**Synnøve Ulseth**

# Parent-offspring association of cardiovascular disease risk factors, and the possible modifying role of physical activity

**BEV3901 Master Thesis**

**Master thesis in Human Movement Science**

**Department of Neuroscience, NTNU**

**Trondheim, spring 2016**

**Abstract**

*Background:* Cardiovascular disease (CVD) is one of the world's major health issues, and there is a worrying trend among young adults that show that the number of first time case hospitalization due to acute myocardial infarctions, is increasing. It is known that some risk factors for CVD are associated across generations. The current guidelines recommend that a positive parental history of CVD must be taken into consideration in the treatment and prevention of offspring CVD. Physical activity has been inversely associated with CVD, and studies have shown that physical activity is one of the most important modifiable factors that may contribute to a decrease in risk of developing CVD. The aim of the current study was to assess the possible parent-offspring associations in CVD risk factors, and to examine the possible modifying role of physical activity on the relationship of CVD risk factors between parents and their adult offspring.

*Methods*: The study was based on data from the two latest surveys from the Nord-Trøndelag Health Study (HUNT2 and HUNT3), where we investigated intergenerational associations of cardiovascular disease risk factor. Generalized linear regression was used to estimate adjusted mean differences in offspring level of body mass index (BMI), blood pressure, blood glucose and total cholesterol between the corresponding parental factors. Further, we used logistic regression to estimate odds ratios for unfavorable risk factor levels in the offspring related to parental risk factor levels. All associations were adjusted for parental age, BMI and levels of physical activity. Additionally, we examined the possible modifying role of offspring physical activity on the relationship of these risk factors in stratified analyses and by statistical test for interaction.

*Results:* There was a positive association between parents and offspring for all risk factors studied. Further, the results showed that offspring were more likely to have high risk factor levels if one of the parents had high levels, compared with normal level parents. Analyses stratified by offspring activity levels (inactive vs active) gave no evidence of effect modification, and this was supported by tests for statistical interaction between physical activity and each of the risk factors (all p-values >0.05).

*Conclusion:* In this populations based family study we found a positive association between parent and offspring risk factors for CVD, pointing to the importance of genetic and shared family environment for CVD risk factor levels. Stratified analyses did not indicate that offspring level off physical activity had an effect modification. This indicates that offspring level of physical activity modified the observed parent-offspring association.

**Sammendrag**

*Bakgrunn*: Kardiovaskulære sykdommer er en av verdens store helseproblemer, og det er en stadig økende trend at unge voksne blir innlagt på sykehus for akutt hjerteinfarkt. Det er kjent at noen kardiovaskulære risikofaktorer føres videre gjennom generasjoner. De nåværende retningslinjene anbefaler å ta foreldres sykdomshistorie i betraktning når man skal forebygge eller behandle kardiovaskulær sykdom hos barn. Det er vist at fysisk aktivitet har en positiv innvirkning på kardiovaskulære sykdommer, og studier viser at fysisk aktivitet er en av de viktigste modifiserbare faktorene som kan bidra til en reduksjon i risiko for å utvikle sykdom. Problemstillingen til dette studiet var å se på en mulig foreldre-barn sammenheng på risikofaktorene for kardiovaskulære sykdommer, og å studere den mulige modifiserbare effekten av fysisk aktivitet på risikofaktorforholdet mellom foreldre og deres voksne barn.

*Metode:* Dette studiet er basert på data fra de to siste HUNT-undersøkelsene (HUNT2 og HUNT3), hvor vi har sett på familiesammenhengen på risikofaktorer for kardiovaskulær sykdom. Det ble brukt lineær regresjon for å estimere justerte forskjeller i gjennomsnittlig nivå av barnas risikofaktorer som kroppsmasseindeks (KMI), blodglukose, blodtrykk og totalkolesterol i forhold til foreldrenes risikofaktornivå. Deretter brukte vi logistisk regresjon for å beregne odds ratio for å ha et ugunstig risikofaktornivå blant barna i forhold til foreldrenes verdier. Alle sammenhengene ble justert for foreldres alder, KMI og aktivitetsnivå. I tillegg ble det sett på om barnas fysiske aktivitet hadde en effekt på disse sammenhengene ved å gjøre stratifiserte analyser samt teste for statistisk interaksjon.

*Resultater:* Det var en positiv sammenheng mellom foreldre og barn for alle de studerte risikofaktorene. Resultatene viste også at andelen barn med høye risikofaktornivå var større dersom foreldrene hadde høye verdier på risikofaktorene, enn dersom foreldrene hadde lavere verdier. De stratifiserte analysene på barns fysisk aktivitets nivå (inaktiv vs aktiv) viste ingen modifiserende effekt av fysisk aktivitet. Dette ble støttet av resultatene fra tester av statistisk interaksjon (alle p-verdier var >0.05).

*Konklusjon:* I dette populasjonsbaserte familiestudiet ble det funnet en positiv foreldre-barn sammenheng på risikofaktorene for kardiovaskulære sykdommer, noe som peker på den viktige betydningen som gener og delt miljø i familien kan ha på nivået av risikofaktorer for kardiovaskulær sykdom. Stratifiserte analyser tyder ikke på at barnets fysiske aktivitetsnivå modifiserte disse foreldre-barn sammenhengene.

**Acknowledgements**

I would like to express my gratitude to my supervisor Tom Ivar Lund Nilsen, for his guidance, useful comments, remarks and engagement through the writing process of this master´s thesis. Furthermore, I would like to thank my boss and colleagues for their understanding and support during this process. I would also like to thank my family and friends for their encouragements and for believing in me.

I am grateful for all your help.

# Contents

## Introduction

Cardiovascular disease (CVD) is one of the world´s major contributors to disease burden (1, 2) and remains the number one global cause of death (17.3 million deaths per year), and the numbers are expected to grow (>23.6 million by 2030) (2). In Europe, CVD accounts for more than 4 million deaths each year, which are nearly half of all deaths (47%), 42% men and 52% women (1, 3). Overall, CVD is estimated to cost the EU economy almost 196 billion Euro a year (3). In 2012, about 66 000 people in Norway consulted a physician or stayed in hospital due to cardiovascular disease. In 2013, 5975 men and 7035 women died due to CVD in Norway (4). Developments over time show that the mortality rates from CVD have fallen in the last 40 years. There is a worrying trend of an increasing number of young people being hospitalized after acute myocardial infractions (4). Among seniors, the number of first time cases is decreasing. The Norwegian Institute of Public Health (4) also reports that the overall numbers are expected to rise due to an aging population and improved survival after acute illness.

There are several possible mechanisms contributing to CVD, and more than 75% of CVD can be attributed to risk factors such as tobacco use, alcohol use, high blood pressure, high cholesterol, obesity, physical inactivity, or a combination of these (4-6). Recent studies have focused on the family linkage of these risk factors, and the results showed that some risk factors could be associated through generations (5-8). A study from the US (9) showed that having a parent with a CVD history doubles the offspring´s risk for the disease. The current guidelines (7), recommend that a parental history of CVD must be taken into consideration in the treatment and prevention of offspring´s CVD. However, reporting CVD history among relatives may lead to incorrect estimates of risks. It is important to use objective measures of body mass index (BMI), blood pressure, blood lipids and diabetes to strengthen the validity to the observed associations (6). The topic of genetic determinants of cardiovascular risk and parent-offspring association is still under discussion and further studies are necessary to determine this relationship. However, the aforementioned factors can all be affected by both genetic and environmental factors.

A shared family environment may have effects into adulthood and could also contribute to the observed parent-offspring associations in CVD risk factors (6). Lifestyle factors, such as physical activity and dietary habits, have been associated with CVD (6, 10). Studies show that leisure time physical activity is one of the most important modifiable factors that may contribute to a decrease in risk of developing CVD (5, 8, 11). It is also known that physical

activity is associated with a reduction in risk factors of CVD and risk of CVD death (7, 11). Studies have shown an inverse dose-response association between volume of physical activity, all-cause mortality and CVD mortality (11-13). According to the World Health Report (5), the impact of many risk factors can be reversed quickly, and even modest changes in risk factor levels could give large benefits for the individual and for the society. By identifying environmental factors that can decrease the risk factors for CVD, these factors can be used as prevention of early age onset of CVD and reduce the number of deaths caused by CVD.

The majority of research so far has focused on offspring factors at a young age. As far as we know, few studies have examined whether these factors persists into the offspring´s adult life. It is important to study the associations between parents and their adult offspring to minimize the potential risk factors.

The aim of the present study was to assess possible parent-offspring associations in CVD risk factors. Additionally, this study examined the possible modifying role of physical activity on the relationship of CVD risk factors between parents and offspring. Identifying these relations can be important for reduction of CVD risk factors and for prevention of CVD.

## Materials and methods

### Study population

The Nord-Trøndelag Health Study (HUNT) is a large population-based longitudinal study conducted in the county of Nord- Trøndelag in Norway, where the adult population of 20 years and older was invited to participate. All participants were inhabitants of Nord-Trøndelag county, a limited geographical area. The population is relatively homogeneous and relatively stable (14, 15). The study consists of three cross-sectional surveys conducted in 1984-86 (HUNT1), 1995-97 (HUNT2) and 2006-08 (HUNT3). Since the first survey did not obtain information on blood lipid values, the present study includes data from HUNT2 and 3. In HUNT2, 94 194 individuals were invited of which 71 % (n= 66 140) accepted; in HUNT3, 93 860 were invited of which 54 % (n=50 839) accepted (14, 16).

All participants completed a questionnaire on health and lifestyle factors, including information such as current CVD, use of blood pressure medications and leisure-time physical activity. At a clinical examination, standardized measures of anthropometry and blood pressure were obtained by trained personal, and non-fasting serum blood-sample was drawn. A more detailed description of procedures and methods can be found at http://www.ntnu.edu/hunt.

### Record linkage

Norwegian citizens have been assigned a unique personal identification number, which HUNT use in their record. This was used to establish a family linkage to the Family Registry at Statistics Norway between parents and their biological offspring who had participated in either HUNT2 or HUNT3. A total of 66 000 parent-offspring linkages within the HUNT Study (i.e. offspring and mother and/or father) have participated. The parent-offspring linkages were constructed separately for fathers and mothers.

### Study variables

### Anthropometric factors

Anthropometric factors were measured with participants wearing light clothes without shoes. Weight was measured to the nearest half-kilo and the height to the nearest cm. BMI was calculated as body weight (kg) divided by the square of the individual´s height (m). BMI was

subdivided into four categories (17): underweight (<18.5 kg/m$^2$), normal weight (18.5-24.9 kg/m$^2$), overweight (25-29.9 kg/m$^2$) and obese (>30 kg/m$^2$).

**Blood pressure**

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured three times at 1 min intervals using Dinamap 845XT (Citricon, Tampa, Florida, USA). The mean of the second and third measures was used in the analyses to avoid an artificially high reading at the first measure. SBP was then categorized into normal blood pressure (<120 mm Hg), prehypertension (120-139 mm Hg) and hypertension (>140 mm Hg) (18). Correspondingly, DBP was categorized into normal blood pressure (<80 mm Hg), prehypertension (80-89 mm Hg) and hypertension (>90 mm Hg) (18).

**Total cholesterol**

Total cholesterol was classified according to quartiles based on the specific distribution among offsprings, mothers and fathers, respectively. This resulted in the following offspring categories: 1 (<4.6 mmol/l), 2 (4.6-5.2 mmol/l), 3 (5.3-6.0 mmol/l) and 4 (>6.1 mmol/l). The corresponding categories among mothers and fathers were; 1 (<5.5 and <5.3 mmol/l), 2 (5.5-6.2 and 5.3-5.9 mmol/l), 3 (6.3-7.2 and 6.0-6.7 mmol/l) and 4 (>7.3 and >6.8 mmol/l).

**Blood glucose**

Blood glucose was classified according to quartiles based on the specific distribution among offsprings, mothers and fathers, respectively. Blood glucose in offsprings were categorized into: 1 (<4.7 mmol/l), 2 (4.7-5.1 mmol/l), 3 (5.2-5.6 mmol/l) and 4 (>5.7 mmol/l); whereas blood glucose levels for mother and father was categorized into; 1 (<4.9 and <4.9 mmol/l), 2 (4.9-5.2 and 4.9-5.3 mmol/l), 3 (5.3-5.8 and 5.4-6.0 mmol/l), 4 (>5.9 and >6.1 mmol/l).

**Leisure time physical activity**

In HUNT2 the parents were asked about their leisure time physical activity levels. They were asked to estimate the average number of hours per week (0, <1, 1-2, >3) with low and hard levels of physical activity.

In HUNT3, the offspring were asked about their average frequency of leisure time physical activity in a week, with five response alternatives (0, <1, 1, 2-3, ≥ 4 times). Subjects who reported to exercise once a week or more were also asked about the average intensity (light,

moderate, vigorous) and the duration (<15, 15-30, 30-60, >60 min) of the activity. The answers to these questions were recorded into an index variable and classified into 4 categories; “no activity”, “low”, “medium” and “high”, which was then collapsed into inactive (no and low activity) and active (medium and high activity) for the purpose of the stratified analyses.

**Offspring´s factors**

Offspring´s risk factors were classified into dichotomous variables (unfavorable level; yes or no), where the highest risk factor levels were set as “yes” and the lowest categories were collapsed into “no”. For the risk factors described above, the highest risk factor level for BMI was defined as >30 kg/$m^2$, hypertension as >140 and >90 mm HG, high cholesterol as >6.1 mmol/l and blood glucose >5,7 mmol/l. These dichotomous variables were then used as outcome variables in logistic regression.

**Statistical methods**

Characteristics of the study population were obtained from descriptive statistics and presented as means with standard deviations (SD). The association between parental and offspring´s risk factors of CVD was studied in two different models. First, we used generalized linear regression to estimate the adjusted mean differences in offspring´s level of BMI, blood pressure (systolic and diastolic), blood glucose and total cholesterol between different levels of the corresponding parental factor. Next, we used logistic regression to calculate the odds ratio for an unfavorable risk factor level in offspring associated with parental risk factor levels. All associations were adjusted for parental age, parental BMI and parental level of physical activity.

To assess the possible modifying effect of offspring´s physical activity on the parent-offspring associations in CVD risk factors, the logistic regression analyses were stratified on offspring´s level of physical activity (inactive and active). Statistical interaction test was assessed to test for differences between active and inactive. We tested for statistical interaction by including a product term of physical activity and the relevant risk factor in the regression model. The precision of the estimated associations was assessed by a 95% confidence interval (CI). All statistical analyses were conducted using SPSS software (version 20 for Mac; SPSS Institute, Chicago, Illinois, USA).

**Results**

A total of 17155 fathers, 23327 mothers and 25696 offsprings were included in this study. The average age of fathers was 60.8 years, and for mother 60.0 years. For offspring the average age was 44.8 years. Descriptive results of the 65767 parent-offspring pairs are shown in table 1.

**Table 1:** Descriptive statistics* of father, mother and offspring

| | Father | Mother | Offspring |
|---|---|---|---|
| Number of participants | 17155 | 23327 | 25696 |
| Age (years) (SD) | 60.84 (13.30) | 60.04 (13.80) | 44.80 (12.51) |
| BMI (kg/m$^2$) (SD) | 26.83 (3.41) | 27.21 (4.53) | 26.93 (4.43) |
| SBP (mm Hg) (SD) | 144.88 (21.05) | 144.46 (24.70) | 126.75 (16.16) |
| DBP (mm Hg) (SD) | 85.00 (11.77) | 82.19 (12.64) | 72.68 (11.01) |
| BG (mg/DL) (SD) | 5.81 (1.78) | 5.63 (1.66) | 5.41 (1.40) |
| TC (mmol/l) (SD) | 6.09 (1.13) | 6.42 (1.31) | 5.37 (1.08) |

*Data presented as mean with SD, unless otherwise specified.

BMI, body mass index, TC, total cholesterol, SBP, systolic blood pressure, DBP, diastolic blood pressure, BG, blood glucose

Table 2 (father-offspring) and table 3 (mother-offspring) show crude and adjusted coefficients from generalized linear regression for the continuously measured risk factors. All measures showed a statically significant association between parents and offspring. Offspring with an obese father or mother (BMI >30 kg/m$^2$) had a BMI that was 3.18 (95% CI 1.73-4.63) and 3.31 (95% CI 2.45-4.18) kg/m$^2$ higher than the reference group.

The corresponding analyses for total cholesterol show that offsprings of parents with high cholesterol (>6.8 mmol/l for father and >7.3 mmol/l for mother) have a total cholesterol level 0.16 (95% CI 0.09-0.23) and 0.63 (95% CI 0.59-0.68) mmol/l higher the reference group. Similar analyses comparing variables such as blood glucose, SBP and DBP show that high levels in both parents are associated with higher levels in offspring, compared with the reference group for blood glucose, SBP and DBP. For blood glucose, the analyses show that offspring of parents with high levels of blood glucose (>6,1 and >5.9 mg/DL) had a blood glucose level that was 0.16 (95% CI 0.09-0.23) and 0.20 (95% CI 0.14-0.26) mg/DL higher than the reference group. For SBP and DBP, corresponding analyses gave a 4.37 (95% CI 3.38-5.35) and 2.77 (95% CI 2.31-3.24) mmHg difference for father-offspring associations, and a 4.07 (95% CI 3.93-5.49) and 3.32 (95% CI 2.89-3.70) mmHg difference for mother-offspring associations, respectively.

**Table 2:** Generalized linear model father and offspring

| Variable | N | Mean (offspring value) | Mean diff | Adj mean diff.* | 95% CI |
|---|---|---|---|---|---|
| BMI (kg/m$^2$) | | | | ** | |
| <18.5 | 62 | 25.21 | 0.0 | 0.0 | 0.0(reference) |
| 18.5-24.9 | 5175 | 25.75 | 0.54 | 0.56 | -0.90-2.01 |
| 24.9-29.9 | 9195 | 26.76 | 1.55 | 1.52 | 0.08-2.97 |
| >30 | 2818 | 28.44 | 3.23 | 3.18 | 1.73-4.63 |
| SBP (mm Hg) | | | | | |
| <120 | 1335 | 121.12 | 0.0 | 0.0 | 0.0(reference) |
| 120-139 | 5348 | 122.75 | 1.63 | 1.61 | 0.61-2.62 |
| >140 | 8511 | 127.54 | 6.42 | 4.37 | 3.38-5.35 |
| DBP (mm Hg) | | | | | |
| <80 | 5522 | 70.13 | 0.0 | 0.0 | 0.0(reference) |
| 80-89 | 4720 | 71.83 | 1.70 | 1.48 | 1.02-1.94 |
| >90 | 4956 | 73.93 | 3.80 | 2.77 | 2.31-3.24 |
| BG (mg/DL) | | | | | |
| <4.9 | 3612 | 5.19 | 0.0 | 0.0 | 0.0(reference) |
| 4.9-5.3 | 3672 | 5.25 | 0.06 | 0.03 | -0.36-0.97 |
| 5.4-6.0 | 4258 | 5.38 | 0.19 | 0.90 | 0.03-0.16 |
| >6.1 | 4198 | 5.49 | 0.30 | 0.16 | 0.09-0.23 |
| TC (mmol/l) | | | | | |
| <5.3 | 3804 | 4.98 | 0.0 | 0.0 | 0.0(reference) |
| 5.3-5.9 | 3470 | 5.15 | 0.17 | 0.15 | 0.09-0.20 |
| 6.0-6.7 | 4628 | 5.34 | 0.36 | 0.34 | 0.29-0.39 |
| >6.8 | 4456 | 5.60 | 0.62 | 0.57 | 0.52-0.62 |

* adjusted for parental age, BMI and physical activity

**adjusted for parental age and physical activity

BMI, body mass index, TC, total cholesterol, SBP, systolic blood pressure, DBP, diastolic blood pressure, BG, blood glucose

**Table 3:** Generalized linear model mother and offspring

| Variable | N | Mean (offspring value) | Mean diff | Adj mean diff.* | 95% CI |
|---|---|---|---|---|---|
| BMI (kg/m$^2$) | | | | ** | |
| <18.5 | 145 | 25.03 | 0.0 | 0.0 | Reference |
| 18.5-24.9 | 7755 | 25.64 | 0.61 | 0.74 | -0.14-1.59 |
| 24.9-29.9 | 9374 | 26.95 | 1.92 | 1.91 | 1.04-2.77 |
| >30 | 5513 | 28.42 | 3.39 | 3.31 | 2.45-4.18 |
| SBP (mm Hg) | | | | | |
| <120 | 3134 | 120.12 | 0.0 | 0.0 | Reference |
| 120-139 | 6362 | 123.84 | 3.72 | 2.02 | 1.28-2.76 |
| >140 | 10688 | 129.78 | 9.66 | 4.071 | 3.93-5.49 |
| DBP (mm Hg) | | | | | |
| <80 | 9764 | 70.38 | 0.0 | 0.0 | Reference |
| 80-89 | 5252 | 73.52 | 3.14 | 2.15 | 1.74-2.56 |
| >90 | 5175 | 75.50 | 5.12 | 3.32 | 2.89-3.7 |
| BG (mg/DL) | | | | | |
| <4.9 | 5622 | 5.24 | 0.0 | 0.0 | Reference |
| 4.9-5.2 | 5430 | 5.32 | 0.08 | 0.03 | -0.03-0.09 |
| 5.3-5.8 | 4955 | 5.40 | 0.16 | 0.04 | -0.02-1.01 |
| >5.9 | 6013 | 5.63 | 0.39 | 0.20 | 0.14-0.26 |
| TC (mmol/l) | | | | | |
| <5.5 | 5857 | 4.89 | 0.0 | 0.0 | Reference |
| 5.5-6.29 | 4898 | 5.25 | 0.36 | 0.24 | 0.19-0.29 |
| 6.3-7.2 | 6193 | 5.50 | 0.61 | 0.42 | 0.38-0.46 |
| >7.3 | 5706 | 5.79 | 0.90 | 0.63 | 0.59-0.68 |

* adjusted for parental age, BMI and physical activity

**adjusted for parental age and physical activity

BMI, body mass index, TC, total cholesterol, SBP, systolic blood pressure, DBP, diastolic blood pressure, BG, blood glucose

Table 4 (father-offspring) and table 5 (mother-offspring) show odds ratio for an unfavorable offspring risk factor level using dichotomous variables. Offspring were 2.63 (95% CI 2.31-2.90) times more likely to be obese if the father was obese, and three times (2.99, 95% CI 2.69-3.33) more if the mother was obese, compared with the reference group. For total cholesterol, the results showed that offsprings were 2.09 (95% CI 1.83-2.38) (father) and 2.30 (95% CI 2.04-2.59) (mother) more likely to have high levels of cholesterol when their parents have high cholesterol levels. The results for blood glucose show that offsprings were 1.43 (95% CI 1.25-1.64) and 1.26 (95% CI 1.13-1.14) times more likely to have high levels of blood glucose if their parents had high blood glucose levels. For SBP and DBP, the analysis shows that offsprings were 1.84 (95% CI 1.46-2.31) (father) and 1.90 (95% CI 1.59-2.27) (mother) more likely to have high levels of SBP, and 1.91 (95% CI 1.13-1.14) (father) and 1.79 (95% CI 1.51-2.12) (mother) times more likely to have high levels of DBP when their parents report high levels of SBP and DBP.

**Table** 4: Odds ratio offspring and father

| | Unfavorable level | | OR | OR adjusted* | 95% CI |
|---|---|---|---|---|---|
| | no | yes | | | |
| BMI (kg/m$^2$) | | | | ** | |
| <18.5 | 58 | 4 | 0.41 | 0.48 | 0.15-1.6 |
| 18.5-24.9 | 4436 | 739 | 1.00 | 1.00 | Reference |
| 24.9-29.9 | 7399 | 1796 | 1.46 | 1.45 | 1.31-1.63 |
| >30 | 1929 | 889 | 2.77 | 2.63 | 2.31-2.99 |
| SBP (mm Hg) | | | | | |
| <120 | 1204 | 131 | 1.17 | 1.19 | 0.94-1.52 |
| 120-139 | 4745 | 603 | 1.00 | 1.00 | Reference |
| >140 | 6780 | 1731 | 2.35 | 1.84 | 1.46-2.31 |
| DBP (mm Hg) | | | | | |
| <80 | 5294 | 228 | 1.81 | 1.40 | 1.12-1.76 |
| 80-89 | 4455 | 265 | 1.00 | 1.00 | Reference |
| >90 | 4557 | 399 | 2.22 | 1.91 | 1.54-2.35 |
| BG (mg/DL) | | | | | |
| <4.9 | 2670 | 631 | 1.23 | 1.17 | 1.01-1.34 |
| 4.9-5.3 | 2585 | 754 | 1.00 | 1.00 | Reference |
| 5.4-6.0 | 2874 | 1031 | 1.52 | 1.34 | 1.17-1.54 |
| >6.1 | 2694 | 1131 | 1.78 | 1.43 | 1.25-1.64 |
| TC (mmol/l) | | | | | |
| <5.3 | 2390 | 838 | 1.24 | 1.24 | 1.08-1.42 |
| 5.3-5.9 | 1970 | 858 | 1.00 | 1.00 | Reference |
| 6.0-6.7 | 2303 | 1255 | 1.55 | 1.53 | 1.35-1.74 |
| >6.8 | 1781 | 1307 | 2.09 | 2.09 | 1.83-2.38 |

* adjusted for parental age, BMI and physical activity

**adjusted for parental age and physical activity

BMI, body mass index, TC, total cholesterol, SBP, systolic blood pressure, DBP, diastolic blood pressure, BG, blood glucose

**Table 5:** Odds ratio offspring and mother

| | Unfavorable level | | OR | OR adjusted* | 95% CI |
|---|---|---|---|---|---|
| | no | yes | | | |
| BMI (kg/m$^2$) | | | | ** | |
| <18.5 | 133 | 12 | 0.61 | 0.77 | 0.40-1.49 |
| 18.5-24.9 | 6757 | 997 | 1.00 | 1.00 | Reference |
| 24.9-29.9 | 7481 | 1891 | 1.71 | 1.67 | 1.51-1.85 |
| >30 | 3760 | 5513 | 3.16 | 2.99 | 2.69-3.33 |
| SBP (mm Hg) | | | | | |
| <120 | 2895 | 239 | 1.86 | 1.41 | 1.18-1.69 |
| 120-139 | 5514 | 848 | 1.00 | 1.00 | Reference |
| >140 | 8030 | 2658 | 4.01 | 1.90 | 1.59-2.27 |
| DBP (mm Hg) | | | | | |
| <80 | 9317 | 447 | 1.81 | 1.58 | 1.33-1.87 |
| 80-89 | 4833 | 419 | 1.00 | 1.00 | Reference |
| >90 | 4677 | 498 | 2.22 | 1.79 | 1.51-2.12 |
| BG (mg/DL) | | | | | |
| <4.9 | 4027 | 1114 | 1.13 | 0.99 | 0.89-1.11 |
| 4.9-5.2 | 3744 | 1168 | 1.00 | 1.00 | Reference |
| 5.3-5.8 | 3305 | 1215 | 1.33 | 1.06 | 0.95-1.19 |
| >5.9 | 3719 | 1764 | 1.71 | 1.26 | 1.13-1.41 |
| TC (mmol/l) | | | | | |
| <5.5 | 3970 | 1155 | 1.74 | 1.48 | 1.32-1.66 |
| 5.5-6.29 | 2594 | 1315 | 1.00 | 1.00 | Reference |
| 6.3-7.2 | 2651 | 1822 | 2.36 | 1.82 | 1.63-2.03 |
| >7.3 | 1820 | 1711 | 3.23 | 2.30 | 2.04-2.59 |

* adjusted for parental age, BMI and physical activity
**adjusted for parental age and physical activity
BMI, body mass index, TC, total cholesterol, SBP, systolic blood pressure, DBP, diastolic blood pressure, BG, blood glucose

Table 6 (father- offspring) and 7 (mother-offspring) show analyses stratified by offsprings level of physical activity (inactive vs. active). Overall, there was no evidence that offspring physical activity modified the parent-offspring associations of the various risk factors. Stratified analyses for offsprings BMI (>30 kg/m$^2$) show an odds ratio of 2.48 (95% CI 2.13-2.89) for inactive and 3.07 (95% CI 2.37-3.98) for active in the father-offspring association, and 3.04 (95% CI 2.67-3.45) and 2.79 (95% CI 2.27-3.42) for the mother-offspring association. For total cholesterol the results show an odds ratio at 2.08 (95% CI 1.79-2.41) and 2.09 (95% CI 1.59-2.76) for father-offspring, and 2.39 (95% CI 2.08-2.74) and 1.97 (95% CI 1.52-2.55) for mother-offspring.

The corresponding results for blood glucose, show an adjusted odds ratio of 1.41 (95% CI 1.21-1.66) for inactive and 1.52 (95% CI 1.15-2.02) for active offsprings in the father-offspring association. For the mother-offspring association, the odds ratio for inactive offsprings was 1.24 (95% CI 1.09-1.40) and 1.34 (95% CI 1.07-1.68) for active offsprings. For SBP, the results show 1.90 (95% CI 1.46-2.52) and 1.46 (95% CI .94-2.25) for father-offspring, and 1.88 (95% CI 1.53-2.33) and1.82 (95% CI 1.30-2.56) for mother-offspring association. The adjusted odds ratio for DBP was 1.73 (95% CI 1.35-2.21) and 2.21 (95% CI 1.49-3.27) for father-offspring, and 1.77 (95% CI 1.45-2.16) and 1.84 (95% CI 1.33-2.54) for mother-offspring. There was no evidence of statistical interaction between physical activity and each of the risk factors (all p-values > 0.05).

**Table 6:** Odds ratio father- offspring, stratified by offsprings level of PA

| | Offspring | | | | | | |
|---|---|---|---|---|---|---|---|
| | Inactive | | | Active | | | Interaction test |
| | OR | OR adjusted * | 95% CI | OR | OR adjusted * | 95% CI | p-value* |
| BMI (kg/m$^2$) | | ** | | | ** | | |
| <18.5 | 0.29 | 0.46 | 0.11-1.94 | 0.69 | 0.52 | 0.06-4.21 | 0.59 |
| 18.5-24.9 | 1.00 | 1.00 | Reference | 1.00 | 1.00 | Reference | |
| 24.9-29.9 | 1.41 | 1.39 | 1.22-1.58 | 1.60 | 1.66 | 1.34-2.06 | |
| >30 | 2.66 | 2.48 | 2.13-2.89 | 3.07 | 3.07 | 2.37-3.98 | |
| SBP (mm Hg) | | | | | | | |
| <120 | 1.17 | 1.27 | 0.95-1.69 | 1.07 | 0.93 | 0.58-1.47 | 0.39 |
| 120-139 | 1.00 | 1.00 | Reference | 1.00 | 1.00 | Reference | |
| >140 | 2.38 | 1.90 | 1.46-2.52 | 2.01 | 1.46 | 0.94-2.25 | |
| DBP (mm Hg) | | | | | | | |
| <80 | 1.38 | 1.44 | 1.11-1.87 | 1.29 | 0.17 | 0.75-1.81 | 0.18 |
| 80-89 | 1.00 | 1.00 | Reference | 1.00 | 1.00 | Reference | |
| >90 | 1.89 | 1.73 | 1.45-2.16 | 2.27 | 2.21 | 1.49-3.27 | |
| BG (mg/DL) | | | | | | | |
| <4.9 | 1.26 | 1.16 | 0.98-1.36 | 1.21 | 1.27 | 0.96-1.70 | 0.85 |
| 4.9-5.2 | 1.00 | 1.00 | Reference | 1.00 | 1.00 | Reference | |
| 5.3-5.8 | 1.52 | 1.31 | 1.12-1.53 | 1.50 | 1.47 | 1.12-1.95 | |
| >5.9 | 1.80 | 1.41 | 1.21-1.66 | 1.73 | 1.52 | 1.15-2.02 | |
| TC (mmol/l) | | | | | | | |
| <5.5 | 1.33 | 1.29 | 1.10-1.50 | 0.97 | 1.04 | 1.09-1.76 | 0.25 |
| 5.5-6.29 | 1.00 | 1.00 | Reference | 1.00 | 1.00 | Reference | |
| 6.3-7.2 | 1.57 | 1.48 | 1.28-1.72 | 1.47 | 1.68 | 1.24-2.21 | |
| >7.3 | 2.09 | 2.08 | 1.79-2.41 | 2.08 | 2.09 | 1.59-2.76 | |

* adjusted for parental age, BMI and physical activity

**adjusted for parental age and physical activity

BMI, body mass index, TC, total cholesterol, SBP, systolic blood pressure, DBP, diastolic blood pressure, BG, blood glucose

**Table 7:** Odds ratio mother- offspring, stratified by offsprings level of PA

| | Offspring | | | | | | |
|---|---|---|---|---|---|---|---|
| | Inactive | | | Active | | | Interaction test |
| | OR | OR adjusted * | 95% CI | OR | OR adjusted * | 95% CI | p-value* |
| BMI (kg/m$^2$) | | ** | | | ** | | |
| <18.5 | 0.57 | 0.59 | 0.24-1.48 | 0.69 | 1.13 | 0.42-3.06 | 0.67 |
| 18.5-24.9 | 1.00 | 1.00 | Reference | 1.00 | 1.00 | Reference | |
| 24.9-29.9 | 1.79 | 1.71 | 1.52-1.92 | 1.50 | 1.54 | 1.27-1.86 | |
| >30 | 3.27 | 3.04 | 2.67-3.45 | 2.79 | 2.79 | 2.27-3.42 | |
| SBP (mm Hg) | | | | | | | |
| <120 | 1.97 | 1.47 | 1.18-1.82 | 1.53 | 1.25 | 0.89-1.75 | 0.33 |
| 120-139 | 1.00 | 1.00 | Reference | 1.00 | 1.00 | Reference | |
| >140 | 4.35 | 1.88 | 1.53-2.33 | 3.05 | 1.82 | 1.30 -2.56 | |
| DBP (mm Hg) | | | | | | | |
| <80 | 1.84 | 1.58 | 1.29-1.93 | 1.69 | 1.65 | 1.18-2.29 | 1.0 |
| 80-89 | 1.00 | 1.00 | Reference | 1.00 | 1.00 | Reference | |
| >90 | 2.21 | 1.77 | 1.45-2.16 | 2.19 | 1.84 | 1.33-2.54 | |
| BG (mg/DL) | | | | | | | |
| <4.9 | 1.17 | 1.99 | 0.87-1.13 | 1.04 | 0.99 | 0.79-1.26 | 0.84 |
| 4.9-5.2 | 1.00 | 1.00 | Reference | 1.00 | 1.00 | Reference | |
| 5.3-5.8 | 1.36 | 1.05 | 0.92-1.20 | 1.23 | 1.11 | 0.87-1.41 | |
| >5.9 | 1.77 | 1.24 | 1.09-1.40 | 1.51 | 1.34 | 1.07-1.68 | |
| TC (mmol/l) | | | | | | | |
| <5.5 | 1.80 | 1.52 | 1.33-1.74 | 1.55 | 1.38 | 1.09-1.76 | 0.52 |
| 5.5-6.29 | 1.00 | 1.00 | Reference | 1.00 | 1.00 | Reference | |
| 6.3-7.2 | 2.38 | 1.81 | 1.60-2.06 | 2.21 | 1.79 | 1.42-2.26 | |
| >7.3 | 3.35 | 2.39 | 2.08-2.74 | 2.76 | 1.97 | 1.52-2.55 | |

* adjusted for parental age, BMI and physical activity

**adjusted for parental age and physical activity

BMI, body mass index, TC, total cholesterol, SBP, systolic blood pressure, DBP, diastolic blood pressure, BG, blood glucose

## Discussion

### Main results

In this population-based family linkage study, we found positive associations between parental and offspring risk factors for CVD. The results suggest that parental BMI, SBP, DBP blood glucose and total cholesterol levels were associated with offsprings levels of the same risk factor. The odds ratio adjusted for parental age, BMI and level of physical activity, show that high levels of BMI, SBP, DBP, blood glucose and total cholesterol in parents were associated with increased prevalence of an unfavorable risk factor level in the offspring, compared to if parents had the lowest risk factor levels. Further, there was no statistical evidence of effect modification for offspring level of physical activity, suggesting that the familial contribution to offspring´s risk factor levels is not influenced by physical activity.

### Comparison with existing literature

Previous studies have reported a positive association between parental and offspring CVD risk factors (6, 8-10, 19). Li et al. (19) examined the influences of parental childhood BMI on offspring childhood BMI. They found that parental BMI across all ages, from childhood to adulthood, had a strong positive association with offspring BMI. Fasting et.al (8) found that parental lifestyle factors (weight, smoking and physical activity) were associated with offspring adiposity, and that offsprings with overweight parents had a higher odds ratio for overweight, compared with normal weight parents. Their results also showed that parental weight gain during offspring childhood were an important risk factor for offsprings to become overweight in later life. Further, Lloyd-jones et al. (9) have found a positive parent-offspring association in SBP, total cholesterol, BMI and other CVD risk factors (diabetes, smoking, age). Their results showed that parental CVD increased offspring´s risk across all strata of total cholesterol and blood pressure. Our results support previous studies, and showed that there was a positive association between parental and offspring´s risk factor levels.

It has been suggested that the parent-offspring association of CVD risk factors occurs in early pregnancy phase, and that the maternal BMI and body weight can increase the fetus´ risk of adiposity in later life (20). A population-based cohort study from Australia (21) have found an association between high maternal pregnancy BMI and high adolescent BMI, waist circumference, waist-to-hip ratio, blood pressure, and total cholesterol. They did also find that high prepregnancy BMI and early pregnancy weight gain were associated with increased risks

of cardio metabolic disease in offspring. Further, Fleten et al. (22) have examined the association between parental BMI and offspring BMI at age 3, and the influence of the intrauterine environment on early life BMI. Their findings showed that there was no strong difference in paternal and maternal association on offspring BMI. Smith et al. (23) also compared the relative strength of association of maternal-offspring and paternal-offspring BMI, and their finding showed that the strength was the same for both maternal and paternal, which supports the findings of Fleten et al. (22). This can indicate that the intrauterine environment had no strong effect, and that genetic factors from both parents and shared familial environment could be a cause of exposure of risk factors of obesity.

Our study differs from existing literature in that the offsprings were adults (>20 years), whilst most other studies have examined the association between parents and their offspring at young age, when still living at home and sharing environment with their parents (8, 19, 22). It takes time to develop CVD and CVD risk factors, and by looking at offsprings at young age it could make the parent-offspring associations less clear.

Although several studies have examined the association between parental and offspring´s risk factors, we are not aware previous studies that have included the offsprings level of physical activity. It is well established that physical activity plays an important role in preventing CVD and decreasing several of the risk factors for CVD. Findings show that even low levels of physical activity can reduce the risk of CVD (24, 25). The intensity and volume of the activity is debated, but studies conclude that physical activity has a dose-response relation to CVD risk factors, and that just a single bout of exercise could be enough (24-26). Despite this, our study did not show differential parent-offspring associations when stratifying on offspring activity level. This may indicate that the familial associations (genetic and environmental) are stronger than the contribution of offspring activity level on this association.

**Possible mechanisms**

It is not possible to distinguish between the genetic and environmental contribution to the offspring´s CVD risk factor levels in this study, since we had no information on genetic markers. Risk factors such as high cholesterol, high levels of SBP and DBP, high BMI and blood glucose are all partly explained by genetic and partly due to environmental and behavioral factors (10). The term epigenetic refers to the study field of genetic variations that are caused by environmental factors that switches genes on and off (6, 27). This affects how genes are transcripted, without making any changes in the DNA-sequence. CVD can therefore

be influenced by changes in epigenetic structures, which provide a mechanic link between genes and environment (27). Turan et.al (27) concluded that because of epigenetic information, the individual variety could not be explained by genotypes alone, but rather as a combination of genes and environment.

By looking at twin and adoption studies it is possible to investigate the effect of sharing genes in shared and different environments. Most twin studies have found evidence for genetic factors of obesity, and estimated effects in adolescents tend to be higher than those from adults (28). Grilo et al. (29) investigated the effect of sharing genes in shared environment versus shared genes in different environments, and found a greater correlation in BMI between adopted children and their biological parents compared with their adoptive parents. They stated that even though they did not share the same environment, they still had shared genes that influenced the risk factors. Hunt et al. (30) found that shared environmental factors did not appear to contribute to the variation in BMI. Similar studies on blood pressure indicate less familial contribution and stronger environmental effects (31)

Maes et al. (28) emphasized that when examining the topic of heritability in family, twin and adoption studies, they can not exclude environmental pathways. They also wrote that a genetic predisposition to select or request fatty foods in the diet is dependent on the availability of such foods. Predisposition to obesity might be due to individual differences in metabolism, but also affected by environmental pathways (28). Other possible mechanisms and environmental factors involve childhood and early life events. There is evidence showing that shared environment and family characteristics such as smoking, alcohol consumption, physical activity and diet are associated between parents and their offspring (6, 28). Fasting et al. (8) found that parental weight gain during offspring´s childhood is an important factor for offspring´s risk for becoming overweight and develop CVD.

Cooper et al. (32) examined the associations between parental BMI and risk factors for CVD among their offspring in mid-life, and whether associations of offspring´s BMI and CVD risk factors were modified by parental BMI. Their findings showed that obese offspring were more likely to have had an overweight or obese parent during their childhood and higher CVD risk factor levels, compared with normal weight offsprings. After adjusting for offspring lifestyle factors the associations were no longer found. It is possible that the lifestyle association between parents and offspring are strongest during childhood, and lesser when offspring are adult and more independent.

**Strengths and limitations**

The strength of this study includes the large study size, population-based design and a large number of standardized and objectively measured CVD risk factors (14). The representative sample is from a population with a wide age range, and the information was collected using questionnaires and clinical examinations. The data are linked to the national family register, which makes it possible to link and study biological parent-offspring history.

It is difficult to disentangle the relative contributions of genes and environment, and there was no information on whether the offspring shared an environment with one or both of their biological parents, either in adulthood or in childhood. Since the offspring were adults at the time the data was collected, it can be assumed that the offspring did not share household environment with their parents at that time.

The strength of the HUNT-surveys is that it has a good participation rate (16). However, there is a possibility that families in which both parents and offspring have participated could be a selected and more health conscious sample than the general population. This study found statistical significant associations between parents and their adult offspring for all CVD risk factors studied. Offspring were more likely to have a high level of risk factors if their parents had similarly high levels, compared with the reference group.

It must be taken into consideration that the information on physical activity were obtained from self-reported questionnaires, which can lead to recall bias and subjective interpretation of questions and response options. Physical activity was reported just one time, and if the questionnaire was answered in the middle of the winter they might report a lower level of physical activity, compared with what they might report during the summer. Offspring´s physical activity level was categorized into inactive (no and low activity) and active (medium and high activity). Splitting offspring´s physical activity levels into two broad categories might make it difficult to detect possible effects of being vigorously active, or alternatively, of being highly inactive.

## Conclusion

In conclusion, we found a positive association between parents and offspring in CVD risk factor levels, and points to the importance of genetic and shared family environment for CVD risk factor levels. Stratified analyses did not indicate that offspring´s level of physical activity had an effect modification. This indicates that offspring´s activity level does not modify the familial contribution to CVD risk factor levels. These findings suggest that future studies should focus on family history in the role of evaluating and develop strategies for prevention risk factors for cardiovascular diseases.

**References**


1. Hardman AE, Stensel DJ. Physical activity and health: The evidence explained: Routledge; 2009.
2. Smith SC, Collins A, Ferrari R, Holmes DR, Logstrup S, McGhie DV, et al. Our Time: A Call to Save Preventable Death From Cardiovascular Disease (Heart Disease and Stroke). Circulation. 2012;126(23):2769-75.
3. Leal J, Luengo-Fernández R, Gray A, Petersen S, Rayner M. Economic burden of cardiovascular diseases in the enlarged European Union. Eur Heart J. 2006;27(13):1610-9.
4. Selmer R, Hovda GE, Graff-Iversen S, Sakshaug S. Folkehelserapporten 2014 http://www.fhi.no/artikler/?id=1104112014 [updated 09.04.2015; cited 2015 09.05].
5. Organization WH. The World Health Report 2002. Reducing Risks, Promoting Healthy Life. 2002.
6. Vik KL. Generational studies of cardiovascular disease risk factors and cardiovascular mortality: the HUNT Study. 2014.
7. Antonopoulos S. Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. Circulation. 2002;106(3143):3421.
8. Fasting MH, Nilsen TIL, Holmen TL, Vik T. Changes in parental weight and smoking habits and offspring adiposity: Data from the HUNT‐study. Int J Pediatr Obes. 2011;6(2Part2):e399-e407.
9. Lloyd-Jones DM, Nam B-H, D'Agostino Sr RB, Levy D, Murabito JM, Wang TJ, et al. Parental cardiovascular disease as a risk factor for cardiovascular disease in middle-aged adults: a prospective study of parents and offspring. JAMA. 2004;291(18):2204-11.
10. Vik KL, Romundstad P, Nilsen TIL. Tracking of cardiovascular risk factors across generations: family linkage within the population-based HUNT study, Norway. J Epidemiol Community Health. 2013:jech-2012-201634.
11. Warburton DE, Nicol CW, Bredin SS. Health benefits of physical activity: the evidence. Can Med Assoc J. 2006;174(6):801-9.
12. Lee I-M, Skerrett PJ. Physical activity and all-cause mortality: what is the dose-response relation? Med Sci Sports Exerc. 2001;33(6; SUPP):S459-S71.
13. Wen CP, Wai JPM, Tsai MK, Yang YC, Cheng TYD, Lee M-C, et al. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. The Lancet. 2011;378(9798):1244-53.
14. Krokstad S, Langhammer A, Hveem K, Holmen T, Midthjell K, Stene T, et al. Cohort profile: the HUNT study, Norway. Int J Epidemiol. 2013;42(4):968-77.
15. HUNT. HUNT Databank https://www.ntnu.edu/hunt/databank: HUNT Research Center; [cited 2015 09.11].
16. HUNT. Participation numbers https://www.ntnu.edu/hunt/participation: HUNT Research Center; [cited 2015 09.11].
17. Organization WH. BMI Classification http://apps.who.int/bmi/index.jsp?introPage=intro_3.html&: World Health Organisation; 2006 [updated 31.03.2016; cited 2015 21.10].
18. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, et al. Recommendations for blood pressure measurement in humans and experimental animals part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Hypertension. 2005;45(1):142-61.

19. Li L, Law C, Conte RL, Power C. Intergenerational influences on childhood body mass index: the effect of parental body mass index trajectories. The American journal of clinical nutrition. 2009;89(2):551-7.
20. Whitaker RC, Dietz WH. Role of the prenatal environment in the development of obesity. The Journal of Pediatrics. 1998;132(5):768-76.
21. Gaillard R, Welten M, Oddy WH, Beilin LJ, Mori TA, Jaddoe V, et al. Associations of maternal prepregnancy body mass index and gestational weight gain with cardio-metabolic risk factors in adolescent offspring: a prospective cohort study. BJOG. 2016;123(2):207-16.
22. Fleten C, Nystad W, Stigum H, Skjærven R, Lawlor DA, Smith GD, et al. Parent-offspring body mass index associations in the Norwegian Mother and Child Cohort Study: a family-based approach to studying the role of the intrauterine environment in childhood adiposity. Am J Epidemiol. 2012;176(2):83-92.
23. Smith GD, Steer C, Leary S, Ness A. Is there an intrauterine influence on obesity? Evidence from parent–child associations in the Avon Longitudinal Study of Parents and Children (ALSPAC). Arch Dis Child. 2007;92(10):876-80.
24. Stensvold D, Nauman J, Nilsen TI, Wisloff U, Slordahl SA, Vatten L. Even low level of physical activity is associated with reduced mortality among people with metabolic syndrome, a population based study (the HUNT 2 study, Norway). BMC Med. 2011;9:109.
25. Yu S, Yarnell JWG, Sweetnam PM, Murray L. What level of physical activity protects against premature cardiovascular death? The Caerphilly study. Heart. 2003;89(5):502-6.
26. Wisløff U, Nilsen TIL, Drøyvold WB, Mørkved S, Slørdahl SA, Vatten LJ. A single weekly bout of exercise may reduce cardiovascular mortality: how little pain for cardiac gain? 'The HUNT study, Norway'. Eur J Cardiovasc Prev Rehabil. 2006;13(5):798-804.
27. Turan N, Katari S, Coutifaris C, Sapienza C. Explaining inter-individual variability in phenotype. Epigenetics. 2010;5(1):1-4.
28. Maes HHM, Neale MC, Eaves LJ. Genetic and environmental factors in relative body weight and human adiposity. Behav Genet. 1997;27(4):325-51.
29. Grilo CM, Pogue-Geile MF. The nature of environmental influences on weight and obesity: a behavior genetic analysis. Psychol Bull. 1991;110(3):520.
30. Hunt SC, HASSTEDT SJ, Kuida H, Stults BM, Hopkins PN, Williams RR. Genetic heritability and common environmental components of resting and stressed blood pressures, lipids, and body mass index in Utah pedigrees and twins. Am J Epidemiol. 1989;129(3):625-38.
31. Xu X, Ding X, Zhang X, Su S, Treiber FA, Vlietinck R, et al. Genetic and environmental influences on blood pressure variability: a study in twins. J Hypertens. 2013;31(4):690-7.
32. Cooper R, Pereira SMP, Power C, Hyppönen E. Parental obesity and risk factors for cardiovascular disease among their offspring in mid-life: findings from the 1958 British Birth Cohort Study. Int J Obes. 2013;37(12):1590-6.