**Table 2.** Mean computational time (in second) of various MR methods

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Trait | #SNP in the exemplary gene | CoMM | PMR-Egger | TWAS | LDA MR-Egger | SMR | PrediXcan | MR-PRESSO |
| T1D from WTCCC (n=4901) | 300 | 0.51(0.19) | 0.80(0.57) | 96.09(72.39) | 0.08(0.02) | 0.0003(0.0005) | 26.74(2.81) | 408.27(74.76) |
| 500 | 1.21(0.41) | 1.42(0.77) | 3.48(1.16) | 0.14(0.03) | 0.0004(0.0005) | 11.77(0.64) | 829.04(135.79) |
| 983 | 5.85(1.50) | 9.79(1.56) | 4.69(1.73) | 0.60(0.09) | 0.0004(0.0005) | 9.96(0.78) | 2023.77(260.43) |
| 2106 | 111.00(12.87) | 97.33(7.63) | 5.87(2.26) | 4.18(0.59) | 0.0005(0.0005) | 22.90(2.63) | 4913.22(554.47) |
| Asthma from GERA (n=61,953) | 300 | 1.47(0.29) | 2.06(0.22) | 2.61(1.48) | 0.05(0.02) | 0.0002(0.0004) | 33.39(3.09) | 464.64(62.18) |
| 500 | 1.21(0.33) | 4.21(0.81) | 2.54(0.87) | 0.09(0.03) | 0.0002(0.0004) | 11.71(0.70) | 919.66(102.83) |
| 1000 | 24.37(5.13) | 21.68(1.66) | 3.07(2.55) | 0.46(0.13) | 0.0002(0.0004) | 14.29(1.30) | 2275.42(263.95) |
| 2008 | 59.01(4.98) | 52.52(4.47) | 4.51(1.48) | 2.33(0.71) | 0.0004(0.0005) | 20.18(3.28) | 5213.73(601.46) |
| Platelet Count from UK Biobank (n=337,199) | 300 | 2.56(0.53) | 5.57(4.54) | 5.04(4.19) | 0.09(0.02) | 0.0008(0.0004) | 10.93(1.96) | 471.55(50.44) |
| 500 | 6.82(2.75) | 7.61(2.30) | 5.44(4.30) | 0.15(0.02) | 0.0007(0.0005) | 12.17(1.04) | 876.06(92.90) |
| 1052 | 24.92(6.28) | 23.59(3.21) | 5.91(4.79) | 0.81(0.09) | 0.0008(0.0004) | 16.05(2.38) | 2133.03(77.56) |
| 2605 | 186.14(28.45) | 178.68(16.75) | 5.37(0.73) | 8.11(1.20) | 0.0008(0.0004) | 9.89(1.74) | 6949.72(245.75) |

Computation is carried out on a single thread of a Xeon Gold 6138 CPU. The computation time is averaged across 20 replicates, with values inside parentheses denoting the standard deviation. #SNP denotes the number of cis-SNPs for four exemplary genes in each study. The computational time for MR-PRESSO is based on 10,000 permutations.