**Supplementary tables**

Table S1: Descriptive Statistics in Partners of Aunts and Uncles

|  |
| --- |
| Mean (SD) |
|  | Partners of maternal aunts (n=45,598)a | Partners of maternal uncles (n=45,618)a | Partners of paternal aunts (n=53,700)a | Partners of paternal uncles (n=46,831)a |
| Age at risk factors measurement | 41.0 (4.2) | 40.5 (4.0) | 41.4 (4.5) | 40.7 (4.0) |
| Height (cm) | 179.2 (6.2) | 165.9 (5.6) | 179.2 (6.2) | 165.8 (5.6) |
| BMI (kg/m2) | 25.5 (3.0) | 24.2 (3.7) | 25.6 (3.0) | 24.2 (3.7) |
| RHR (bpm) | 71.7 (12.4) | 76.4 (12.4) | 71.8 (12.5) | 76.4 (12.5) |
| SBP (mmHg) | 135.5 (13.1) | 125.4 (13.8) | 135.6 (13.3) | 125.7 (13.8) |
| TC (mmol/l) | 5.85 (1.1) | 5.40 (1.0) | 5.85 (1.1) | 5.40 (0.9) |
| TG (mmol/l) | 2.06 (1.3) | 1.30 (0.7) | 2.06 (1.3) | 1.30 (0.7) |
| N (%) |
| Education (≥ 13 years)  | 14,967 (30.9) | 14,221 (29.4) | 17,363 (31.5) | 14,918 (28.8) |
| Obesity (BMI ≥ 30kg/m2)  | 3,901 (9.5) | 4,079 (9.4) | 4,718 (9.2) | 4,086 (8.9) |
| RHR ( ≥ 80 bpm)  | 12,980 (26.7) | 17,038 (35.2) | 15,272 (27.6) | 18,603 (35.8) |
| SBP ( > 140 mmHg)  | 16,249 (33.5) | 6,603 (13.6) | 18,935 (34.2) | 7,424 (14.3) |
| TC ( ≥ 6 mmol/l)  | 19,452 (40.1) | 11,882 (24.5) | 22,645 (41.0) | 12,407 (24.0) |
| TG ( ≥ 2 mmol/l)  | 19,495 (40.2) | 6,327 (13.0) | 21,948 (39.7) | 6,539 (12.6) |
| Current smokers  | 18,480 (38.0) | 16,919 (36.3) | 20,475 (37.0) | 18,230 (36.7) |

BMI; body mass index (weight (kg)/height (m)2), RHR; resting heart rate, SBP; systolic blood pressure, TC; total cholesterol, TG; triglycerides.
Values are presented as mean (standard deviation) and percentages (%). a Number of offspring linked with partners of aunts/uncles who have information of CVD risk factors in the health surveys.

Table S2: Minimally-adjusted Associations between Offspring Birthweight and CVD risk factors of Parents and Aunts/uncles in Trios

|  |  |
| --- | --- |
|  | Mean difference or Odds Ratio (95% CI) per kg birthweight in offspring/niece/nephew |
|  | Risk factor index (0-6) | BMI (kg/m2) | RHR (bpm) | SBP (mmHg) | TC (mmol/l) | TG (mmol/l) | Current smoking | Education ≥ 13 years |
| Mothersa   | -0.14(-0.15, -0.12) | 0.80(0.76,0.82) | -0.84(-0.97,-0.72) | -0.78(-0.91,-0.64) | -0.05(-0.06,-0.04) | -0.05(-0.01,-0.00) | 0.61(0.59, 0.62) | 1.31(1.28, 1.35) |
| Fathersa  | -0.13(-0.14, -0.12) | 0.18(0.12, 0.25) | -0.58(-0.70,-0.46) | -0.35(-0.47,-0.22) | -0.07(0.08,-0.06) | -0.06(-0.07,-0.04) | 0.77(0.76, 0.79) | 1.19(1.16, 1.23) |
| Maternal auntsa  | - 0.09(-0.11,-0.07) | 0.13(0.10, 0.17) | -0.43(-0.65,-0.22) | -0.61(-0.84,-0.38) | -0.05(-0.07,-0.03) | -0.01(-0.03,-0.00) | 0.82(0.79, 0.85) | 1.18(1.15, 1.23) |
| Maternal unclesa  | -0.05(-0.08, -0.03) | 0.15(0.10, 0.20) | -0.21(-0.43,-0.02) | -0.37(-0.60,-0.14) | -0.03(-0.05,-0.02) | - 0.01(-0.03,-0.01) | 0.87(0.84, 0.90) | 1.15(1.10, 1.20) |
| Paternal auntsa  | -0.06(-0.08, -0.04) | 0.06(0.01,0.12) | -0.17(-0.38,-0.10) | -0.28(-0.50,-0.10) | -0.03(-0.05,-0.01) | - 0.01(-0.02,-0.01) | 0.88(0.86, 0.91) | 1.18(1.14,1.24) |
| Paternal unclesa  | -0.07(-0.09, -0.04) | 0.04(0.01, 0.09) | -0.27(-0.49,-0.18) | -0.22(-0.44,-0.12) | -0.04(-0.06,-0.02) | - 0.02(-0.04,-0.01) | 0.87(0.84, 0.90) | 1.11(1.06,1.16) |

BMI; body mass index (weight (kg)/height (m)2), RHR; resting heart rate, SBP; systolic blood pressure, TC; total cholesterol, TG; triglycerides, risk factor index was created from six of the risk factors. a Number of offspring linked with mothers (n=210,417), fathers (n=210,651), maternal aunts (n=77,201), maternal uncles (n=74,551) and paternal aunts (n=78,942), paternal uncles (n=76,805). Associations in parents, aunts and uncles were adjusted for mothers, fathers, aunts and uncles’ age at the time of risk factors measurements.

Table S3: Pearson’s Correlation Coefficients of Mothers and Their Siblings’ Cardiovascular Risk Factors (n=312,683)

|  |  |
| --- | --- |
| Maternal Cardiovascular Risk factors  | Maternal Siblings’ Cardiovascular Risk Factors |
| BMI | Heart Rate | Systolic blood pressure | Diastolic blood pressure | Total Cholesterol | Triglycerides | Smoking |
| BMI | 0.24 | 0.00 | 0.04 | 0.04 | 0.04 | 0.07 | 0.01 |
| RHR | 0.00 | 0.17 | 0.04 | 0.06 | 0.03 | 0.02 | 0.03 |
| SBP | 0.05 | 0.05 | 0.18 | 0.16 | 0.04 | 0.03 | 0.01 |
| DBP | 0.03 | 0.07 | 0.14 | 0.20 | 0.04 | 0.03 | 0.02 |
| TC | 0.04 | 0.03 | 0.03 | 0.05 | 0.28 | 0.06 | 0.04 |
| TG | 0.06 | 0.03 | 0.03 | 0.04 | 0.09 | 0.14 | 0.05 |
| Smoking | 0.03 | 0.04 | 0.01 | 0.02 | 0.06 | 0.03 | 0.20 |

BMI; body mass index (weight (kg)/height (m)2), RHR; resting heart rate, SBP; systolic blood pressure, DBP; diastolic blood pressure, TC; total cholesterol, TG; triglycerides.

Table S4: Pearson’s Correlation Coefficients of Fathers and Their Siblings’ Cardiovascular Risk Factors (n=329,057)

|  |  |
| --- | --- |
| Paternal Cardiovascular Risk factors  | Paternal Siblings’ Cardiovascular Risk Factors |
| BMI | Heart Rate | Systolic blood pressure  | Diastolic blood pressure | Total Cholesterol | Triglycerides | Smoking |
| BMI | 0.23 | 0.01 | 0.04 | 0.04 | 0.04 | 0.06 | 0.02 |
| RHR | 0.01 | 0.17 | 0.04 | 0.07 | 0.03 | 0.02 | 0.05 |
| SBP | 0.04 | 0.05 | 0.18 | 0.14 | 0.03 | 0.02 | 0.00 |
| DBP | 0.04 | 0.06 | 0.15 | 0.19 | 0.04 | 0.03 | 0.01 |
| TC | 0.04 | 0.03 | 0.04 | 0.05 | 0.28 | 0.07 | 0.05 |
| TG | 0.06 | 0.03 | 0.03 | 0.04 | 0.08 | 0.15 | 0.03 |
| Smoking | 0.01 | 0.05 | 0.00 | 0.02 | 0.04 | 0.02 | 0.21 |

BMI; body mass index (weight (kg)/height (m)2), RHR; resting heart rate, SBP; systolic blood pressure, DBP; diastolic blood pressure, TC; total cholesterol, TG; triglycerides.

Table S5 (Figure 2): Minimally-adjusted Associations between Offspring Birthweight (1967-2012) and CVD Risk Factors in Parents, Aunts/uncles and Partners of Aunts/uncles

|  |
| --- |
|  Mean difference or Odds Ratio (95% CI) per kg birthweight in offspring/niece/nephew |
|  | Risk factor Index (0-6)b,d | BMI (kg/m2) | RHR(bpm) | SBP(mmHg) | TC (mmol/l) | TG (mmol/l) | Smoking c | Education≥ 13 years c |
|  |  |  |
| Mothersa | -0.14(-0.15, -0.13) | 0.79 (0.76, 0.82) | -0.82 (-0.91, -0.72) | - 0.71 (-0.82, - 0.60) | -0.05 (-0.06, -0.04) | -0.00 (-0.01, -0.00) | 0.61 (0.60, 0.62) | 1.27(1.25, 1.30) |
| Fathersa | -0.11(-0.12, -0.10) | 0.14 (0.12, 0.17) | - 0.48 (-0.57, -0.38) | - 0.27 (-0.37, -0.17) | -0.06 (-0.07, -0.05) | -0.05(-0.06, -0.04) | 0.78(0.76, 0.79) | 1.20(1.18, 1.23) |
| Maternal auntsa | -0.07(-0.09, -0.06) | 0.20 (0.16, 0.25) | -0.37 (-0.51, -0.23) | -0.40 (-0.56, -0.24) | -0.03(-0.04, -0.02) | -0.01(-0.02, -0.00) | 0.83(0.81, 0.85) | 1.17(1.14, 1.21) |
| Partners of maternal auntsa | -0.03 (-0.06, -0.01) | 0.00 (-0.05, 0.06) | -0.05 (-0.31, 0.20) | 0.04 (-0.22, 0.30) | -0.00 (-0.02, 0.01) | -0.01 (-0.04, 0.00) | 0.90 (0.87, 0.94) | 1.11 (1.05, 1.18) |
| Maternal unclesa  | -0.04(-0.06, -0.03) | 0.16 (0.12, 0.20) | -0.14(-0.29, 0.00) | -0.32 (-0.49, -0.16) | -0.03(-0.04, -0.01) | -0.00(-0.02, 0.00) | 0.88(0.86, 0.91) | 1.15(1.12, 1.19) |
| Partners of maternal unclesa | -0.02 (-0.05,-0.00)  | -0.00 (-0.08, 0.07) | 0.11 (-0.14, 0.37) | -0.12 (-0.41, 0.15) | 0.00 (-0.01, 0.02) | -0.01 (-0.03, -0.00) | 0.94 (0.90, 0.98) | 1.10 (1.04, 1.17) |
| Paternal auntsa  | -0.06(-0.07,-0.04) | 0.09 (0.05, 0.13) | -0.24 (-0.37, -0.11) | -0.16 (-0.31, -0.02) | -0.03(-0.04, -0.01) | -0.02(-0.03, -0.01) | 0.87(0.85, 0.89) | 1.18(1.15, 1.21) |
| Partners of paternal auntsa | -0.02 (-0.05, -0.00) | 0.01(-0.03, 0.07) | -0.18 (-0.43, 0.05) | -0.10 (-0.35, 0.15) | -0.01 (-0.03, 0.00) | -0.00 (-0.02, 0.02) | 0.91 (0.87, 0.95) | 1.14 (1.08, 1.20) |
| Paternal unclesa  | -0.07(-0.08,-0.06) | 0.04(0.01, 0.08) | -0.29 (-0.43, -0.15) | -0.23 (-0.37, -0.08) | -0.04(-0.05, -0.03) | -0.03(-0.04, -0.01) | 0.88(0.86, 0.90) | 1.14(1.11, 1.17) |
| Partners of paternal unclesa | -0.02 (-0.05, -0.00) | 0.05 (-0.02, 0.12) | -0.01 (-0.25, 0.23) | -0.02 (-0.29, 0.23) | -0.01 (-0.03, 0.00) | -0.00 (-0.02, 0.00) | 0.90(0.86, 0.94) | 1.16 (1.10, 1.23) |

BMI; Body mass index (weight (kg)/height (m) 2), RHR; resting heart rate, SBP; systolic blood pressure, TC; total cholesterol, TG; triglycerides. a Number of offspring linked with mothers (n=331,369), fathers(n=330,803), maternal aunts(n=162,690), maternal uncles(n=149,933) and paternal aunts (n=166,221), paternal uncles(n=162,836), partners of maternal aunts (n= 45,598), maternal uncles (n=45,618), paternal aunts (n=53,700), paternal uncles (n=46,831).
b Risk factor index was created from six of the risk factors (BMI, RHR, SBP, TC, TG and current smoking). CI; confidence interval. The association for risk factor index, BMI, RHR, SBP, TC and TG was examined by linear regression models adjusted for the age of the parent, aunt or uncle.
c The association for smoking habit and higher education level was examined by logistic regression models adjusted for the age of the parent, aunt or uncle.
d *P* value for difference in associations for risk factor index between mothers and fathers (p < 0.001), aunts and uncles (*P* < 0.001), and between aunts/uncles and their partners (p < 0.001). *P* value for difference in associations between mothers and fathers for BMI, RHR, SBP and TG (*P* < 0.001), TC (0.750).

Table S6 (Figure 3): Association Between Offspring Birthweight (1967-2012) and CVD Risk Factors in Parents, Aunts/uncles and Their Partners After Adjusting for Age, Offspring Sex and Gestational Age, and Maternal Parity

|  |
| --- |
| Mean difference or Odds Ratio (95% CI) per kg birthweight in offspring/niece/nephew |
|  | Risk factor Index (0-6)b | BMI (kg/m2) | RHR(bpm) | SBP(mmHg) | TC (mmol/l) | TG (mmol/l) | Current smoking  | Education≥ 13 years  |
|  |  |  |
|  Mothersa | -0.17(-0.18, -0.16) | 0.95 (0.91, 0.99) | -0.87(-0.98, -0.75) | -0.61 (-0.74, -0.48) | -0.05(-0.06, -0.04) | -0.00(-0.01, 0.00) | 0.52(0.51, 0.53) | 1.37(1.33,1.40) |
|  Fathersa | -0.14(-0.16, -0.13) | 0.21 (0.18, 0.24) | - 0.57 (- 0.68, -0.45) | -0.39 (-0.51, -0.27) | -0.08(-0.09, -0.07) | -0.08(-0.09, -0.06) | 0.73(0.72, 0.74) | 1.24(1.21, 1.27) |
| Maternal auntsa | -0.08(-0.10, -0.06) | 0.25(0.20, 0.31) | -0.45 (-0.63, -0.28) | -0.37 (-0.56, -0.18) | -0.04(-0.05, -0.02) | -0.01(-0.02, -0.00) | 0.80 (0.78, 0.83) | 1.23(1.19, 1.28) |
| Partners of maternal auntsa | -0.05 (-0.08, -0.02) | 0.01 (-0.06, 0.08) | -0.09 (-0.40, 0.21) | 0.07 (-0.24, 0.38) | -0.01 (-0.04, 0.00) | -0.01 (-0.05, 0.01) | 0.88 (0.83, 0.92) | 1.12 (1.04, 1.20) |
| Maternal unclesa  | -0.04(-0.06,-0.02) | 0.20 (0.15, 0.25) | -0.19 (-0.37, -0.01) | -0.34 (-0.54, -0.15) | -0.03(-0.05, -0.01) | -0.00(-0.02, 0.01) | 0.86(0.83, 0.88) | 1.21(1.16, 1.26) |
| Partners of maternal unclesa | -0.03(-0.06, -0.00) | -0.00 (-0.09, 0.08) | 0.13 (-0.17, 0.44) | -0.17 (-0.50, 0.16) | -0.00 (-0.03, 0.01) | -0.02 (-0.04, -0.00) | 0.91 (0.87, 0.96) | 1.14 (1.06, 1.22) |
| Paternal auntsa  | -0.08(-0.10, -0.07) | 0.13 (0.08, 0.18) | -0.36 (-0.52 , -0.20) | -0.27 (-0.45, -0.09) | -0.04(-0.05, -0.03) | -0.02(-0.03, -0.01) | 0.85(0.83, 0.87) | 1.24(1.20, 1.28) |
| Partners of paternal auntsa | -0.04 (-0.07, -0.01) | -0.00(-0.07, 0.06) | -0.30 (-0.59, -0.01) | -0.18 (-0.47, 0.11) | -0.03 (-0.05, -0.00) | -0.01 (-0.04, 0.00) | 0.90 (0.86, 0.94) | 1.16 (1.09, 1.23) |
| Paternal unclesa  | -0.09(-0.11, -0.07) | 0.10 (0.05, 0.14) | -0.40 (-0.57, -0.23) | -0.27 (-0.45, -0.10) | -0.06(-0.07, -0.04) | -0.04(-0.06, -0.02) | 0.86(0.84, 0.88) | 1.16(1.12, 1.21) |
| Partners of paternal unclesa | -0.03 (-0.06, -0.01) | 0.06 (-0.02, 0.15) | -0.07 (-0.37, 0.21) | -0.13 (-0.46, 0.18) | -0.01 (-0.04, -0.00) | -0.00 (-0.02, 0.01) | 0.87(0.83, 0.91) | 1.18 (1.10, 1.26) |

BMI; Body mass index, RHR; resting heart rate, SBP; systolic blood pressure, TC; total cholesterol, TG; triglycerides.  a Number of offspring linked with mothers (n=331,369), fathers(n=330,803), maternal aunts(n=162,690), maternal uncles(n=149,933) and paternal aunts (n=166,221), paternal uncles(n=162,836), partners of maternal aunts (n= 45,598), maternal uncles (n=45,618), paternal aunts (n=53,700), paternal uncles (n=46,831). b Risk factor index was created from six of the risk factors (BMI, RHR, SBP, TC, TG and current smoking). CI; confidence interval. The association for risk factor index, BMI, RHR, SBP, TC and TG was examined by linear regression models adjusted for the age, offspring sex and gestational age, and maternal parity.
The association for smoking habit and higher education level was examined by logistic regression models adjusted for the age, offspring sex and gestational age, and maternal parity.

Table S7: Number of offspring whose parents, aunts and uncles had missing data on CVD risk factors

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Number participated in health surveys | BMI (kg/m2) | RHR(bpm) | SBP(mmHg) | TC (mmol/l) | TG (mmol/l) | Smoking | Total number excluded |
|  |  |  |  |
| Mothers | 345,264 | 1,023 | 8,254 | 792 | 323 | 829 | 2,674 | 13,895 |
| Fathers | 347,063 | 934 | 10,622 | 1,946 | 258 | 750 | 1,750 | 16,260 |
| Maternal aunts and uncles | 331,477 | 1,030 | 12,799 | 1,751 | 447 | 800 | 2,027 | 18,854 |
| Paternal aunts and uncles | 350,897 | 1,143 | 15,357 | 1,904 | 421 | 947 | 2,068 | 21,840 |

BMI; body mass index (weight (kg)/height (m)2), RHR; resting heart rate, SBP; systolic blood pressure, DBP; diastolic blood pressure, TC; total cholesterol, TG; triglycerides.