**Table S2**

Results from using lower quality ancestry estimations on meta-analysis and RUTH.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Data set** | **Variant set** | **GenotypeFormat** | **HWE Test** | **PCs** | **Proportion of Significant Variants** | **Total Variant Count** |
| **P < 0.01** | **P < 10-3** | **P < 10-4** | **P < 10-5** | **P < 10-6** |
| **1000G** | **LQ** | **raw GT** | **Meta-analysis** | **n/a** | 0.392 | 0.343 | 0.307 | 0.283 | 0.262 | 10,966 |
| **Meta-analysis (k-means)** | **n/a** | 0.405 | 0.356 | 0.319 | 0.292 | 0.269 | 10,966 |
| **LD-aware GT** | **Meta-analysis** | **n/a** | 0.184 | 0.149 | 0.127 | 0.111 | 0.098 | 10,966 |
| **Meta-analysis (k-means)** | **n/a** | 0.221 | 0.169 | 0.136 | 0.116 | 0.102 | 10,966 |
| **HQ** | **raw GT** | **Meta-analysis** | **n/a** | 0.298 | 0.161 | 0.084 | 0.042 | 0.020 | 17,740 |
| **Meta-analysis (k-means)** | **n/a** | 0.427 | 0.279 | 0.180 | 0.112 | 0.067 | 17,740 |
| **LD-aware GT** | **Meta-analysis** | **n/a** | 0.019 | 3.1x10-3 | 5.6x10-4 | 1.7x10-4 | 1.1x10-4 | 17,740 |
| **Meta-analysis (k-means)** | **n/a** | 0.107 | 0.043 | 0.020 | 9.5x10-3 | 5.0x10-3 | 17,740 |
| **TOPMed** | **LQ** | **GT** | **Meta-analysis** | **n/a** | 0.553 | 0.523 | 0.501 | 0.485 | 0.471 | 329,699 |
| **Meta-analysis (k-means)** | **n/a** | 0.557 | 0.526 | 0.505 | 0.488 | 0.474 | 329,699 |
| **HQ** | **Meta-analysis** | **n/a** | 0.064 | 0.022 | 9.2x10-3 | 5.0x10-3 | 3.3x10-3 | 17,524 |
| **Meta-analysis (k-means)** | **n/a** | 0.224 | 0.121 | 0.074 | 0.047 | 0.033 | 17,524 |
| **1000G** | **LQ** | **GL** | **RUTH-LRT** | **2** | 0.357 | 0.304 | 0.271 | 0.243 | 0.224 | 10,966 |
| **4** | 0.358 | 0.306 | 0.270 | 0.243 | 0.225 | 10,966 |
| **RUTH-Score** | **2** | 0.336 | 0.293 | 0.263 | 0.241 | 0.221 | 10,966 |
| **4** | 0.336 | 0.295 | 0.264 | 0.242 | 0.223 | 10,966 |
| **LD-aware GT** | **RUTH-LRT** | **2** | 0.220 | 0.177 | 0.149 | 0.128 | 0.113 | 10,966 |
| **4** | 0.215 | 0.177 | 0.151 | 0.131 | 0.115 | 10,966 |
| **RUTH-Score** | **2** | 0.211 | 0.169 | 0.143 | 0.124 | 0.109 | 10,966 |
| **4** | 0.211 | 0.172 | 0.147 | 0.130 | 0.112 | 10,966 |
| **raw GT** | **RUTH-LRT** | **2** | 0.438 | 0.377 | 0.338 | 0.308 | 0.284 | 10,966 |
| **4** | 0.431 | 0.373 | 0.335 | 0.305 | 0.28 | 10,966 |
| **RUTH-Score** | **2** | 0.424 | 0.372 | 0.335 | 0.309 | 0.286 | 10,966 |
| **4** | 0.418 | 0.367 | 0.333 | 0.305 | 0.284 | 10,966 |
| **HQ** | **GL** | **RUTH-LRT** | **2** | 0.110 | 0.040 | 0.016 | 7.3x10-3 | 3.3x10-3 | 17,740 |
| **4** | 0.036 | 6.4x10-3 | 1.3x10-3 | 5.1x10-4 | 3.4x10-4 | 17,740 |
| **RUTH-Score** | **2** | 0.087 | 0.026 | 9.2x10-3 | 3.4x10-3 | 1.6x10-3 | 17,740 |
| **4** | 0.026 | 3.3x10-3 | 7.9x10-4 | 4.5x10-4 | 3.4x10-4 | 17,740 |
| **LD-aware GT** | **RUTH-LRT** | **2** | 0.041 | 0.014 | 5.4x10-3 | 2.4x10-3 | 1.4x10-3 | 17,740 |
| **4** | 0.011 | 1.1x10-3 | 2.3x10-4 | 5.6x10-5 | 0 | 17,740 |
| **RUTH-Score** | **2** | 0.034 | 9.5x10-3 | 2.8x10-3 | 1.2x10-3 | 5.1x10-4 | 17,740 |
| **4** | 0.011 | 1.9x10-3 | 1.1x10-4 | 0 | 0 | 17,740 |
| **raw GT** | **RUTH-LRT** | **2** | 0.299 | 0.176 | 0.098 | 0.055 | 0.03 | 17,740 |
| **4** | 0.200 | 0.095 | 0.044 | 0.021 | 9.7x10-3 | 17,740 |
| **RUTH-Score** | **2** | 0.276 | 0.155 | 0.083 | 0.044 | 0.023 | 17,740 |
| **4** | 0.183 | 0.083 | 0.036 | 0.015 | 7.4x10-3 | 17,740 |
| **TOPMed** | **LQ** | **GL** | **RUTH-LRT** | **2** | 0.646 | 0.610 | 0.584 | 0.563 | 0.547 | 329,699 |
| **4** | 0.652 | 0.614 | 0.588 | 0.567 | 0.55 | 329,699 |
| **RUTH-Score** | **2** | 0.634 | 0.607 | 0.589 | 0.574 | 0.562 | 329,699 |
| **4** | 0.635 | 0.608 | 0.590 | 0.575 | 0.562 | 329,699 |
| **GT** | **RUTH-LRT** | **2** | 0.603 | 0.573 | 0.551 | 0.533 | 0.518 | 329,699 |
| **4** | 0.610 | 0.580 | 0.556 | 0.538 | 0.552 | 329,699 |
| **RUTH-Score** | **2** | 0.608 | 0.586 | 0.571 | 0.558 | 0.548 | 329,699 |
| **4** | 0.608 | 0.587 | 0.572 | 0.559 | 0.549 | 329,699 |
| **HQ** | **GL** | **RUTH-LRT** | **2** | 0.130 | 0.067 | 0.039 | 0.024 | 0.016 | 17,524 |
| **4** | 0.041 | 0.018 | 8.7x10-3 | 4.2x10-3 | 3.1x10-3 | 17,524 |
| **RUTH-Score** | **2** | 0.130 | 0.065 | 0.036 | 0.021 | 0.014 | 17,524 |
| **4** | 0.034 | 0.011 | 4.9x10-3 | 3.1x10-3 | 2.5x10-3 | 17,524 |
| **GT** | **RUTH-LRT** | **2** | 0.079 | 0.028 | 0.012 | 7.6x10-3 | 5.9x10-3 | 17,524 |
| **4** | 0.125 | 0.036 | 0.012 | 5.0x10-3 | 2.7x10-3 | 17,524 |
| **RUTH-Score** | **2** | 0.093 | 0.033 | 0.015 | 8.8x10-3 | 6.0x10-3 | 17,524 |
| **4** | 0.145 | 0.047 | 0.017 | 7.1x10-3 | 3.5x10-3 | 17,524 |

In both 1000G and TOPMed, the false positive rate was much higher when k-means-based groupings were used for meta-analysis, compared to when high quality ancestry groupings were used. Similarly, the false positive rate was much higher when only 2 PCs were used, compared to when 4 PCs were used. Surprisingly, in TOPMed, using 4 PCs led to both a lower false positive rate and higher true positive rate when compared to using 2 PCs.