**Supplementary Material:**

**Genetically low vitamin D concentrations and myopic refractive error: a Mendelian randomization study**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | European Descent | | | | Asian Descent | | | |
| SNP | Gene | Reference Allele | Other Allele | Beta | s.e. | P-value | Number of studies | Beta | s.e. | P-value | Number of studies |
| rs10741657 | CYP2R1 | G | A | 0.007 | 0.017 | 0.691 | 25 | 0.024 | 0.050 | 0.626 | 5 |
| rs10766197 | CYP2R1 | A | G | -0.005 | 0.016 | 0.734 | 27 | 0.019 | 0.037 | 0.605 | 4 |
| rs12794714 | CYP2R1 | G | A | 0.015 | 0.016 | 0.365 | 26 | -0.015 | 0.042 | 0.717 | 5 |
| rs1562902 | CYP2R1 | T | C | -0.011 | 0.016 | 0.480 | 27 | -0.008 | 0.034 | 0.804 | 5 |
| rs2060793 | CYP2R1 | G | A | 0.008 | 0.016 | 0.643 | 27 | 0.023 | 0.050 | 0.638 | 5 |
| rs2282679 | GC | T | G | -0.022 | 0.018 | 0.217 | 28 | 0.039 | 0.039 | 0.324 | 5 |
| rs7041 | GC | C | A | -0.009 | 0.017 | 0.591 | 29 | -0.007 | 0.035 | 0.840 | 5 |
| rs705117 | GC | T | C | 0.027 | 0.028 | 0.350 | 28 | -0.051 | 0.036 | 0.158 | 5 |
| rs7944926 | DHCR7 | G | A | 0.011 | 0.018 | 0.537 | 27 | -0.020 | 0.042 | 0.630 | 5 |
| rs11234027 | DHCR7 | G | A | -0.014 | 0.022 | 0.513 | 25 | -0.040 | 0.036 | 0.260 | 5 |
| rs12785878 | DHCR7 | T | G | 0.010 | 0.019 | 0.600 | 25 | -0.025 | 0.042 | 0.554 | 5 |
| rs3829251 | DHCR7 | G | A | -0.012 | 0.022 | 0.589 | 27 | -0.037 | 0.036 | 0.296 | 5 |
| rs6013897 | CYP24A1 | A | T | 0.012 | 0.067 | 0.567 | 27 | -0.032 | 0.042 | 0.448 | 5 |

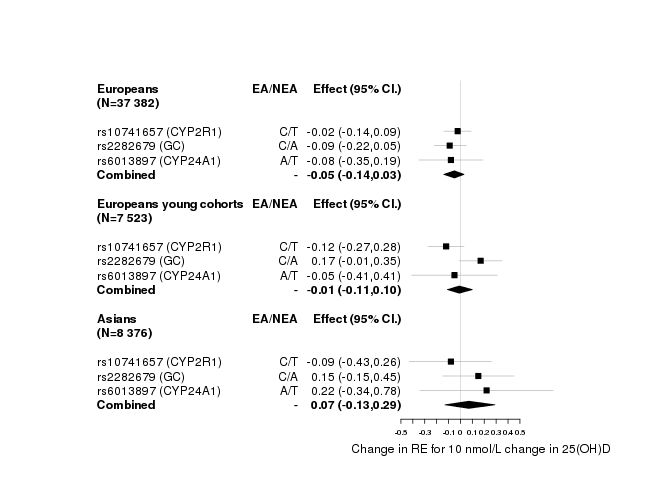
**Supplementary Table 1.** Association between vitamin D SNPs and refractive error obtained from a genome-wide association study (GWAS) meta-analysis carried out by the Consortium for Refractive Error and Myopia (CREAM)[1](#_ENREF_1).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| European Cohorts | | | | | |
| Study | N | Mean age | age s.d. | Mean SPHEQ | SPHEQ s.d. |
| 1985 British Birth Cohort | 1658 | 42 | 0 | -0.96 | 2 |
| ALSPAC (Mothers) | 1865 | 45 | 4.5 | -0.76 | 2.16 |
| ANZRAG | 402 | 79.9 | 12 | -0.26 | 2.36 |
| AREDS1a1b | 485 | 73.4 | 24.2 | 0.73 | 1.9 |
| AREDS1c | 1877 | 67.9 | 4.7 | 0.56 | 2.15 |
| BMES | 1550 | 73.8 | 7.76 | 0.62 | 2.12 |
| CROATIA Korcula | 822 | 56.3 | 13.3 | -0.15 | 1.6 |
| CROATIA Split | 344 | 51.2 | 13 | -1.68 | 1.61 |
| CROATIA Vis | 527 | 56.3 | 13.3 | -0.13 | 1.75 |
| DCCT | 791 | 31.4 | 4.1 | -1.47 | 1.8 |
| EGCUT | 782 | 57.2 | 17.8 | 0.48 | 3.18 |
| ERF | 2028 | 48.5 | 14.3 | 0.08 | 2.14 |
| FECD | 412 | 71.5 | 9.2 | 0.14 | 2.49 |
| FITSA | 98 | 68.1 | 3.7 | 1.54 | 1.7 |
| Framingham | 1497 | 55.6 | 8.9 | 0.03 | 2.41 |
| Gutenberg Health Study 1 | 2750 | 55.6 | 10.8 | -0.38 | 2.44 |
| Gutenberg Health Study 2 | 1143 | 54.8 | 10.8 | -0.41 | 2.58 |
| KORA | 1860 | 55.6 | 11.8 | -0.82 | 7.33 |
| OGP Talana | 627 | 52.6 | 16.3 | -0.2 | 2.04 |
| ORCADES | 504 | 57.6 | 13.5 | 0.03 | 2.08 |
| RS1 | 5328 | 68.5 | 8.6 | 0.86 | 2.44 |
| RS2 | 2009 | 64.2 | 7.4 | 0.48 | 2.51 |
| RS3 | 1970 | 60.8 | 5.5 | -0.35 | 2.62 |
| TEST/BATS | 403 | 38.7 | 13.7 | -0.28 | 1.05 |
| TwinsUK | 3865 | 53.8 | 11 | -0.4 | 2.73 |
| WESDR | 306 | 34.7 | 8.2 | -1.5 | 2.02 |
| Young Finns Study | 1479 | 41.9 | 5 | -1.04 | 2.01 |
| Asian Cohorts | | | | | |
| Beijing Eye Study | 578 | 62.1 | 8.8 | 2.45 | 15.73 |
| SCES | 1723 | 57.5 | 9 | -0.77 | 2.65 |
| SIMES | 2273 | 58 | 10.8 | -0.05 | 1.86 |
| SINDI | 2108 | 55.8 | 8.8 | 0.01 | 2.14 |
| SP2 | 1694 | 47.7 | 10.8 | -1.66 | 2.93 |

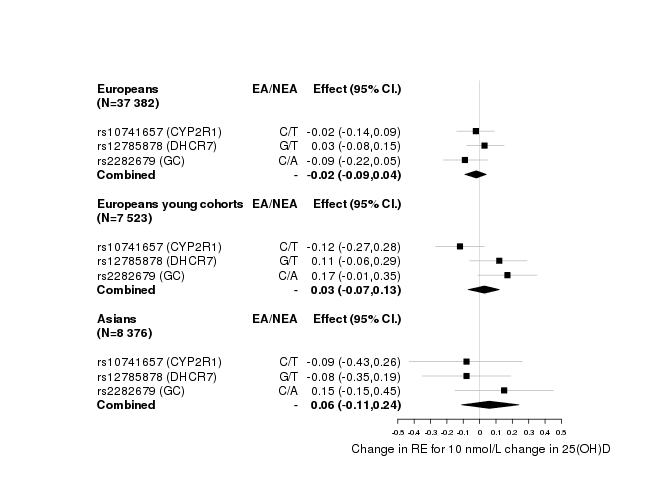
**Supplementary Table 2.** Description of cohorts included in the GWAS meta-analysis carried out by CREAM[1](#_ENREF_1).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Body Mass Index[2](#_ENREF_2) | | | | |
| SNP | EA | NEA | Effect | P |
| rs10741657 | G | A | -0.0086 | 0.02363 |
| rs11234027 | A | G | 0.0041 | 0.4027 |
| rs12785878 | G | T | 0.0017 | 0.6857 |
| rs12794714 | G | A | 0.0092 | 0.0129 |
| rs2282679 | T | G | 0.0027 | 0.5203 |
| rs6013897 | T | A | -0.0014 | 0.7609 |
| rs7944926 | A | G | 0.0016 | 0.7032 |
| Cigars Per Day[3](#_ENREF_3) | | | | |
| rs10741657 | A | G | 0.0109 | 0.8965 |
| rs11234027 | A | G | -0.1132 | 0.3023 |
| rs12785878 | T | G | 0.1218 | 0.1834 |
| rs12794714 | A | G | -0.0013 | 0.9871 |
| rs2282679 | T | G | 0.0232 | 0.8012 |
| rs6013897 | A | T | 0.0354 | 0.7253 |
| rs7944926 | A | G | -0.1154 | 0.2077 |
| Education Years[4](#_ENREF_4) | | | | |
| rs10741657 | A | G | -0.002 | 0.429 |
| rs11234027 | A | G | -0.005 | 0.1307 |
| rs12785878 | T | G | 0.005 | 0.05727 |
| rs12794714 | A | G | 0.003 | 0.184 |
| rs2282679 | T | G | -0.002 | 0.5373 |
| rs6013897 | A | T | -0.003 | 0.2904 |
| rs7944926 | A | G | -0.005 | 0.05595 |

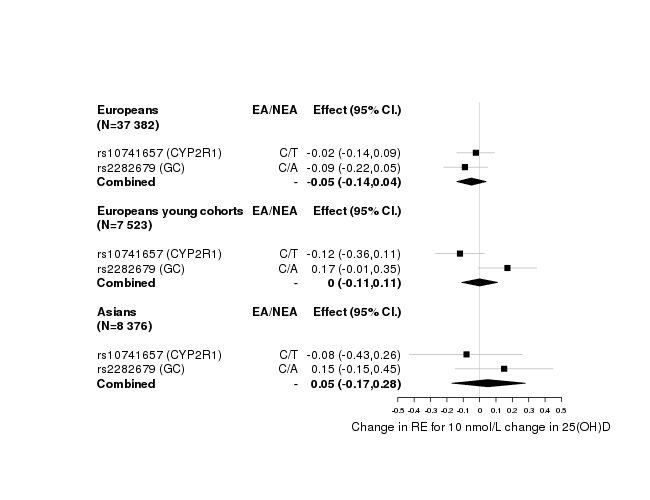
**Supplementaty Table 3.** Association between the SNPs using in the Mendelian Randomization and potential confounders.



**Supplementary Figure 1.** Mendelian Randomization results excluding the SNP in DHCR7.



**Supplementary Figure 2.** Mendelian Randomization results excluding the SNP in CYP24A1.



**Supplementary Figure 3.** Mendelian Randomization excluding SNPs in DHCR7 and CYP24A1.

1. Verhoeven VJ, Hysi PG, Wojciechowski R, et al. Genome-wide meta-analyses of multiancestry cohorts identify multiple new susceptibility loci for refractive error and myopia. *Nature genetics* 2013; **45**: 314-8.

2. Locke AE, Kahali B, Berndt SI, et al. Genetic studies of body mass index yield new insights for obesity biology. *Nature* 2015; **518**: 197-206.

3. Vink JM, Smit AB, de Geus EJ, et al. Genome-wide association study of smoking initiation and current smoking. *Am J Hum Genet* 2009; **84**: 367-79.

4. Okbay A, Beauchamp JP, Fontana MA, et al. Genome-wide association study identifies 74 loci associated with educational attainment. *Nature* 2016; **533**: 539-42.