**Table S4 Anthropometry and Physical Capability by rs2943641 (*IRS1*) Genotype and Cohort**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Variable | Cohort | C/C | C/T | T/T | Total | b (95% CI) a | p-value | Heterogeneity |
| mean (sd) [n] | mean (sd) [n] | mean (sd) [n] | mean (sd) [n] | I2%; p-value |
|  | NSHD | 167.8 (9.1) [1082] | 168.4 (8.7) [1176] | 168.3 (9.2) [339] | 168.2 (8.9) [2597] | 0.04 (0.00- 0.08) | 0.0294 |  |
|  | ELSA | 165.8 (9.5) [2217] | 165.5 (9.6) [2426] | 165.9 (9.1) [659] | 165.7 (9.5) [5302] | 0.01 (-0.01- 0.04) | 0.38 |  |
|  | HCS | 167.8 (9.1) [1146] | 168.1 (9.1) [1298] | 167.7 (9.1) [337] | 167.9 (9.1) [2781] | 0.02 (-0.02- 0.06) | 0.27 |  |
| Height, cm | HAS | 167.5 (8.9) [219] | 166.0 (9.1) [227] | 168.4 (8.6) [73] | 167.0 (9.0) [519] | 0.01 (-0.07- 0.10)† | 0.74 |  |
|  | Boyd Orr | 164.4 (9.1) [148] | 164.3 (9.4) [189] | 163.3 (8.4) [53] | 164.2 (9.1) [390] | -0.03 (-0.13- 0.07) | 0.58 |  |
|  | CaPS | 169.7 (6.2) [339] | 170.3 (6.2) [354] | 170.8 (6.2) [101] | 170.1 (6.2) [794] | 0.10 (-0.01- 0.20) | 0.06 |  |
|  | LBC1921 | 163.3 (9.5) [217] | 163.1 (9.2) [234] | 163.2 (9.5) [62] | 163.2 (9.3) [513] | -0.06 (-0.15- 0.02) | 0.16 |  |
|  | **Pooled** | [5368] | [5904] | [1624] | [12896] | 0.018 (-0.005- 0.042) | 0.12 | 27.5; 0.22 |
|  | NSHD | 77.3 (14.7) [1082] | 78.0 (14.9) [1171] | 76.4 (15.0) [337] | 77.5 (14.8) [2590] | -0.00 (-0.06- 0.05)† | 0.85 |  |
|  | ELSA | 76.7 (15.4) [2231] | 76.1 (15.2) [2427] | 76.7 (15.2) [660] | 76.4 (15.3) [5318] | 0.00 (-0.03- 0.04) | 0.80 |  |
|  | HCS | 76.7 (14.2) [1146] | 77.7 (14.1) [1299] | 77.4 (14.8) [337] | 77.2 (14.2) [2782] | 0.04 (-0.01- 0.10) | 0.09 |  |
| Weight, kg | HAS | 75.3 (13.7) [219] | 74.1 (13.0) [227] | 77.1 (12.8) [73] | 75.0 (13.3) [519] | 0.04 (-0.08- 0.15) | 0.51 |  |
|  | Boyd Orr | 72.6 (13.3) [148] | 76.2 (14.5) [189] | 73.3 (13.6) [53] | 74.4 (14.0) [390] | 0.11 (-0.02- 0.25)† | 0.10 |  |
|  | CaPS | 80.1 (13.6) [340] | 81.2 (12.6) [356] | 81.3 (10.6) [103] | 80.8 (12.8) [799] | 0.07 (-0.03- 0.17) | 0.20 |  |
|  | LBC1921 | 69.4 (12.3) [217] | 70.2 (13.0) [235] | 70.1 (13.6) [62] | 69.8 (12.8) [514] | 0.00 (-0.11- 0.12) | 0.96 |  |
|  | **Pooled** | [5383] | [5904] | [1625] | [12912] | 0.019 (-0.005- 0.042) | 0.12 | 0.0; 0.50 |
|  | NSHD | 27.4 (4.6) [1080] | 27.4 (4.8) [1170] | 26.9 (4.4) [337] | 27.4 (4.7) [2587] | -0.04 (-0.09- 0.02) | 0.22 |  |
|  | ELSA | 27.8 (4.8) [2193] | 27.7 (4.7) [2387] | 27.9 (5.0) [650] | 27.8 (4.7) [5230] | 0.00 (-0.04- 0.04) | 0.86 |  |
|  | HCS | 27.2 (4.4) [1146] | 27.4 (4.3) [1297] | 27.5 (4.6) [337] | 27.4 (4.4) [2780] | 0.04 (-0.02- 0.09) | 0.18 |  |
| BMI, kg/m2 | HAS | 26.8 (3.9) [219] | 26.9 (4.2) [227] | 27.1 (3.7) [73] | 26.9 (4.0) [519] | 0.04 (-0.08- 0.17) | 0.51 |  |
|  | Boyd Orr | 26.8 (4.4) [148] | 28.1 (4.3) [189] | 27.5 (4.9) [53] | 27.5 (4.5) [390] | 0.15 (0.01- 0.30) | 0.0417 |  |
|  | CaPS | 27.8 (4.4) [339] | 28.0 (3.9) [354] | 27.8 (3.0) [101] | 27.9 (4.0) [794] | 0.02 (-0.08- 0.12) | 0.74 |  |
|  | LBC1921 | 26.0 (3.7) [217] | 26.4 (4.3) [234] | 26.3 (4.7) [62] | 26.2 (4.1) [513] | 0.06 (-0.07- 0.19) | 0.36 |  |
|  | **Pooled** | [5342] | [5858] | [1613] | [12813] | 0.017 (-0.016- 0.049) | 0.32 | 25.0; 0.24 |
|  | NSHD | 0.87 (0.09) [1082] | 0.87 (0.09) [1173] | 0.86 (0.09) [340] | 0.87 (0.09) [2595] | -0.02 (-0.06- 0.02)† | 0.29 |  |
|  | ELSA | 0.89 (0.08) [2231] | 0.89 (0.08) [2449] | 0.89 (0.08) [658] | 0.89 (0.08) [5338] | 0.01 (-0.02- 0.04) | 0.68 |  |
|  | HCS | 0.91 (0.08) [1144] | 0.92 (0.08) [1293] | 0.91 (0.09) [337] | 0.91 (0.08) [2774] | 0.05 (0.01- 0.09) | 0.0086 |  |
| Waist-hip ratio | HAS | 0.89 (0.08) [219] | 0.87 (0.08) [226] | 0.88 (0.09) [73] | 0.88 (0.08) [518] | -0.05 (-0.13- 0.02) | 0.17 |  |
|  | Boyd Orr | 0.90 (0.10) [147] | 0.92 (0.09) [189] | 0.90 (0.08) [53] | 0.91 (0.09) [389] | 0.05 (-0.07- 0.17)† | 0.41 |  |
|  | CaPS | 0.93 (0.06) [339] | 0.93 (0.06) [356] | 0.93 (0.06) [103] | 0.93 (0.06) [798] | 0.04 (-0.06- 0.15) | 0.40 |  |
|  | **Pooled** | [5162] | [5686] | [1564] | [12412] | 0.009 (-0.023- 0.042) | 0.57 | 52.8; 0.06 |
|  | NSHD | 37.7 (14.1) [1055] | 37.9 (14.6) [1126] | 38.0 (14.3) [327] | 37.8 (14.4) [2508] | 0.02 (-0.02- 0.06) | 0.27 |  |
|  | ELSA | 32.3 (11.6) [2263] | 31.9 (11.6) [2485] | 31.6 (11.0) [675] | 32.0 (11.5) [5423] | -0.01 (-0.03- 0.02) | 0.54 |  |
| Grip strength, kg | HCS | 35.7 (11.2) [1146] | 35.9 (11.0) [1299] | 36.0 (10.8) [338] | 35.8 (11.1) [2783] | 0.03 (-0.01- 0.06) | 0.11 |  |
|  | HAS | 32.0 (10.3) [218] | 31.8 (10.0) [227] | 32.4 (9.4) [73] | 32.0 (10.0) [518] | 0.03 (-0.04- 0.11) | 0.41 |  |
|  | LBC1921 | 26.8 (9.3) [217] | 26.0 (9.1) [234] | 27.5 (8.8) [62] | 26.5 (9.1) [513] | -0.05 (-0.14- 0.03) | 0.22 |  |
|  | **Pooled** | [4899] | [5371] | [1475] | [11745] | 0.008 (-0.014- 0.031) | 0.47 | 30.2; 0.22 |
| Timed 2.44m walk, m/s | ELSA | 0.94 (0.29) [1433] | 0.93 (0.31) [1601] | 0.92 (0.27) [448] | 0.93 (0.30) [3482] | -0.01 (-0.06- 0.03) | 0.62 |  |
| Timed 3m get up and go, m/s | HCS | 0.57 (0.10) [893] | 0.57 (0.10) [993] | 0.58 (0.10) [247] | 0.57 (0.10) [2133] | 0.02 (-0.04- 0.08) | 0.50 |  |
| Timed 3m get up and go, m/s | HAS | 0.51 (0.11) [85] | 0.50 (0.12) [87] | 0.52 (0.14) [31] | 0.51 (0.12) [203] | 0.04 (-0.15- 0.22) | 0.69 |  |
| Timed 3m get up and go, m/s | Boyd Orr | 0.69 (0.14) [148] | 0.65 (0.16) [189] | 0.65 (0.16) [53] | 0.67 (0.16) [390] | -0.09 (-0.24- 0.05) | 0.20 |  |
| Timed 3m get up and go, m/s | CaPS | 0.60 (0.13) [324] | 0.60 (0.13) [328] | 0.59 (0.14) [102] | 0.60 (0.13) [754] | -0.01 (-0.11- 0.09) | 0.85 |  |
| Timed 6m walk, m/s | LBC1921 | 1.40 (0.37) [216] | 1.41 (0.38) [233] | 1.42 (0.40) [61] | 1.40 (0.37) [510] | 0.01 (-0.12- 0.13) | 0.91 |  |
|  | **Pooled** | [3099] | [3431] | [942] | [7472] | -0.004 (-0.036- 0.027) | 0.79 | 0.0; 0.78 |
| Timed chair risesb-10 rises | NSHD | 5.21 (1.72) [1020] | 5.17 (1.66) [1084] | 5.28 (1.68) [323] | 5.20 (1.69) [2427] | 0.01 (-0.05- 0.07) | 0.79 |  |
| Timed chair risesb-5 rises | ELSA | 9.72 (3.20) [2014] | 9.54 (3.13) [2136] | 9.58 (3.13) [570] | 9.62 (3.16) [4720] | -0.01 (-0.05- 0.03) | 0.53 |  |
| Timed chair risesb-5 rises | HCS | 6.15 (1.45) [630] | 6.24 (1.50) [670] | 6.43 (1.52) [167] | 6.22 (1.48) [1467] | 0.09 (0.02- 0.16) | 0.0168 |  |
| Timed chair risesb-5 rises | HAS | 5.50 (1.57) [78] | 5.22 (1.57) [84] | 5.54 (1.35) [28] | 5.38 (1.54) [190] | -0.02 (-0.22- 0.19) | 0.88 |  |
|  | **Pooled** | [3742] | [3974] | [1088] | [8804] | 0.018 (-0.030- 0.066) | 0.46 | 49.0; 0.12 |
|  |  |  |  |  |  |  |  |  |
| Variable | Cohort | C/C | C/T | T/T | Total | OR (95% CI) a | p-value | Heterogeneity |
| n (%)c | n (%)c | n (%)c | n (%)c | I2%; p-value |
| Balance <5s-One legged | NSHD | 43 (4.1) | 47 (4.1) | 10 (3.0) | 100 (4.0) | 0.90 (0.67- 1.21) | 0.49 |  |
| Balance <5s-Tandem | ELSA | 288 (12.6) | 333 (13.3) | 88 (13.0) | 709 (13.0) | 0.96 (0.84- 1.09) | 0.50 |  |
| Balance <5s-Flamingo | HCS | 120 (18.4) | 132 (19.0) | 28 (16.3) | 280 (18.4) | 0.97 (0.79- 1.18) | 0.75 |  |
| Balance <5s-Flamingo | HAS | 26 (30.6) | 29 (33.0) | 10 (32.3) | 65 (31.9) | 1.04 (0.68- 1.59) | 0.87 |  |
| Balance <5s-Flamingo | Boyd Orr | 50 (33.8) | 77 (41.0) | 24 (45.3) | 151 (38.8) | 1.21 (0.89- 1.66) | 0.22 |  |
| Balance <5s-Flamingo | CaPS | 119 (36.3) | 122 (36.4) | 40 (40.4) | 281 (36.9) | 1.05 (0.84- 1.31) | 0.68 |  |
|  | **Pooled**d | [646/4552] | [740/4957] | [200/1368] | [1586/10877] | 0.99 (0.91- 1.08) | 0.79 | 0.0; 0.75 |

†Full genotype model representing a significantly better fit than the given per allele model.

a: Beta coefficients or odds ratios based on z-scores per minor allele adjusted for age and sex.

b: Reciprocal of time taken in sec x 100.

c: #participants unable to balance for at least 5s (%).

d: Pooled: [#participants unable to balance for at least 5s /total # participants with relevant data].

WHR in CaPS from Phase III. Balance, timed walk and chair rises in HCS from both phases. Balance, timed get up and go and chair rises in HAS from Phase II.