## **Online Supporting Materials**

**Supplemental Table 1.** Genotype distribution of vitamin D related SNPs and their association with serum 25(OH)D during autumn

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | | **Minor allele frequency** | **Hardy-Weinberg equilibrium** | **25(OH)D** (nmol/L) |  |  |  |  |
| **SNP** | **Genotype** | **n** | **%** | | ***P*** | **Mean±SD** | ***P*** | **β1 (95% CI)** | | ***P*** |
| *DHCR7* | |  |  | |  |  |  |  | |  |
| rs12785878 | MM | 297 | 35.8 | | 0.068 | 63 ± 17.5 |  | Ref. | |  |
|  | Mm | 297 |  | |  | 61 ± 18.4 | 0.260 | -2.2 (-5.1, 0.7) | | 0.131 |
|  | mm | 100 |  | |  | 58 ± 21.0 | 0.027 | -5.5 (-9.6, -1.4) | | 0.009 |
| rs3829251 | MM | 422 | 22.0 | | 0.92 | 62 ± 18.5 |  | Ref. | |  |
|  | Mm | 237 |  | |  | 60 ± 19.0 | 0.319 | -1.8 (-4.7, 1.1) | | 0.21 |
|  | mm | 34 |  | |  | 60 ± 20.0 | 0.655 | -1.5 (-8.0, 5.0) | | 0.66 |
| *GC* |  |  |  | |  |  |  |  | |  |
| rs4588 | MM | 355 | 28.2 | | 0.60 | 65 ± 19.0 |  | Ref. | |  |
|  | Mm | 271 |  | |  | 58 ± 16.6 | <0.001 | -8.1 (-10.8, -5.3) | | <0.001 |
|  | mm | 57 |  | |  | 51 ± 17.0 | <0.001 | -14.2 (-19.2, -9.2) | | <0.001 |
| rs12512631 | MM | 282 | 36.7 | | 0.34 | 58 ± 18.6 |  | Ref. | |  |
|  | Mm | 309 |  | |  | 63 ± 18.3 | 0.002 | 4.3 (1.3, 7.2) | | 0.004 |
|  | mm | 99 |  | |  | 65 ± 17.1 | 0.001 | 7.3 (3.2, 11.5) | | <0.001 |
| rs7041 | MM | 238 | 42.8 | | 0.076 | 66 ± 18.6 |  | Ref. | |  |
|  | Mm | 316 |  | |  | 59 ± 17.2 | <0.001 | -7.0 (-10.0, -4.0) | | <0.001 |
|  | mm | 138 |  | |  | 57 ± 19.2 | <0.001 | -8.9 (-12.6, -5.1) | | <0.001 |
| *CYP2R1* |  |  |  | |  |  |  |  | |  |
| rs10741657 | MM | 258 | 39.6 | | 0.38 | 57 ± 16.7 |  | Ref. | |  |
|  | Mm | 320 |  | |  | 61 ± 17.9 | 0.005 | 3.9 (1.0, 6.8) | | 0.009 |
|  | mm | 114 |  | |  | 69 ± 21.1 | <0.001 | 11.3 (7.4, 15.2) | | <0.001 |
| rs10500804 | MM | 237 | 41.4 | | 0.89 | 65 ± 20.6 |  | Ref. | |  |
|  | Mm | 338 |  | |  | 60 ± 17.2 | 0.001 | -4.8 (-7.7, -1.8) | | 0.002 |
|  | mm | 118 |  | |  | 55 ± 15.4 | <0.001 | -9.0 (-12.9, -5.0) | | <0.001 |
| rs1562902 | MM | 202 | 45.2 | | 0.35 | 59 ± 16.6 |  | Ref. | |  |
|  | Mm | 355 |  | |  | 61 ± 18.2 | 0.389 | 1.9 (-1.3, 5.0) | | 0.24 |
|  | mm | 135 |  | |  | 65 ± 21.1 | 0.003 | 6.3 (2.4, 10.2) | | 0.002 |
| *CYP24A1* |  |  |  | |  |  |  |  | |  |
| rs2296241 | MM | 186 | 36.9 | | 0.88 | 63 ± 20.6 |  | Ref. | |  |
|  | Mm | 354 |  | |  | 61 ± 18.2 | 0.320 | -2.1 (-5.3, 1.2) | | 0.22 |
|  | mm | 157 |  | |  | 59 ± 16.9 | 0.076 | -2.9 (-6.8, 1.0) | | 0.140 |

1 Association between genotype and serum 25(OH)D concentrations with major homozygosity as reference. Linear regression model adjusted for fat mass index (kg/m2), vitamin D dietary intake (µg/d), vitamin D supplements intake (yes/no) and moderate-to-vigorous physical activity (min/d).

## **Online Supporting Materials**

**Supplemental Table 2.** Linkage disequilibrium for SNPs in *GC* and *CYP2R1*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| SNP | rs4588 | rs12512631 | rs7041 | rs10741657 | rs10500804 |
| *GC* |  |  |  |  |  |
| rs4588 |  |  |  |  |  |
| rs12512631 | -0.514a |  |  |  |  |
| rs7041 | 0.736a | -0.655a |  |  |  |
| *CYP2R1* |  |  |  |  |  |
| rs10741657 | 0.007b | 0.030b | 0.003b |  |  |
| rs10500804 | 0.017b | 0.002b | 0.002b | -0.674a |  |

a Linkage disequilibrium between polymorphisms in the same gene evaluated using Pearson’s r.

b D’ values of calculated Linkage disequilibrium between polymorphisms in two different genes.

## **Online Supporting Materials**

**Supplemental Table 3.** Effect modification by SNPs in the *VDR* gene on associations between the genetic risk score and cardiometabolic risk markers

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Genotype** | | |  | | | | **n** | | | **Risk score** | | | **β (95% CI)** | | ***P*** | | **βa (95% CI)** | | ***P*** |
| **Systolic blood pressure** (mmHg) | | | | | | | | | | | | | | | | | | | |
| rs757343 | | | | | | |  | | |  | | | *P-*interaction = 0.76 | |  | |  |  |  |
| MM | | | GG | | | | 514 | | | 0 - 2 | | | Ref. | |  | | Ref. | |  |
|  | | |  | | | |  | | | 3 - 5 | | | 0.8 (-0.9, 2.6) | | 0.36 | | 0.8 (-1.1, 2.6) | | 0.41 |
|  | | |  | | | |  | | | 6 - 8 | | | -0.4 (-2.6, 1.9) | | 0.76 | | 0.1 (-2.2, 2.4) | | 0.95 |
| Mm + mm | | | GA+AA | | | | 151 | | | 0 - 2 | | | Ref. | |  | | Ref. | |  |
|  | | |  | | | |  | | | 3 - 5 | | | 0.2 (-2.9, 3.4) | | 0.88 | | 1.3 (-2.0, 4.7) | | 0.44 |
|  | | |  | | | |  | | | 6 - 8 | | | -1.0 (-5.0, 3.0) | | 0.61 | | 0.3 (-4.0, 4.6) | | 0.89 |
| rs2228570 | | | | | | | | | |  | | | *P-*interaction = 0.98 | |  | |  |  |  |
| MM | | | CC | | | | 274 | | | 0 - 2 | | | Ref. | |  | | Ref. | |  |
|  | | |  | | | |  | | | 3 - 5 | | | 0.1 (-2.3, 2.4) | | 0.97 | | 0.4 (-2.0, 2.8) | | 0.75 |
|  | | |  | | | |  | | | 6 - 8 | | | -0.7 (-3.7, 2.2) | | 0.63 | | -0.6 (-3.6, 2.5) | | 0.71 |
| Mm | | | TC | | | | 304 | | | 0 - 2 | | | Ref. | |  | | Ref. | |  |
|  | | |  | | | |  | | | 3 - 5 | | | 1.6 (-0.7, 3.9) | | 0.18 | | 2.2 (-0.2, 4.6) | | 0.073 |
|  | | |  | | | |  | | | 6 - 8 | | | -0.6 (-3.6, 2.4) | | 0.70 | | 0.3 (-2.8, 3.5) | | 0.83 |
| mm | | | TT | | | | 91 | | | 0 - 2 | | | Ref. | |  | | Ref. | |  |
|  | | |  | | | |  | | | 3 - 5 | | | -0.4 (-4.4, 3.6) | | 0.83 | | -1.3 (-4.6, 3.2) | | 0.73 |
|  | | |  | | | |  | | | 6 - 8 | | | -0.2 (-5.2, 4.8) | | 0.93 | | -0.7 (-2.2, 7.7) | | 0.27 |
| rs11568820 | | |  | | | |  | | |  | | | *P-*interaction = 0.038 | |  | |  |  |  |
| MM | | | GG | | | | 460 | | | 0 - 2 | | | Ref. | |  | | Ref. | |  |
|  | | |  | | | |  | | | 3 - 5 | | | 1.5 (-0.4, 3.3) | | 0.117 | | 1.4 (-0.5, 3.3) | | 0.150 |
|  | | |  | | | |  | | | 6 - 8 | | | 1.0 (-1.3, 3.4) | | 0.40 | | 1.5 (-1.0, 3.9) | | 0.23 |
| Mm + mm | | | GA+AA | | | | 209 | | | 0 - 2 | | | Ref. | |  | | Ref. | |  |
|  | | |  | | | |  | | | 3 - 5 | | | -0.7 (-3.6, 2.1) | | 0.61 | | 0.4 (-2.4, 3.2) | | 0.79 |
|  | | |  | | | |  | | | 6 - 8 | | | -3.2 (-6.7, 0.3) | | 0.070 | | -2.0 (-5.4, 1.4) | | 0.25 |
| **Diastolic blood pressure** (mmHg) | | | | | | | | | | | | | | | | | | | |
| rs757343 | | | | | | | | | |  | | | *P*-interaction = 0.99 | |  | |  |  |  |
| MM | | | | GG | | | 514 | | | 0 - 2 | | | Ref. | |  | | Ref. | |  |
|  | | | |  | | |  | | | 3 - 5 | | | 1.2 (-0.2, 2.6) | | 0.095 | | 0.9 (-0.6, 2.3) | | 0.236 |
|  | | | |  | | |  | | | 6 - 8 | | | 1.3 (-0.5, 3.1) | | 0.159 | | 1.2 (-0.6, 3.0) | | 0.193 |
| Mm + mm | | | | GA+AA | | | 151 | | | 0 - 2 | | | Ref. | |  | | Ref. | |  |
|  | | | |  | | |  | | | 3 - 5 | | | 0.1 (-2.3, 2.6) | | 0.92 | | -0.1 (-2.7, 2.6) | | 0.96 |
|  | | | |  | | |  | | | 6 - 8 | | | 1.4 (-1.7, 4.5) | | 0.37 | | 1.2 (-2.1, 4.6) | | 0.47 |
| rs2228570 | | | | | | |  | | |  | | | *P*-interaction = 0.37 | |  | |  |  |  |
| MM | | | | CC | | | 274 | | | 0 - 2 | | | Ref. | |  | | Ref. | |  |
|  | | | |  | | |  | | | 3 - 5 | | | 1.2 (-0.7, 3.2) | | 0.22 | | 0.8 (-1.3, 3.0) | | 0.44 |
|  | | | |  | | |  | | | 6 - 8 | | | 2.1 (-0.3, 4.6) | | 0.090 | | 1.7 (-0.9, 4.4) | | 0.193 |
| Mm | | | | TC | | | 304 | | | 0 - 2 | | | Ref. | |  | | Ref. | |  |
|  | | | |  | | |  | | | 3 - 5 | | | 1.1 (-0.7, 3.0) | | 0.22 | | 1.8 (-0.0, 3.6) | | 0.052 |
|  | | | |  | | |  | | | 6 - 8 | | | 1.3 (-1.0, 3.6) | | 0.27 | | 1.7 (-0.6, 4.0) | | 0.156 |
| mm | | | | TT | | | 91 | | | 0 - 2 | | | Ref. | |  | | Ref. | |  |
|  | | | |  | | |  | | | 3 - 5 | | | -0.8 (-4.3, 2.7) | | 0.65 | | -1.2 (-4.7, 2.2) | | 0.48 |
|  | | | |  | | |  | | | 6 - 8 | | | -1.4 (-5.7, 2.9) | | 0.53 | | -0.6 (-5.0, 3.8) | | 0.79 |
| rs11568820 | | | | | | |  | | |  | | | *P-*interaction = 0.132 | |  | |  |  |  |
| MM | | | GG | | | | 460 | | | 0 - 2 | | | Ref. | |  | | Ref. | |  |
|  | | |  | | | |  | | | 3 - 5 | | | 1.8 (0.2, 3.3) | | 0.024 | | 1.4 (-0.2, 3.0) | | 0.087 |
|  | | |  | | | |  | | | 6 - 8 | | | 2.2 (0.2, 4.2) | | 0.029 | | 2.1 (0.17, 4.1) | | 0.043 |
| Mm + mm | | | GA+AA | | | | 209 | | | 0 - 2 | | | Ref. | |  | | Ref. | |  |
|  | | |  | | | |  | | | 3 - 5 | | | -0.5 (-2.6, 1.6) | | 0.62 | | 0.0 (-2.1, 2.2) | | 0.97 |
|  | | |  | | | |  | | | 6 - 8 | | | -0.2 (-2.8, 2.4) | | 0.891 | | 0.1 (-2.5, 2.7) | | 0.93 |
| **Insulin** (pmol/L) **b,c** | | | | | | | | | | | | | | | | | | | |
| rs757343 | | | | | | |  | | |  | | | *P-*interaction = 0.099 | | |  |  |  |  |
| MM | | GG | | | 514 | | | | | | 0 - 2 | Ref. | | | |  | Ref. | |  |
|  | |  | | |  | | | | | | 3 - 5 | 3.5 (-1.0, 8.0) | | | | 0.127 | 1.5 (-2.6, 5.6) | | 0.48 |
|  | |  | | |  | | | | | | 6 - 8 | 3.2 (-2.5, 9.0) | | | | 0.27 | 3.2 (-2.0, 8.3) | | 0.23 |
| Mm + mm | | GA+AA | | | 151 | | | | | | 0 - 2 | Ref. | | | |  | Ref. | |  |
|  | |  | | |  | | | | | | 3 - 5 | -12.1 (-20.5, -3.8) | | | | 0.005 | -9.2 (-17.4, -1.1) | | 0.027 |
|  | |  | | |  | | | | | | 6 - 8 | -6.2 (-16.7, 4.3) | | | | 0.25 | -4.8 (-15.1, 5.5) | | 0.36 |
| rs2228570 | | | | | | |  | | |  | | | *P-*interaction = 0.44 | | |  |  |  |  |
| MM | CC | | | | | 274 | | | | 0 - 2 | | | Ref. | | |  | Ref. | |  |
|  |  | | | | |  | | | | 3 - 5 | | | 1.4 (-4.9, 7.6) | | | 0.66 | -1.9 (-7.9, 4.1) | | 0.53 |
|  |  | | | | |  | | | | 6 - 8 | | | 4.3 (-3.6, 2.2) | | | 0.29 | 1.1 (-6.3, 8.6) | | 0.77 |
| Mm | TC | | | | | 304 | | | | 0 - 2 | | | Ref. | | |  | Ref. | |  |
|  |  | | | | |  | | | | 3 - 5 | | | -2.0 (-7.7, 3.7) | | | 0.49 | -0.4 (-5.6, 4.9) | | 0.90 |
|  |  | | | | |  | | | | 6 - 8 | | | -1.8 (-9.2, 5.5) | | | 0.62 | 0.9 (-5.8, 7.7) | | 0.79 |
| mm | TT | | | | | 91 | | | | 0 - 2 | | | Ref. | | |  | Ref. | |  |
|  |  | | | | |  | | | | 3 - 5 | | | 3.2 (-8.5, 15.0) | | | 0.59 | -0.6 (-11.8, 10.5) | | 0.91 |
|  |  | | | | |  | | | | 6 - 8 | | | 2.3 (-12.4, 17.0) | | | 0.76 | 2.8 (-11.2, 16.9) | | 0.69 |
| rs11568820 | | | | | | |  | | |  | | | *P-*interaction = 0.053 | | |  |  |  |  |
| MM | | GG | | | | | | 460 | 0 - 2 | | | | | Ref. | |  | Ref. | |  |
|  | |  | | | | | |  | 3 - 5 | | | | | 1.9 (-3.0, 6.7) | | 0.45 | 0.1 (-4.5, 4.6) | | 0.98 |
|  | |  | | | | | |  | 6 - 8 | | | | | 4.4 (-1.8, 10.6) | | 0.167 | 3.2 (-2.6, 9.1) | | 0.28 |
| Mm + mm | | GA+AA | | | | | | 209 | 0 - 2 | | | | | Ref. | |  | Ref. | |  |
|  | |  | | | | | |  | 3 - 5 | | | | | -4.0 (-10.9, 3.1) | | 0.27 | -2.2 (-8.2, 3.9) | | 0.48 |
|  | |  | | | | | |  | 6 - 8 | | | | | -4.8 (-13.4, 3.8) | | 0.27 | -2.4 (-9.8, 5.0) | | 0.52 |
| **Triacylglycerol** (mmol/L) **b,c** | | | | | | | | | | | | | | | | | | | |
| rs757343 | | | | | | |  | | |  | | | *P*-interaction = 0.52 | | |  |  |  |  |
| MM | | GG | | | 514 | | | | | | 0 - 2 | Ref. | | | |  | Ref. | |  |
|  | |  | | |  | | | | | | 3 - 5 | 0.02 (-0.03, 0.07) | | | | 0.51 | 0.01 (-0.04, 0.06) | | 0.72 |
|  | |  | | |  | | | | | | 6 - 8 | 0.02 (-0.05, 0.08) | | | | 0.65 | 0.02 (-0.05, 0.08) | | 0.65 |
| Mm + mm | | GA+AA | | | 151 | | | | | | 0 - 2 | Ref. | | | |  | Ref. | |  |
|  | |  | | |  | | | | | | 3 - 5 | -0.00 (-0.10, 0.09) | | | | 0.95 | 0.03 (-0.06, 0.10) | | 0.49 |
|  | |  | | |  | | | | | | 6 - 8 | -0.07 (-0.04, 0.20) | | | | 0.24 | 0.10 (-0.02, 0.20) | | 0.106 |
| rs2228570 | | | | | | |  | | |  | | | *P-*interaction = 0.187 | | |  |  |  |  |
| MM | CC | | | | | 274 | | | | 0 - 2 | | | Ref. | | |  | Ref. | |  |
|  |  | | | | |  | | | | 3 - 5 | | | 0.06 (-0.01, 0.10) | | | 0.099 | 0.05 (-0.07, 0.03) | | 0.151 |
|  |  | | | | |  | | | | 6 - 8 | | | 0.09 (-0.01, 0.20) | | | 0.070 | 0.08 (-0.06, 0.08) | | 0.083 |
| Mm | TC | | | | | 304 | | | | 0 - 2 | | | Ref. | | |  | Ref. | |  |
|  |  | | | | |  | | | | 3 - 5 | | | -0.03 (-0.09, 0.03) | | | 0.27 | -0.04 (-0.10, 0.03) | | 0.25 |
|  |  | | | | |  | | | | 6 - 8 | | | -0.01 (-0.09, 0.07) | | | 0.83 | 0.00 (-0.08, 0.08) | | 0.98 |
| mm | TT | | | | | 91 | | | | 0 - 2 | | | Ref. | | |  | Ref. | |  |
|  |  | | | | |  | | | | 3 - 5 | | | 0.01 (-0.10, 0.10) | | | 0.90 | -0.02 (-0.10, 0.10) | | 0.78 |
|  |  | | | | |  | | | | 6 - 8 | | | -0.03 (-0.20, 0.10) | | | 0.71 | -0.07 (-0.20, 0.10) | | 0.41 |
| rs11568820 | | | | | | |  | | |  | | | *P-*interaction = 0.42 | | |  |  |  |  |
| MM | | GG | | | | | | 460 | 0 - 2 | | | | | Ref. | |  | Ref. | |  |
|  | |  | | | | | |  | 3 - 5 | | | | | -0.02 (-0.07, 0.03) | | 0.47 | -0.02 (-0.07, 0.03) | | 0.46 |
|  | |  | | | | | |  | 6 - 8 | | | | | 0.01 (-0.06, 0.08) | | 0.81 | 0.01 (-0.06, 0.08) | | 0.76 |
| Mm + mm | | GA+AA | | | | | | 209 | 0 - 2 | | | | | Ref. | |  | Ref. | |  |
|  | |  | | | | | |  | 3 - 5 | | | | | 0.06 (-0.02, 0.10) | | 0.125 | 0.08 (-0.00, 0.20) | | 0.063 |
|  | |  | | | | | |  | 6 - 8 | | | | | 0.05 (-0.04, 0.20) | | 0.27 | 0.06 (-0.03, 0.20) | | 0.21 |

a Linear regression model adjusted for age, sex, parental education, entered puberty (yes/no), fat mass index (kg/m2) and moderate-to-vigorous physical activity (min/d). Regression coefficients are presented as cardiometabolic outcome change per genetic risk score group

b Analysis with log transformed values and back transformed to normal units.

c Subjects with fasting status.