshold (Bayesian FDR) | Empirical | | | |  |  | Simulation | | |
| a | Positives | | eFDRc |  | d | Positives | | eFDR |
| False | Trueb |  | False | True |
| HDL (ntest=19,840 ntruth=188,577) | 1% | 1.3×10-4 | 0 | 14 | 0% |  | 8.7×10-5 | 0.18 | 7.5 | 2.3% |
| 3% | 1 | 16 | 5.9% |  | 0.30 | 9.0 | 3.2% |
| 20% | 8 | 18 | 31% |  | 1.8 | 14 | 11% |
| 25% | 9 | 19 | 32% |  | 2.5 | 15 | 14% |
| LDL (ntest=19,840 ntruth=188,577) | 1% | 1.3×10-4 | 0 | 15 | 0% |  | 9.6×10-5 | 0.12 | 11 | 1.1% |
| 3% | 1 | 16 | 5.9% |  | 0.26 | 13 | 1.9% |
| 20% | 7 | 19 | 27% |  | 2.2 | 19 | 10% |
| 25% | 9 | 20 | 31% |  | 3.2 | 20 | 13% |
| TG (ntest=19,840 ntruth=188,577) | 1% | 2.1×10-4 | 0 | 8 | 0% |  | 1.6×10-4 | 0.07 | 8.1 | 0.85% |
| 3% | 1 | 9 | 10% |  | 0.20 | 9.2 | 2.1% |
| 20% | 4 | 14 | 22% |  | 2.6 | 12 | 17% |
| 25% | 6 | 14 | 30% |  | 3.6 | 13 | 22% |
| Height  (ntest=133,653 ntruth693,529) | 1% | 2.0×10-3 | 1 | 234 | 0.43% |  | 2.9×10-3 | 8.7 | 254 | 3.3% |
| 3% | 2 | 299 | 0.66% |  | 18 | 294 | 5.9% |
| 20% | 16 | 523 | 3.0% |  | 106 | 410 | 21% |
| 25% | 20 | 584 | 3.3% |  | 141 | 433 | 25% |
| BMI (ntest=123,865 ntruth=681,275) | 1% | 3.6 ×10-4 | 0 | 25 | 0% |  | 5.2×10-4 | 1.1 | 46 | 2.2% |
| 3% | 0 | 31 | 0% |  | 2.6 | 59 | 4.1% |
| 20% | 1 | 57 | 1.7% |  | 15 | 103 | 13% |
| 25% | 1 | 65 | 1.5% |  | 21 | 112 | 16% |

*Note:* a is the estimated prior probability of association at a variant site equal to the proportion of tested variants with P-value less than 5×10-8.

b Number of loci in truth set for HDL: 89, LDL: 72, TG: 60, height: 1100, BMI: 724.

c eFDR is calculated as number of false positives divided by sum of true and false positives.

d Average in 1,000 replicate datasets.

**Table S9.** Combined univariate and multivariate empirical results for lipids

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Metric | | Threshold | Combined univariate | | |  | Multivariate | | |
|  | Positives | | eFDRb |  | Positives | | eFDR |
|  | False | Truea |  | False | True |
| HDL,LDL,TG (ntest=19,840 ntruth=188,577) | P-value | Unadjusted | 5×10-8 | 2 | 38 | 5.0% |  | 0 | 41 | 0% |
| 5×10-7 | 6 | 47 | 11% |  | 0 | 45 | 0% |
| 5×10-6 | 24 | 58 | 29% |  | 2 | 52 | 3.7% |
| Adjusted | 1.67×10-8 | 0 | 35 | 0% |  | *Not applicable* | | |
| 1.67×10-7 | 2 | 40 | 4.8% |  |
| 1.67×10-6 | 13 | 53 | 20% |  |
| B-H | | 5% | 6 | 53 | 10% |  | 2 | 52 | 3.7% |
| 10% | 14 | 60 | 19% |  | 5 | 52 | 8.8% |
| 15% | 18 | 60 | 23% |  | 8 | 53 | 13% |
| BFDPc | | 5% | 7 | 57 | 11% |  | 5 | 58 | 7.9% |
| 10% | 15 | 61 | 20% |  | 10 | 61 | 14% |
| 15% | 19 | 66 | 22% |  | 14 | 65 | 18% |

*Note:* a Number of loci in truth set for all three lipids: 139 (non-overlapping), height: 1100, BMI: 724.

b eFDR is calculated as number of false positives divided by sum of true and false positives.

c ’s for univariate analyses is 1.3×10-4 for HDL, 1.3×10-4 for LDL, and 2.1×10-4 for TG. is 1.7×10-4, the average of the ’s for the three lipid traits.

**Table S10.** Combined univariate and multivariate simulation results for lipids

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Metric | | Threshold | Combined univariate | | |  | Multivariate | | |
|  | Positives | | eFDRb |  | Positives | | eFDR |
|  | False | Truea |  | False | True |
| HDL,LDL,TG (ntest=19,840 ntruth=188,577) | P-value | Unadjusted | 5×10-8 | 0.43 | 22 | 1.9% |  | 0.57 | 30 | 1.9% |
| 5×10-7 | 1.7 | 28 | 5.7% |  | 1.6 | 37 | 4.1% |
| 5×10-6 | 10 | 36 | 22% |  | 6.4 | 47 | 12% |
| Adjusted | 1.67×10-8 | 0.26 | 20 | 1.3% |  | *Not applicable* | | |
| 1.67×10-7 | 0.78 | 25 | 3.0% |  |
| 1.67×10-6 | 4.4 | 32 | 12% |  |
| B-H | | 5% | 1.1 | 32 | 3.3% |  | 2.4 | 40 | 5.7% |
| 10% | 2.2 | 35 | 5.9% |  | 3.9 | 43 | 8.3% |
| 15% | 3.2 | 37 | 8.0% |  | 5.2 | 46 | 10% |
| BFDPc | | 5% | 1.2 | 31 | 3.7% |  | 1.6 | 34 | 4.5% |
| 10% | 2.6 | 35 | 6.9% |  | 3.1 | 38 | 7.5% |
| 15% | 4.1 | 38 | 9.7% |  | 4.8 | 40 | 11% |

*Note:* a Number of loci in truth set for all three lipids: 139 (non-overlapping), height: 1100, BMI: 724.

b eFDR is calculated as number of false positives divided by sum of true and false positives.

c Average ’s for univariate analyses is 7.7×10-5 for HDL, 8.7×10-5 for LDL, and 1.4×10-4 for TG. is 9.9×10-5,the average of the ’s for the three lipid traits.

**Table S11.** Simulation results for P-value threshold results under distance-based definitions

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Threshold  P-value | FDR | P-value threshold | | |  | B-H | | |  | BFDP | | |
|  | Positives | | eFDR |  | Positives | | eFDR |  | Positives | | eFDR |
| False | Truea |  | False | True |  | False | True |
| HDL (ntest = 19,840 ntruth = 188,577) | 5×10-8 | 5% | 0.07 | 7.8 | 0.89% |  | 0.20 | 9.4 | 2.1% |  | 0.06 | 8.0 | 0.75% |
| 5×10-7 | 10% | 0.35 | 10 | 3.4% |  | 0.41 | 10 | 3.8% |  | 0.19 | 9.3 | 2.0% |
| 5×10-6 | 15% | 2.9 | 14 | 17% |  | 0.69 | 11 | 5.9% |  | 0.46 | 10 | 4.2% |
| LDL (ntest = 19,840 ntruth = 188,577) | 5×10-8 | 5% | 0.02 | 12 | 0.17% |  | 0.24 | 13 | 1.8% |  | 0.12 | 12 | 0.96% |
| 5×10-7 | 10% | 0.33 | 14 | 2.3% |  | 0.53 | 14 | 3.5% |  | 0.43 | 14 | 3.0% |
| 5×10-6 | 15% | 3.2 | 17 | 16% |  | 0.85 | 15 | 5.4% |  | 0.90 | 15 | 5.6% |
| TG (ntest = 19,840 ntruth = 188,577) | 5×10-8 | 5% | 0.05 | 8.7 | 0.57% |  | 0.18 | 9.5 | 1.9% |  | 0.17 | 9.2 | 1.8% |
| 5×10-7 | 10% | 0.32 | 9.8 | 3.2% |  | 0.35 | 9.9 | 3.4% |  | 0.58 | 10 | 5.4% |
| 5×10-6 | 15% | 3.0 | 12 | 20% |  | 0.58 | 10 | 5.4% |  | 1.3 | 11 | 10% |
| Height (ntest = 133,653 ntruth = 693,529) | 5×10-8 | 5% | 0.08 | 172 | 0.05% |  | 3.7 | 263 | 1.4% |  | 8.7 | 291 | 2.9% |
| 5×10-7 | 10% | 0.49 | 207 | 0.24% |  | 7.3 | 284 | 2.5% |  | 20 | 324 | 5.8% |
| 5×10-6 | 15% | 2.8 | 255 | 1.1% |  | 11 | 297 | 3.6% |  | 34 | 348 | 9.0% |
| BMI (ntest = 123,865 ntruth = 681,275) | 5×10-8 | 5% | 0.14 | 38 | 0.37% |  | 2.5 | 75 | 3.2% |  | 1.3 | 67 | 1.9% |
| 5×10-7 | 10% | 0.81 | 57 | 1.4% |  | 4.7 | 90 | 5.0% |  | 2.9 | 82 | 3.4% |
| 5×10-6 | 15% | 4.9 | 90 | 5.1% |  | 6.9 | 101 | 6.4% |  | 4.8 | 94 | 4.8% |

*Note:* a Locus defined as variants within ±1Mb of the lead variant

b True positive defined as a locus whose lead variant was within ±50kb of a variant with *P* < 5×10-8 in the truth set.

**Table S12.** BFDP results using alternative estimation of prior

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Trait | Threshold (Bayesian FDR) | Empirical | | | |  |  | Simulation | | |
| a | Positives | | eFDRc |  | d | Positives | | eFDR |
| False | Trueb |  | False | True |
| HDL (ntest = 19,840 ntruth = 188,577) | 5% | 2.0×10-5 | 0 | 17 | 0% |  | 9.9×10-6 | 0.14 | 7.2 | 1.9% |
| 10% | 1 | 19 | 5.0% |  | 0.28 | 8.2 | 3.3% |
| 15% | 1 | 22 | 4.3% |  | 0.35 | 9.2 | 3.7% |
| LDL (ntest = 19,840 ntruth = 188,577) | 5% | 1.5×10-5 | 0 | 14 | 0% |  | 1.1×10-5 | 0.02 | 9.2 | 0.22% |
| 10% | 0 | 16 | 0% |  | 0.10 | 10 | 0.95% |
| 15% | 1 | 16 | 5.9% |  | 0.19 | 11 | 1.6% |
| TG (ntest = 19,840 ntruth = 188,577) | 5% | 1.6×10-5 | 0 | 14 | 0% |  | 9.7×10-6 | 0.02 | 7.6 | 0.26% |
| 10% | 0 | 16 | 0% |  | 0.10 | 8.4 | 1.2% |
| 15% | 0 | 18 | 0% |  | 0.17 | 9.1 | 1.8% |
| Height (ntest = 133,653 ntruth = 693,529) | 5% | 1.4×10-4 | 1 | 170 | 0.58% |  | 1.7×10-4 | 4.3 | 218 | 2.0% |
| 10% | 1 | 190 | 0.52% |  | 7.6 | 241 | 3.1% |
| 15% | 1 | 207 | 0.48% |  | 12 | 260 | 4.3% |
| BMI (ntest = 123,865 ntruth = 681,275) | 5% | 8.8×10-6 | 0 | 22 | 0% |  | 4.0×10-5 | 0.62 | 39 | 1.6% |
| 10% | 0 | 22 | 0% |  | 1.1 | 47 | 2.3% |
| 15% | 0 | 28 | 0% |  | 1.8 | 53 | 3.2% |

*Note:* a is the estimated prior probability of association at a variant site equal to the number of loci with lead variant P-value less than 5×10-8 divided by 1,000,000 (estimated total number of independent common variants in genome).

b Number of loci in truth set for HDL: 89, LDL: 72, TG: 60, height: 1100, BMI: 724.

c eFDR is calculated as number of false positives divided by sum of true and false positives.

d Average in 1,000 replicate datasets.

Table S13. Null simulations for P-value threshold

|  |  |  |  |
| --- | --- | --- | --- |
| Sample size | P-value threshold | eFWERa | Mean # of false positives |
| 19,840 | 5×10-8 | 0.043 | 0.045 |
| 5×10-7 | 0.338 | 0.402 |
| 5×10-6 | 0.974 | 3.64 |
| 133,653 | 5×10-8 | 0.045 | 0.048 |
| 5×10-7 | 0.344 | 0.423 |
| 5×10-6 | 0.964 | 3.71 |

*Note*: a eFWER is calculated as proportion of 1,000 null simulations with at least 1 false positive.