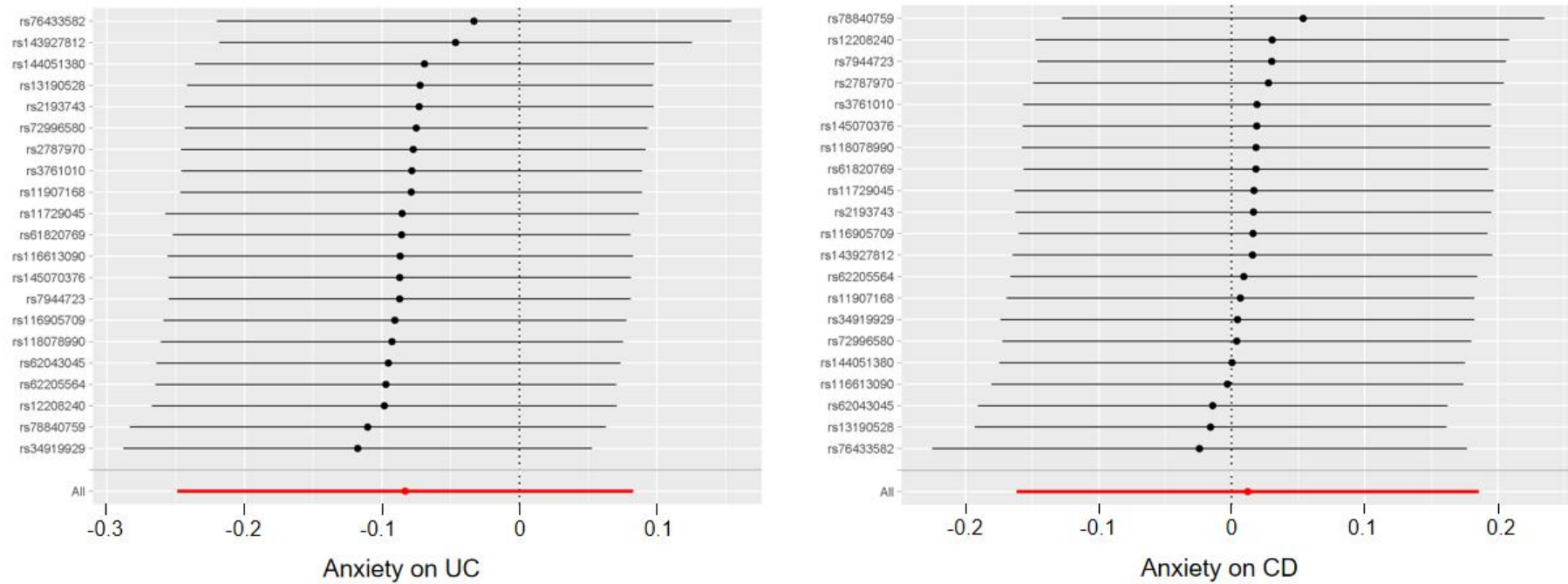


**Supplementary Figure 1** Leave-one-out analyses for the effects of ulcerative colitis and Crohn's disease on anxiety. UC: Ulcerative colitis; CD: Crohn's disease; PGC: Psychiatric Genomics Consortium



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**Supplementary Figure 2** Leave-one-out analyses for the effects of anxiety on ulcerative colitis and Crohn's disease. UC: Ulcerative colitis; CD: Crohn's disease.

**Supplementary Table 1 genome-wide association studies summary statistics of ulcerative colitis, Crohn's disease and anxiety.**

| <b>Trait</b> | <b>Case (N)</b> | <b>Control (N)</b> | <b>Ancestry</b> | <b>Consortium</b> | <b>Download website</b>   |
|--------------|-----------------|--------------------|-----------------|-------------------|---|
| UC           | 6968            | 20,464             | European        | IIBDGC            | <a href="https://gwas.mrcieu.ac.uk/datasets/ieu-a-32/">https://gwas.mrcieu.ac.uk/datasets/ieu-a-32/</a>   |
| CD           | 5956            | 14,927             | European        | IIBDGC            | <a href="https://gwas.mrcieu.ac.uk/datasets/ieu-a-30/">https://gwas.mrcieu.ac.uk/datasets/ieu-a-30/</a>   |
| Anxiety      | 2565            | 14,745             | European        | PGC               | <a href="https://figshare.com/articles/dataset/anx2016/14842689">https://figshare.com/articles/dataset/anx2016/14842689</a>   |
| Anxiety      | 20992           | 197,800            | European        | FinnGen           | <a href="https://storage.googleapis.com/finngen-public-data-r7/summary_stats/finngen_R7_KRA_PSY_ANXIETY.gz">https://storage.googleapis.com/finngen-public-data-r7/summary_stats/finngen_R7_KRA_PSY_ANXIETY.gz</a> |

**Supplementary Table 2 Detailed information of confounders-independent single-nucleotide polymorphisms of ulcerative colitison anxiety**

| SNP        | effect_allele<br>exposure | other_allele<br>exposure | beta.<br>exposure | eaf.<br>exposure | se.<br>exposure | pval.<br>outcome | pval.<br>exposure | F       | R2    |
|------------|---------------------------|--------------------------|-------------------|------------------|-----------------|------------------|-------------------|---------|-------|
| rs10182512 | A                         | G                        | 0.161             | 0.350            | 0.022           | 0.169            | 5.19E-13          | 51.995  | 0.012 |
| rs10272963 | T                         | C                        | -0.172            | 0.426            | 0.022           | 0.470            | 1.69E-15          | 63.338  | 0.014 |
| rs10737481 | G                         | T                        | 0.250             | 0.556            | 0.022           | 0.577            | 4.37E-31          | 134.071 | 0.031 |
| rs10917545 | A                         | G                        | -0.185            | 0.882            | 0.034           | 0.451            | 3.29E-08          | 30.530  | 0.007 |
| rs11209026 | A                         | G                        | -0.562            | 0.059            | 0.052           | 0.296            | 1.58E-27          | 118.039 | 0.035 |
| rs12612675 | G                         | A                        | 0.123             | 0.403            | 0.022           | 0.955            | 1.98E-08          | 31.494  | 0.007 |
| rs12817473 | G                         | A                        | 0.191             | 0.382            | 0.022           | 0.888            | 1.71E-18          | 77.230  | 0.017 |
| rs1359946  | A                         | G                        | 0.158             | 0.196            | 0.027           | 0.317            | 3.84E-09          | 34.631  | 0.008 |
| rs137845   | G                         | A                        | 0.118             | 0.515            | 0.021           | 0.638            | 2.38E-08          | 31.085  | 0.007 |
| rs1801274  | G                         | A                        | -0.183            | 0.483            | 0.022           | 0.856            | 3.78E-17          | 71.038  | 0.017 |
| rs1886731  | C                         | T                        | -0.141            | 0.481            | 0.022           | 0.011            | 2.25E-10          | 40.418  | 0.010 |
| rs1887428  | C                         | G                        | -0.177            | 0.623            | 0.022           | 0.272            | 3.36E-15          | 62.227  | 0.015 |
| rs2212434  | T                         | C                        | 0.142             | 0.460            | 0.021           | 0.503            | 2.46E-11          | 44.381  | 0.010 |
| rs254559   | A                         | C                        | 0.124             | 0.404            | 0.022           | 0.855            | 7.63E-09          | 33.427  | 0.007 |

|            |   |   |        |       |       |       |          |         |       |
|------------|---|---|--------|-------|-------|-------|----------|---------|-------|
| rs28383456 | T | C | -0.337 | 0.335 | 0.026 | 0.627 | 1.07E-39 | 173.608 | 0.051 |
| rs3024493  | A | C | 0.236  | 0.168 | 0.028 | 0.679 | 1.09E-17 | 73.299  | 0.016 |
| rs35730213 | C | G | -0.167 | 0.267 | 0.025 | 0.030 | 8.81E-12 | 46.462  | 0.011 |
| rs3829111  | A | G | 0.156  | 0.417 | 0.021 | 0.895 | 2.89E-13 | 53.347  | 0.012 |
| rs4574921  | T | C | 0.151  | 0.741 | 0.026 | 0.497 | 4.24E-09 | 34.607  | 0.009 |
| rs4676410  | A | G | 0.208  | 0.197 | 0.028 | 0.257 | 2.46E-13 | 53.538  | 0.014 |
| rs483905   | A | G | 0.129  | 0.294 | 0.023 | 0.399 | 1.57E-08 | 31.964  | 0.007 |
| rs484356   | G | C | -0.134 | 0.328 | 0.023 | 0.974 | 3.95E-09 | 34.644  | 0.008 |
| rs56167332 | A | C | 0.152  | 0.342 | 0.023 | 0.415 | 5.30E-11 | 43.068  | 0.010 |
| rs6017342  | C | A | 0.191  | 0.538 | 0.024 | 0.934 | 1.38E-15 | 63.538  | 0.018 |
| rs6062496  | A | G | 0.158  | 0.573 | 0.022 | 0.375 | 1.47E-12 | 50.067  | 0.012 |
| rs6933404  | C | T | 0.167  | 0.216 | 0.025 | 0.182 | 3.68E-11 | 43.811  | 0.009 |
| rs7282490  | A | G | -0.140 | 0.604 | 0.021 | 0.144 | 7.08E-11 | 42.615  | 0.009 |
| rs7752873  | T | C | 0.182  | 0.137 | 0.030 | 0.649 | 1.83E-09 | 36.197  | 0.008 |
| rs7911680  | C | A | -0.172 | 0.490 | 0.021 | 0.751 | 8.27E-16 | 65.056  | 0.015 |
| rs798502   | C | A | -0.136 | 0.283 | 0.024 | 0.070 | 1.21E-08 | 32.617  | 0.008 |
| rs9272514  | T | C | -0.402 | 0.298 | 0.027 | 0.396 | 4.00E-51 | 226.235 | 0.067 |
| rs9823546  | A | T | 0.177  | 0.310 | 0.022 | 0.892 | 2.29E-15 | 62.928  | 0.013 |

|           |   |   |        |       |       |       |          |        |       |
|-----------|---|---|--------|-------|-------|-------|----------|--------|-------|
| rs989960  | T | C | -0.129 | 0.425 | 0.022 | 0.717 | 1.77E-09 | 36.054 | 0.008 |
| rs9977672 | A | G | -0.245 | 0.251 | 0.026 | 0.142 | 6.21E-21 | 88.120 | 0.023 |

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**Supplementary Table 3 Detailed information of confounders-independent single-nucleotide polymorphisms of Crohn's disease on anxiety.**

| SNP         | effect_allele<br>. exposure | other_allele<br>e. exposure | beta.<br>exposure | eaf.<br>exposure | se.<br>exposur<br>e | pval.<br>outcome | pval.<br>exposure | F       | R2    |
|-------------|-----------------------------|-----------------------------|-------------------|------------------|---------------------|------------------|-------------------|---------|-------|
| rs1056441   | C                           | T                           | 0.167             | 0.698            | 0.026               | 0.349            | 5.44E-11          | 42.890  | 0.012 |
| rs10761659  | G                           | A                           | 0.212             | 0.553            | 0.024               | 0.659            | 3.42E-19          | 80.020  | 0.022 |
| rs11209026  | A                           | G                           | -0.995            | 0.056            | 0.064               | 0.296            | 1.05E-54          | 242.559 | 0.105 |
| rs11236797  | A                           | C                           | 0.181             | 0.473            | 0.023               | 0.603            | 4.85E-15          | 61.466  | 0.016 |
| rs112401990 | A                           | G                           | 0.132             | 0.373            | 0.024               | 0.070            | 2.35E-08          | 31.116  | 0.008 |
| rs12194825  | A                           | T                           | -0.172            | 0.186            | 0.030               | 0.967            | 8.00E-09          | 33.277  | 0.009 |
| rs1250573   | A                           | G                           | -0.171            | 0.287            | 0.026               | 0.846            | 9.01E-11          | 41.904  | 0.012 |
| rs12717899  | T                           | G                           | 0.159             | 0.794            | 0.029               | 0.898            | 3.59E-08          | 30.344  | 0.008 |
| rs1297271   | T                           | C                           | -0.155            | 0.430            | 0.024               | 0.427            | 6.28E-11          | 42.718  | 0.012 |
| rs13135092  | G                           | A                           | 0.221             | 0.095            | 0.039               | 0.360            | 1.21E-08          | 32.421  | 0.008 |
| rs1332099   | C                           | T                           | -0.212            | 0.515            | 0.023               | 0.564            | 4.36E-20          | 83.906  | 0.022 |
| rs1456896   | T                           | C                           | 0.139             | 0.698            | 0.025               | 0.113            | 2.90E-08          | 30.801  | 0.008 |
| rs147018773 | T                           | C                           | 0.322             | 0.097            | 0.038               | 0.847            | 8.89E-18          | 73.593  | 0.018 |

|             |   |   |        |       |       |       |          |         |       |
|-------------|---|---|--------|-------|-------|-------|----------|---------|-------|
| rs147684209 | C | T | 0.155  | 0.369 | 0.024 | 0.581 | 2.34E-10 | 40.302  | 0.011 |
| rs151314883 | A | G | -0.224 | 0.158 | 0.033 | 0.495 | 7.12E-12 | 46.922  | 0.013 |
| rs1873625   | A | C | 0.181  | 0.320 | 0.024 | 0.851 | 1.09E-13 | 55.300  | 0.014 |
| rs1887428   | C | G | -0.168 | 0.623 | 0.024 | 0.272 | 4.22E-12 | 47.854  | 0.013 |
| rs1932990   | T | C | 0.153  | 0.254 | 0.026 | 0.040 | 6.02E-09 | 33.799  | 0.009 |
| rs2076756   | G | A | 0.400  | 0.284 | 0.024 | 0.387 | 3.24E-61 | 272.940 | 0.065 |
| rs2129944   | G | T | -0.156 | 0.291 | 0.027 | 0.861 | 7.81E-09 | 33.222  | 0.010 |
| rs2188962   | T | C | 0.212  | 0.440 | 0.023 | 0.925 | 1.36E-20 | 86.782  | 0.022 |
| rs2505640   | G | A | -0.146 | 0.644 | 0.024 | 0.504 | 7.61E-10 | 37.794  | 0.010 |
| rs281379    | A | G | 0.140  | 0.489 | 0.024 | 0.278 | 4.26E-09 | 34.502  | 0.010 |
| rs28701841  | A | G | 0.224  | 0.117 | 0.037 | 0.599 | 1.85E-09 | 36.162  | 0.010 |
| rs3024505   | A | G | 0.178  | 0.162 | 0.030 | 0.137 | 3.90E-09 | 34.702  | 0.009 |
| rs3091315   | G | A | -0.180 | 0.266 | 0.026 | 0.785 | 9.52E-12 | 46.582  | 0.013 |
| rs3810936   | C | T | 0.208  | 0.698 | 0.026 | 0.406 | 2.46E-15 | 62.427  | 0.018 |
| rs4077515   | T | C | 0.216  | 0.420 | 0.024 | 0.638 | 4.37E-20 | 84.406  | 0.023 |
| rs444210    | G | A | 0.163  | 0.547 | 0.023 | 0.767 | 1.02E-12 | 50.915  | 0.013 |
| rs4851586   | C | T | -0.169 | 0.760 | 0.026 | 0.995 | 9.94E-11 | 41.877  | 0.010 |



|            |   |   |        |       |       |       |          |         |       |
|------------|---|---|--------|-------|-------|-------|----------|---------|-------|
| rs4902642  | A | G | -0.129 | 0.409 | 0.024 | 0.318 | 4.34E-08 | 29.970  | 0.008 |
| rs56062135 | T | C | 0.193  | 0.234 | 0.027 | 0.138 | 7.45E-13 | 51.528  | 0.013 |
| rs6588243  | C | A | 0.132  | 0.590 | 0.023 | 0.628 | 1.78E-08 | 31.679  | 0.008 |
| rs6704109  | T | C | 0.202  | 0.256 | 0.026 | 0.286 | 2.77E-15 | 62.263  | 0.016 |
| rs6873866  | C | T | -0.168 | 0.535 | 0.024 | 0.537 | 2.06E-12 | 49.467  | 0.014 |
| rs697693   | A | G | 0.172  | 0.201 | 0.028 | 0.677 | 8.36E-10 | 37.596  | 0.010 |
| rs7276302  | G | A | -0.172 | 0.608 | 0.023 | 0.222 | 1.23E-13 | 55.182  | 0.014 |
| rs72798422 | C | T | 0.590  | 0.048 | 0.051 | 0.347 | 3.19E-31 | 135.068 | 0.032 |
| rs744166   | G | A | -0.129 | 0.408 | 0.023 | 0.883 | 2.92E-08 | 30.795  | 0.008 |
| rs7543234  | T | C | 0.155  | 0.239 | 0.027 | 0.248 | 6.10E-09 | 33.918  | 0.009 |
| rs7713270  | T | C | 0.297  | 0.624 | 0.024 | 0.479 | 6.97E-35 | 151.466 | 0.041 |
| rs78487399 | C | G | 0.226  | 0.101 | 0.037 | 0.923 | 1.03E-09 | 37.276  | 0.009 |
| rs80262450 | A | G | 0.283  | 0.113 | 0.035 | 0.888 | 1.08E-15 | 64.319  | 0.016 |
| rs8178977  | C | G | 0.193  | 0.239 | 0.027 | 0.353 | 2.06E-12 | 49.512  | 0.014 |
| rs907092   | A | G | 0.130  | 0.471 | 0.023 | 0.024 | 1.01E-08 | 32.708  | 0.008 |
| rs921720   | G | A | 0.163  | 0.619 | 0.024 | 0.198 | 6.40E-12 | 47.241  | 0.012 |

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**Supplementary Table 4 Detailed information of confounders-independent single-nucleotide polymorphisms of anxiety on ulcerative colitis**

| SNP         | effect_allele.<br>exposure | other_allele.<br>exposure | beta.<br>exposure | eaf.<br>exposure | se.<br>exposure | pval.<br>exposure | pval.<br>outcome | F      | R     |
|-------------|----------------------------|---------------------------|-------------------|------------------|-----------------|-------------------|------------------|--------|-------|
| rs116613090 | T                          | A                         | 0.157             | 0.030            | 0.033           | 1.78E-06          | 0.998            | 22.859 | 0.001 |
| rs116905709 | A                          | G                         | 0.180             | 0.022            | 0.039           | 3.18E-06          | 0.757            | 21.730 | 0.001 |
| rs11729045  | A                          | C                         | -0.114            | 0.074            | 0.022           | 1.45E-07          | 0.859            | 27.550 | 0.002 |
| rs118078990 | T                          | C                         | -0.118            | 0.050            | 0.026           | 4.85E-06          | 0.631            | 20.827 | 0.001 |
| rs11907168  | A                          | G                         | -0.085            | 0.111            | 0.018           | 2.67E-06          | 0.636            | 22.018 | 0.001 |
| rs12208240  | A                          | G                         | -0.127            | 0.051            | 0.026           | 1.19E-06          | 0.501            | 23.677 | 0.002 |
| rs13190528  | G                          | A                         | 0.114             | 0.062            | 0.023           | 1.11E-06          | 0.429            | 23.729 | 0.002 |
| rs143927812 | A                          | G                         | 0.335             | 0.007            | 0.073           | 3.93E-06          | 0.076            | 21.305 | 0.001 |
| rs144051380 | A                          | G                         | 0.131             | 0.050            | 0.026           | 5.37E-07          | 0.145            | 25.193 | 0.002 |
| rs145070376 | C                          | G                         | 0.343             | 0.007            | 0.073           | 2.60E-06          | 0.925            | 22.064 | 0.002 |
| rs2193743   | G                          | A                         | 0.063             | 0.263            | 0.013           | 8.70E-07          | 0.478            | 24.148 | 0.002 |
| rs2787970   | C                          | T                         | -0.063            | 0.255            | 0.013           | 1.07E-06          | 0.593            | 23.700 | 0.001 |
| rs34919929  | A                          | G                         | -0.064            | 0.711            | 0.012           | 2.40E-07          | 0.157            | 26.556 | 0.002 |
| rs3761010   | C                          | A                         | -0.057            | 0.313            | 0.012           | 2.60E-06          | 0.597            | 22.136 | 0.001 |

|            |   |   |        |       |       |          |       |        |       |
|------------|---|---|--------|-------|-------|----------|-------|--------|-------|
| rs61820769 | T | C | -0.151 | 0.037 | 0.030 | 4.12E-07 | 0.828 | 25.639 | 0.002 |
| rs62043045 | G | A | 0.060  | 0.262 | 0.013 | 2.82E-06 | 0.578 | 21.950 | 0.001 |
| rs62205564 | T | C | -0.156 | 0.029 | 0.034 | 4.15E-06 | 0.355 | 21.149 | 0.001 |
| rs72996580 | A | G | 0.085  | 0.113 | 0.018 | 1.69E-06 | 0.481 | 22.953 | 0.001 |
| rs76433582 | G | A | 0.443  | 0.004 | 0.095 | 2.77E-06 | 0.145 | 21.959 | 0.001 |
| rs78840759 | C | T | -0.183 | 0.021 | 0.040 | 4.07E-06 | 0.467 | 21.211 | 0.001 |
| rs7944723  | G | C | -0.066 | 0.812 | 0.015 | 4.98E-06 | 0.903 | 20.718 | 0.001 |

**Supplementary Table 5 Detailed information of confounders-independent single-nucleotide polymorphism of anxiety on Crohn's disease**

| SNP         | effect_allele.<br>exposure | other_allele.<br>exposure | beta.<br>exposure | eaf.<br>exposure | se.<br>exposure | pval.<br>exposure | pval.<br>outcome | F      | R     |
|-------------|----------------------------|---------------------------|-------------------|------------------|-----------------|-------------------|------------------|--------|-------|
| rs116613090 | T                          | A                         | 0.157             | 0.030            | 0.033           | 1.78E-06          | 0.389            | 22.859 | 0.001 |
| rs116905709 | A                          | G                         | 0.180             | 0.022            | 0.039           | 3.18E-06          | 0.814            | 21.730 | 0.001 |
| rs11729045  | A                          | C                         | -0.114            | 0.074            | 0.022           | 1.45E-07          | 0.882            | 27.550 | 0.002 |
| rs118078990 | T                          | C                         | -0.118            | 0.050            | 0.026           | 4.85E-06          | 0.690            | 20.827 | 0.001 |
| rs11907168  | A                          | G                         | -0.085            | 0.111            | 0.018           | 2.67E-06          | 0.671            | 22.018 | 0.001 |

|             |   |   |        |       |       |          |       |        |       |
|-------------|---|---|--------|-------|-------|----------|-------|--------|-------|
| rs12208240  | A | G | -0.127 | 0.051 | 0.026 | 1.19E-06 | 0.375 | 23.677 | 0.002 |
| rs13190528  | G | A | 0.114  | 0.062 | 0.023 | 1.11E-06 | 0.119 | 23.729 | 0.002 |
| rs143927812 | A | G | 0.335  | 0.007 | 0.073 | 3.93E-06 | 0.918 | 21.305 | 0.001 |
| rs144051380 | A | G | 0.131  | 0.050 | 0.026 | 5.37E-07 | 0.268 | 25.193 | 0.002 |
| rs145070376 | C | G | 0.343  | 0.007 | 0.073 | 2.60E-06 | 0.656 | 22.064 | 0.002 |
| rs2193743   | G | A | 0.063  | 0.263 | 0.013 | 8.70E-07 | 0.871 | 24.148 | 0.002 |
| rs2787970   | C | T | -0.063 | 0.255 | 0.013 | 1.07E-06 | 0.383 | 23.700 | 0.001 |
| rs34919929  | A | G | -0.064 | 0.711 | 0.012 | 2.40E-07 | 0.684 | 26.556 | 0.002 |
| rs3761010   | C | A | -0.057 | 0.313 | 0.012 | 2.60E-06 | 0.629 | 22.136 | 0.001 |
| rs61820769  | T | C | -0.151 | 0.037 | 0.030 | 4.12E-07 | 0.508 | 25.639 | 0.002 |
| rs62043045  | G | A | 0.060  | 0.262 | 0.013 | 2.82E-06 | 0.107 | 21.950 | 0.001 |
| rs62205564  | T | C | -0.156 | 0.029 | 0.034 | 4.15E-06 | 0.809 | 21.149 | 0.001 |
| rs72996580  | A | G | 0.085  | 0.113 | 0.018 | 1.69E-06 | 0.571 | 22.953 | 0.001 |
| rs76433582  | G | A | 0.443  | 0.004 | 0.095 | 2.77E-06 | 0.498 | 21.959 | 0.001 |
| rs78840759  | C | T | -0.183 | 0.021 | 0.040 | 4.07E-06 | 0.140 | 21.211 | 0.001 |
| rs7944723   | G | C | -0.066 | 0.812 | 0.015 | 4.98E-06 | 0.243 | 20.718 | 0.001 |

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