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Moderately elevated body mass index is associated with metabolic variables and cardiovascular risk factors in Swedish children

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Running title: Metabolic risk factors in overweight children

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ABSTRACT

Aim: To evaluate associations between anthropometrics and metabolic variables as well as cardiovascular risk factors among children. **Methods:** Subjects were recruited from a cohort of 274 healthy children in Umeå, Sweden. Anthropometric measures, blood pressure and venous blood samples were collected at age 10 y, and simultaneously from parents. **Results:** Altogether 144 children (53%), 142 mothers and 123 fathers participated. The prevalence of overweight and obesity among the children was 18% and 2%, respectively. Overweight children (above age- and sex-specific cut offs corresponding adult BMI≥25 kg/m^2), compared to normal weight children, had significantly higher BMI already during infancy, and higher S-insulin and HOMA index at 10 y. The children's BMI was positively associated with waist (boys´ r=0.67, girls´ r=0.81), hip (r=0.68), waist/hip ratio (girls´ r=0.37), waist/height ratio (boys´ r=0.59, girls´ r=0.80), sagittal abdominal diameter (r=0.75), S-insulin (r=0.45), HOMA index (r=0.49), systolic blood pressure (r=0.24), mothers´ BMI (girls´ r=0.42) and mothers´ waist (girls´ r=0.42). **Conclusion** Children at 10 y of age with moderately elevated BMI had higher levels of some metabolic variables and cardiovascular risk factors than did normal weight children, and there was a correlation between BMI and some metabolic variables as well as cardiovascular risk factors.

Keywords: Overweight, obesity, metabolic syndrome, children, BMI.

INTRODUCTION

Although recent studies (1, 2) indicate that the increase in overweight and obesity among 10-year-olds may be levelling off or even declining in Sweden, the prevalence still remains much higher than it was about 25 years ago. In the town of Umeå in northern Sweden, a two-fold increase in the prevalence of overweight and obesity among children aged 6-13 y occurred between 1986 and 2001 (3), with 23% of the children being overweight or obese in 2001, and a statistically significant higher prevalence among girls (26%) compared to boys (20%).

In children as well as in adults, obesity is associated with a number of health problems, including increased insulin resistance, type 2 diabetes, abnormal serum lipids and the metabolic syndrome (4). The prevalence of the metabolic syndrome in childhood differs greatly between studies (5, 6). This variation in prevalence depends not only on the population being studied, but also on different definitions of the syndrome and different biochemical and anthropometric cut-offs being used (6). Today there is limited data on differences in metabolic variables and cardiovascular risk factors between groups of overweight pre-pubertal children, i.e. those having moderately elevated BMI compared to normal weight children. The magnitude of obesity and cardiovascular risk factors during childhood appear to predict the development of the metabolic syndrome later in life (7, 8). Therefore, early recognition of these risk factors is important from clinical and public health perspectives. Furthermore, increased knowledge on variables associated with childhood overweight and obesity is a prerequisite for the development of preventive strategies and intervention programs.

The aim of the present study was to evaluate associations between BMI and variables associated with the metabolic syndrome as well as cardiovascular risk factors among 10-y-old children who had been followed prospectively from infancy. The secondary aims were to examine differences in metabolic variables and cardiovascular risk factors between children with higher and lower BMI, to investigate retrospective BMI data and to evaluate associations with parental anthropometrics, metabolic variables and cardiovascular risk factors.

METHODS

Subjects

Subjects participating in the present study were recruited from a cohort of 274 healthy children born at term in Umeå, Sweden. These children had participated in a randomized trial on phytate-reduced infant cereals from age 6 m to 18 m (9). The source population for the initial study was a convenience sample of 300 children recruited from six well-baby clinics in Umeå. There was no significant difference in growth from 6 to 18 m between the groups. Of the original cohort, four families had moved abroad and were therefore not contacted. Sampling during the survey was seasonally balanced between May 2006 and March 2007. One month after the initial invitation, a reminder and new invitation were sent to the families who had not responded. Thereafter, families who had not responded were contacted by telephone and families rejecting the invitation were asked to complete a short questionnaire. Altogether, 144 (53%) of the invited families participated in the present follow-up study. Written informed consent was obtained from the parents and verbal consent was also ascertained from each child. The study was approved by the Research Ethics Committee, Faculty of Medicine, Umeå University, Sweden.

Of the 126 families rejecting the invitation, 106 (83%) completed the dropout questionnaire. Analyses showed that the children not participating in the study were significantly older compared to participating children, mean (SD) age 11.2 (3.1) vs. 10.0 (0.6) years ($P<0.001$), respectively. However, there were no statistically significant differences between the groups regarding sex, nationality of birth or educational level and occupation of mothers or fathers. The most common reason for not participating in the study was lack of time (44%), or that the child did not want to have a blood sample taken (25%).

Anthropometry and blood values

The families willing to participate had an appointment arranged at the Pediatric Clinical Research Unit, Department of Pediatrics, Umeå University Hospital. Both biological parents were invited to the clinic even when they did not live together. If both parents and the child were unable to visit at the same time, a second appointment was arranged. If the family had moved to another region of Sweden, an appointment was arranged close to their new address.

Anthropometric measures (body weight, height, waist and hip circumferences, sagittal abdominal diameter) and blood pressure of the child and both parents were measured by one of the two research nurses. Measurements of height, weight and waist circumference were taken according to the procedure described in WHO's STEPS Field Manual (10), and sagittal abdominal diameter as described by Zamboni et al. (11). Body weight in light clothing and height standing in bare feet were measured according to standard procedures to the nearest 0.10 kg and 0.1 cm, respectively. BMI was calculated by weight (kg) divided by height squared (m^2) and used to determine whether the child should be classified as being or not being overweight, according to the International Obesity Task Force (IOTF) (12). The BMI cut-offs are age- and sex-specific, and were applied accordingly for each individual. The cut-offs are linked to the widely accepted definition at ≥18 y of age for obesity (BMI ≥30 kg/m^2), overweight (BMI ≥25-<30 kg/m^2), normal weight (BMI ≥18.5-<25 kg/m^2) and underweight grade 1 (BMI <18.5 kg/m^2) (12, 13). The children classified as overweight (n=26) or obese (n=3) in the present study were grouped as overweight children (above age- and sex-specific BMI cut offs corresponding to adult BMI≥25 kg/m^2), and children classified as normal weight (n=114) or underweight (n=1) were grouped as normal weight children (below age- and sex-specific BMI cut offs corresponding to adult BMI<25 kg/m^2). The weight and height at age 6-18 mo of the participating children had been measured in the intervention study by the same investigators. Retrospective weight and height data for the age interval 2-10 y were obtained from routine measurements according to protocols within the school health service and the child health service. At 0-1.5, 4 and 10-11 y of age, data on BMI were obtained for 83-100% of the participating children, and at ages 3, 5.5, 6, 7, 7.5, 9 and 9.5 y (normal weight children) data on BMI were obtained for 24-82%. However, at ages 2, 2.5, 3.5, 4.5, 5, 6.5, 8, 8.5 and 9.5 y (overweight children), data were available for <24%, and are therefore not presented. Puberty stage at 10 y of age was assessed for each child according to Tanner (14), and information was obtained on general health and occurrence of diseases in the family.

Venous blood samples were taken after overnight fasting from the child and both parents. Serum (S) and plasma (P) were stored frozen until analyzed for S-lipids [total cholesterol (S-TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), triglycerides (TG), apolipoproteins A1 (apoA1) and B (apoB)], P-glucose, S-insulin, S-HbA1c, S-alanine amino transferase (S-ALT) and S-aspartate amino transferase (S-AST). All blood analyses were undertaken at the Department of Clinical Chemistry, Umeå University Hospital. Homeostatic Model Assessment (HOMA)-index was calculated according to the equation (S-insulin in mU/L × P-glucose in mmol/L)/22.5 (15). The metabolic syndrome was defined according to the International Diabetes Federation (IDF) (16). According to the IDF, metabolic syndrome should not be diagnosed in children <10 y, but children with a waist circumference ≥90 percentile is a group at risk. For children aged 10 y or older, the metabolic syndrome can be diagnosed in those with a waist circumference ≥90 percentile and the presence of two or more other clinical features (i.e. elevated TG, low HDL-C, high blood pressure, or increased P-glucose). For parents, the IDF's definition of metabolic syndrome was used (17). A waist circumference above the sex- and ethnicity-specific cut-off values (European men ≥94 cm and women ≥80 cm) in combination with two abnormal variables of either raised TG, reduced HDL-C, raised blood pressure, raised fasting P-glucose or previously diagnosed type 2 diabetes is defined as metabolic syndrome.

Statistical analyses

Data are presented as means (SD) for normally distributed variables and median (25^{th}, 75^{th} percentile) for non-normally distributed variable (HDL-C, LDL/HDL ratio, TG, apoB/apoA1 ratio, P-glucose, S-insulin, S-AST, S-ALT). Differences between measurements and groups were analyzed using independent sample t-test for normally distributed variables (Tables 1-2) and the Mann-Whitney U test for non-normally distributed variables (Table 2). Chi-square and Pearson correlation analyses were used. Eighteen blood values not normally distributed were logarithmically transformed before Pearson correlation analyses, presented in Table 3 (the eight blood values mentioned above as well as parental S-TC, TG, S-insulin and diastolic and systolic blood pressure). Interactions between sex and anthropometry, blood pressure and blood values of children and their parents presented in tables 1-3, were tested by linear regression for associations. Scatter matrixes of correlations between children's BMI and anthropometry, blood pressure and blood values of children and their parents, are enclosed in appendix 1. Anthropometrical data were converted to z-scores, comparing with the Centers for Disease Control and Prevention (CDC) 2000 growth data (18). Missing data at follow up was blood pressure for one overweight child, hip circumference for one normal weight child and blood analyses of one normal weight child. Statistically significant results were those with values of $P<0.05$ (Tables 1 and 3, Figures 1-2) and $P<0.01$ (Table 2). Statistical analyses were performed using SPSS for Windows (version 15.0, SPSS, Inc., Chicago, IL, USA).

RESULTS

The analyses are based on data from 144 children aged 10.0±0.62 y (56% girls) and their parents (Table 1). Data were collected for 51% of the families during the first six months of 2006 and 2007 and for 49% of the families during the last six months of 2006. None of the children had entered puberty at the time of data collection and 98% were reported as healthy. Of the three subjects reported as not healthy one had gastritis, one had hypothyreosis and one did not give any further information.

The prevalence of children classified as overweight or obese was 18% and 2%, respectively. In comparison to the CDC 2000 data (18), the mean (SD) z-score for BMI of the overweight children (n=29) was 1.45 (0.27) kg/m^2.

There were no differences in age, sex or height between the groups of overweight children compared with the normal weight children. However, the overweight children had a significantly higher body weight, waist and hip circumference, waist/hip ratio, waist/height ratio and sagittal abdominal diameter than did the normal weight children (Table 1). There were no differences between boys and girls regarding anthropometric measurements and prevalence of overweight and obesity, but there was a significant sex interaction regarding waist circumference, waist/hip ratio and waist/height ratio.

Mothers of overweight children had higher BMI and waist circumference compared with mothers of normal weight children (Table 1). At group level there were no significant differences in risk variables of metabolic syndrome between mothers or fathers of overweight children and normal weight children. In total, three mothers (10%) of overweight children were classified as having metabolic syndrome according to the definition used (17) compared with nine (8%) of the mothers of normal weight children. Of the fathers of overweight children, seven (24%) were classified as having metabolic syndrome, compared with 22 (19%) of the fathers of normal weight children.

Overweight children at age 10 y had significantly higher BMI retrospectively at all ages compared to normal weight children (Figure 1). The confidence intervals show that there is a significant difference between mean BMI in the groups.

Overweight children at 10 y of age had significantly higher S-insulin and HOMA index compared with normal weight children ($P<0.01$) (Table 2). Compared to girls, boys had significantly higher apoA1 ($P<0.01$). On the other hand, girls had higher TG and apoB/apoA1 ratio ($P<0.01$), and there was significant interaction between boys and girls regarding LDL/HDL ratio and P-glucose.

There was a positive correlation between the children's BMI at 10 y of age and several anthropometric parameters and blood values (Table 3, Appendix 1). A positive correlation with no sex interaction was seen for hip circumference (r=0.68), sagittal abdominal diameter (r=0.75), TG (r=0.17), apoB (r=0.17), apoB/apoA1 ratio (r=0.19), S-insulin (r=0.45), HOMA index (r=0.49), ALT (r=0.21), diastolic blood pressure (r=0.17) and systolic blood pressure (r=0.24). A positive correlation with significant sex interaction was seen for waist circumference (boys´ r=0.67, girls´ r=0.81), waist/hip ratio (girls´ r=0.37), waist/height ratio (boys´ r=0.59, girls´ r=0.80), LDL/HDL ratio (boys´ r=0.30) and P-glucose (girls´ r=0.24).

Among girls, but not boys, there was a significant positive correlation between the girls' BMI and their mothers' BMI (r=0.42) and waist circumference (r=0.42) (Table 3). For all children there was a significant correlation between the children's BMI at 10 y of age and fathers' BMI (r=0.20), diastolic blood pressure (r=0.18) and systolic blood pressure (r=0.18) (Table 3).

Of the overweight children, 15 (52%) had a sagittal abdominal diameter >90 percentile within the sample (16.5 cm). Furthermore, the BMI of the participating children explained 56% (R^2=0.56) of the variation in sagittal abdominal diameter (Figure 2).

None of the children in the present study were classified as having metabolic syndrome according to the definitions of the International Diabetes Federation (16), and only one child was classified as having abdominal obesity (>90 percentile within the sample) in combination with one other clinical risk variable. In total, 14 (48%) of the overweight children had a waist circumference >90 percentile within the sample and two overweight children and three normal weight children had HDL-C levels below 1.03 mmol/L.

DISCUSSION

The children grouped as being overweight (26 overweight and 3 obese children) in the present study had an average BMI of 21.7 (1.56) kg/m^2 which may be regarded as moderately high in comparison with the sex and age BMI cut-offs, 24.0 kg/m^2 for boys and 24.1 kg/m^2 for girls, for obesity at age 10 y (12). Based on this, the results of the present study show that even moderately elevated BMI already at 10 y of age, negatively affects the metabolic profile. Significant correlations were found at a young age; in these healthy, pre-pubertal children, there were strong correlations between BMI and S-insulin and HOMA index, respectively. In agreement with reports on other populations of 9-12-y-olds, we found significant positive correlations between children's BMI and TG, S-insulin, HOMA index, diastolic and systolic blood pressure and P-glucose (only for girls), but no significant correlations to, S-TC, HDL- and LDL-C (19, 20). The present study also confirms that overweight children have significantly higher waist circumference, S-insulin and HOMA index compared with normal weight children (20).

Several previous studies have investigated obesity and metabolic variables and cardiovascular risk factors. Studies on obese 12-14-y-old children demonstrated that abdominal obesity is associated with unfavourable lipid profiles (21) and strong associations between S-insulin levels and metabolic-endocrine alterations early in life (22). However, only few studies have investigated the effects of overweight on the metabolic variables and cardiovascular risk factors of school-aged children, and detailed data on serum lipids, P-glucose and S-insulin levels among 10-y-old pre-pubertal children are largely missing (19). For children aged 10-16 y, the metabolic syndrome is diagnosed by abdominal obesity and the presence of two or more other clinical risk variables (i.e. elevated TG, low HDL-C, high blood pressure, or increased P-glucose) (17). In the present study none of the children were classified as having metabolic syndrome, and only one had abdominal obesity (>90 percentile within the sample which may be regarded as a relatively lean population) in combination with another clinical risk variable, but almost half of the overweight children had isolated abdominal obesity. The International Diabetes Federation suggests that metabolic syndrome should not be diagnosed in children younger than 10 y, but that a strong message suggesting weight reduction should be delivered to those with abdominal obesity.

In concordance with previous studies, we observed that there are differences in metabolic variables between overweight children compared to normal weight

children. However, in the present study we have extended previous findings by showing that in a homogenous age group of healthy, pre-pubertal children, those with moderately elevated BMI already at age 10 y had higher levels of some metabolic variables and cardiovascular risk factors compared to children with lower BMI. A limitation of the present study is that the children's diet and physical activity were not investigated thoroughly enough to be taken into consideration.

The BMI of the participating children in the present study explained 56% of the variation in sagittal abdominal diameter (Figure 2), and the correlation between the children's BMI and sagittal abdominal diameter was as strong as the correlation between BMI and waist circumference. Sagittal abdominal diameter has been recognized as a useful alternative to visceral fat measurement in epidemiological studies on adults (23), but has not been widely used in children. In a study on obese 6-14-y-old boys, sagittal abdominal diameter was the best anthropometric diagnostic criterion for detecting early metabolic complication (24). However, the result on sagittal abdominal diameter presented in the present study is not strong enough to draw such a conclusion. The waist/height ratio also showed a strong correlation with BMI in the present study. This is in concordance with a previous study in which the waist/height ratio was used to detect overweight children with a higher risk of metabolic and cardiovascular complications (25).

Overweight children at 10 y of age in the present study had a significantly higher BMI at all ages compared with normal weight children (Figure 1). This is in agreement with the observation that, on the one hand, birth weight and ponderal index (kg/m^3) correlate with BMI and, on the other, high birth weight and normal or high birth length are risk factors for overweight and severe overweight among boys at age 18 y (26). Other studies have also concluded that infants who are at the highest end of the distribution for weight or BMI are at increased risk of subsequent obesity (27). There may be potential limitations of the use of clinical and school-obtained measurements of height and weight in the present study. The measured data at age 6-18 mo and 10 y of age were collected by the same investigators in the present study, but the measurements between 2-10 y of age were conducted by several nurses within the primary health care system (those working at well-baby clinics as well as school nurses), which may have increased the variation of those measurements. Furthermore, since sufficient data for both groups at e.g. ages 2, 2.5, 3.5, 4.5, 5 and 6.5 y were not available, it was not possible to evaluate the age of onset of overweight. However, our data indicate that high BMI during early childhood, perhaps even infancy, may be a strong predictor of later overweight and obesity in a Swedish population as well.

There was a significant positive correlation between the child's BMI and that of the mother and father in the present study. This concurs with a previous study of 10-year-olds (28). Heredity, especially maternal overweight, as well as the degree of overweight of the child is significant predictors for becoming overweight as adult (29). The higher the degree of overweight, and the older the overweight child, the greater the risk is of maintaining overweight into adulthood. The risk of remaining overweight in adulthood was 79% for overweight 10-14-year-olds who had at least one overweight parent (30).

Only about half of the families participating when the child was 6 m were willing to participate when the child was 10 y, giving us a smaller sample size than was aimed for in the follow-up. However, there was no significant difference between the children participating and those not participating regarding sex, nationality of birth or educational level and occupation of mothers or fathers, indicating that selection bias does not appear to be a major concern and that a 53% participation rate can be regarded as acceptable. The proportion of children classified as overweight and obese in the present study is comparable to those shown in a recent survey on 10-y-olds in Umeå conducted by the Swedish National Institute of Public Health (20% and 3%, respectively) (2). Both studies show that overweight and obesity among 10-y-olds is at a high level from a historical perspective (3, 28). In the present study BMI, according to the IOTF (12), was used to classify the children as being or not being overweight. If we instead had used the CDC 2000 growth reference (18), as classification system, only two children instead of 29 would have been classified as overweight or obese (>2 SD). If the CDC reference had been used we would have underestimated the risk of overweight and possibly misclassified those with elevated metabolic risk markers and somewhat elevated BMI into the group of children with lower BMI.

Conclusion

Even moderately elevated BMI already at 10 y of age, negatively affects the metabolic profile among overweight children compared with normal weight children, and there was a positive correlation between BMI and some metabolic variables and cardiovascular risk factors. Among these healthy children, followed prospectively from early infancy, overweight at 10 y of age was significantly associated with higher BMI already during the first year of life. Further research regarding how to prevent overweight early in life is needed.

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LIST OF ABBREVIATIONS

ALT	Alanine amino transferase
apoA1	Apolipoproteins A1
apoB	Apolipoproteins B
AST	Aspartate amino transferase
CDC	Centers for Disease Control and Prevention
HDL-C	High density lipoprotein cholesterol
HOMA	Homeostatic Model Assessment
IDF	International Diabetes Federation
IOTF	International Obesity Task Force
LDL-C	Low density lipoprotein cholesterol
P	Plasma
S	Serum
TG	Triglycerides
TC	Total cholesterol

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Table 1 Characteristics of the participating children and their parents.

	All	Normal weight[1]	Overweight[2]	P[3]	Boys	Girls	P[3]
Children[4]	**(n=144)**	**(n=115)**	**(n=29)**		**(n=63)**	**(n=81)**	
Age at follow-up (y)	10.0 (0.62)	10.0 (0.63)	10.0 (0.59)	0.723			
Sex (% girls)	56.3	56.5	55.2	0.896			
Weight (kg)	35.8 (6.50)	33.6 (4.73)	44.5 (5.11)	<0.0001			
Height (cm)	142 (6.31)	142 (6.33)	143 (6.24)	0.321			
BMI (kg/m^2)	17.7 (2.51)	16.7 (1.47)	21.7 (1.56)	<0.0001			
Waist circumference (cm)	61.9 (7.83)	59.5 (5.55)	71.7 (7.94)	<0.0001	61.9 (8.66)	62.0 (7.16)	0.961
Hip circumference (cm)	73.1 (7.46)	71.2 (5.96)	80.7 (7.95)	<0.0001			
Waist/hip ratio	0.85 (0.08)	0.84 (0.07)	0.89 (0.07)	0.001	0.86 (0.10)	0.84 (0.52)	0.149
Waist/height ratio	0.44 (0.05)	0.42 (0.04)	0.50 (0.06)	<0.0001	0.44 (0.06)	0.44 (0.05)	0.942
Sagittal abdominal diameter (cm)	14.5 (1.60)	14.0 (1.21)	16.3 (1.63)	<0.0001			
1-2 parents with BMI>30 (%)	20.1	17.4	31.0	0.138			
Mothers	**(n=142)**	**(n=113)**	**(n=29)**				
Age at follow-up (y)	39.4 (3.82)	39.4 (4.06)	39.6 (3.74)	0.794			
BMI (kg/m^2)	24.1 (3.81)	23.8 (3.72)	25.6 (3.88)	0.018	23.9 (4.16)	24.3 (3.54)	0.505
Waist circumference (cm)	80.9 (9.44)	80.1 (9.20)	84.3 (9.90)	0.032	79.6 (10.4)	81.9 (8.50)	0.150
Overweight and obesity (%)	30.3	27.4	41.4	0.145			
Smoking (%)	5.0	6.3	0	0.167			
>12 y of education (%)	67.4	67.0	69.0	0.838			
Fathers	**(n=123)**	**(n=96)**	**(n=27)**				
Age at follow-up (y)	41.7 (5.21)	41.7 (5.32)	41.6 (4.93)	0.941			
BMI (kg/m^2)	26.6 (3.65)	26.4 (3.46)	27.5 (4.22)	0.163			
Waist circumference (cm)	94.7 (10.1)	94.2 (9.50)	96.4 (12.0)	0.319			
Overweight and obesity (%)	59.3	56.3	70.4	0.187			
Smoking (%)	5.7	5.4	6.9	0.953			
>12 y of education (%)	54.1	56.6	44.8	0.352			

[1] Includes children with BMI below age- and-sex-specific cut-offs corresponding to adult BMI< 25. One child had BMI corresponding to adult BMI<18.5 (12, 13).
[2] Includes children with BMI above age- and-sex-specific cut-offs corresponding to adult BMI≥ 25. Three children had BMI corresponding to adult BMI>30 (12).
[3] Independent samples t-test or chi square P-values for difference between groups of children and their parents.
[4] Data are presented as mean (SD) or proportion (%). Interaction of sex was tested by linnear regression and for associations significantly different between boys and girls (P<0.05), sex-specific data was provided instead of data of all children..

Table 2 Fasting blood values of participating children.

Blood values[1]	**All (n=144)**	**Normal weight**[2] **(n=115)**	**Overweight**[3] **(n=29)**	**P**[4]	**Boys (n=63)**	**Girls (n=81)**	**P**[4]
Total cholesterol (mmol/L)	4.23 (0.73)	4.20 (0.72)	4.35 (0.76)	0.306			
LDL cholesterol (mmol/L)	2.34 (0.67)	2.30 (0.64)	2.49 (0.78)	0.163			
HDL cholesterol (mmol/L)	1.57 (1.38, 1.73)	1.60 (1.39, 1.73)	1.51 (1.28, 1.72)	0.245			
LDL/HDL ratio	1.45 (1.17, 1.82)	1.42 (1.18, 1.79)	1.52 (1.12, 2.26)	0.186	1.35 (1.05, 1.80)	1.52 (1.24, 1.85)	0.120
S-triglycerides (mmol/L)	0.66 (0.53, 0.82)	0.65 (0.53, 0.78)	0.69 (0.57, 0.94)	0.182			
S-apolipoprotein B (g/L)	709 (165)	697 (156)	752 (191)	0.109			
S-apolipoprotein A_1 (g/L)	1390 (193)	1408 (195)	1339 (173)	0.083			
Apolipoprotein B/A_1 ratio	0.51 (0.43, 0.59)	0.51 (0.43, 0.57)	0.52 (0.43, 0.67)	0.148			
P-glucose (mmol/L)	4.50 (4.30, 4.70)	4.40 (4.20, 4.70)	4.50 (4.40, 4.70)	0.408	4.50 (4.28, 4.73)	4.40 (4.30, 4.60)	0.196
S-insulin (mU/L)	5.40 (3.60, 7.30)	5.00 (3.40, 6.70)	7.50 (5.45, 10.50)	<0.0001			
HOMA index	1.19 (0.66)	1.07 (0.57)	1.65 (0.78)	<0.0001			
HbA1c (%)	4.01 (0.32)	4.00 (0.34)	4.07 (0.25)	0.346			
S-AST (µkat/L)	0.53 (0.48, 0.59)	0.53 (0.48, 0.60)	0.52 (0.48, 0.58)	0.715			
S-ALT (µkat/L)	0.26 (0.19, 0.36)	0.24 (0.18, 0.34)	0.34 (0.22, 0.44)	0.028			
Diastolic blood pressure (mm Hg)	64.4 (5.55)	64.2 (5.69)	65.1 (4.96)	0.476			
Systolic blood pressure (mm Hg)	106 (7.98)	105 (8.23)	108 (6.35)	0.064			

[1] Data are presented as means (SD) for normally distributed variables and as median (25^{th}, 75^{th} percentile) for non-normally distributed variables. Interaction of sex was tested by linear regression and for associations significantly different between boys and girls (P<0.05), sex-specific data was provided instead of data of all children.

[2] Includes children with BMI below age- and-sex-specific cut-offs corresponding to adult BMI< 25. One child had BMI corresponding to adult BMI<18.5 (12, 13).

[3] Includes children with BMI above age- and-sex-specific cut-offs corresponding to adult BMI≥ 25. Three children had BMI corresponding to adult BMI>30 (12).

[4] P-value for difference between groups of children from independent samples t-test for normally distributed variables and from Mann-Whitney U test for non- normally distributed variables.

Table 3 Correlations between children's BMI and anthropometry, blood pressure and blood values of children and their parents.

Pearson correlation coefficient to BMI of children[1]	**All (n=144)**	**P-value**	**Boys (n=63)**	**P-value**	**Girls (=81)**	**P-value**
Children (n=144)						
Waist circumference	0.74	<0.0001	0.67	<0.0001	0.81	<0.0001
Hip circumference	0.68	<0.0001				
Waist/hip ratio	0.24	0.004	0.18	0.161	0.37	0.001
Waist/height ratio	0.69	<0.0001	0.59	<0.0001	0.80	<0.0001
Sagittal abdominal diameter	0.75	<0.0001				
Total cholesterol	0.10	0.252				
LDL cholesterol	0.13	0.116				
Ln HDL cholesterol	-0.13	0.138				
Ln LDL/HDL ratio	0.17	0.045	0.30	0.019	0.07	0.564
Ln S-triglycerides	0.17	0.042				
S-apolipoprotein B	0.17	0.048				
S-apolipoprotein A_1	-0.14	0.104				
Ln Apolipoprotein B/A_1 ratio	0.19	0.023				
Ln P-glucose	0.05	0.563	-0.14	0.286	0.24	0.028
Ln S-insulin	0.45	<0.0001				
HOMA index	0.49	<0.0001				
HbA1c	0.13	0.116				
Ln S-AST	0.10	0.259				
Ln S-ALT	0.21	0.011				
Diastolic blood pressure	0.17	0.038				
Systolic blood pressure	0.24	0.004				
Mothers (n=142)						
BMI	0.24	0.004	0.03	0.839	0.42	<0.001
Waist circumference	0.20	0.016	-0.04	0.748	0.42	<0.001
Ln Total cholesterol	0.11	0.193				
Ln S-triglycerides	0.16	0.062				
Ln S-insulin	0.03	0.771				
Ln Diastolic blood pressure	-0.09	0.278				
Ln Systolic blood pressure	-0.03	0.694				
Fathers (n=122)						
BMI	0.20	0.026				
Waist circumference	0.13	0.154				
Ln Total cholesterol	0.15	0.096				
Ln S-triglycerides	0.11	0.225				
Ln S-insulin	0.16	0.079				
Ln Diastolic blood pressure	0.18	0.049				
Ln Systolic blood pressure	0.18	0.045				

[1]Interaction of sex was tested by linear regression and for associations significantly different between boys and girls (P<0.05), sex-specific data was provided instead of data of all children.

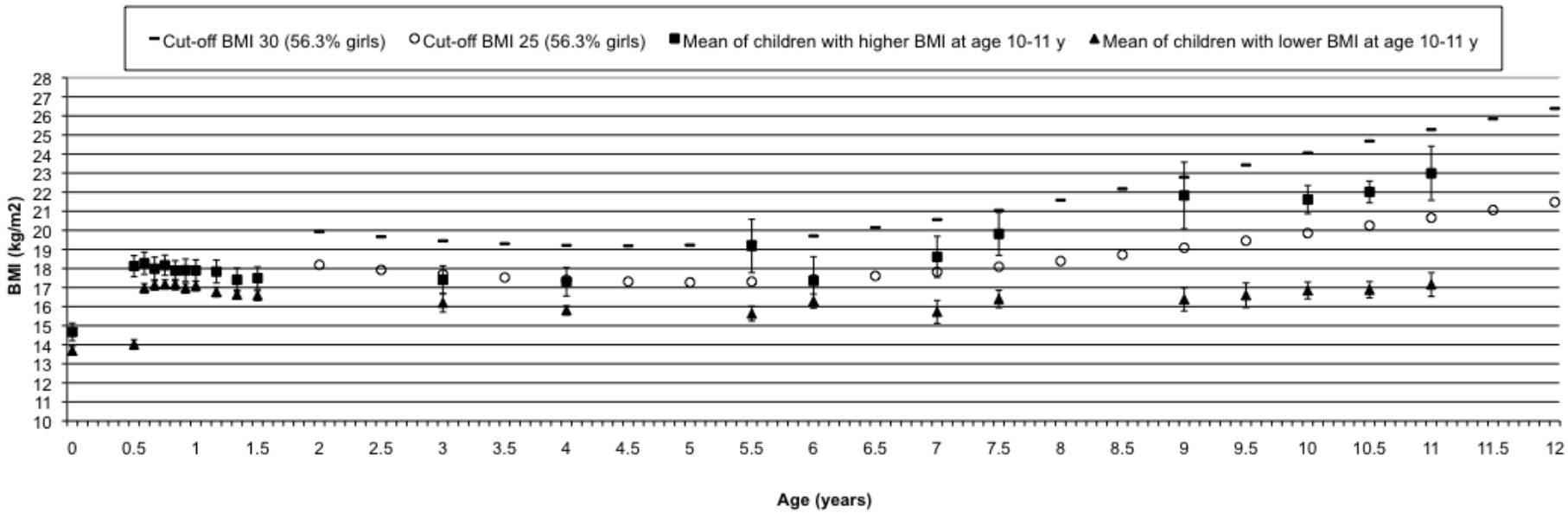

Figure 1 Retrospective data, from birth to 11 y of age, on body mass index (BMI) and 95% confidence interval in children having either lower BMI (114 normal weight and 1 underweight child) or higher BMI (29 overweight and 1 obese child) at age 10-11 y. The cut-off BMI 30 and 25 corresponds to BMI 30 or 25 kg/m^2 at age ≥18 y according to the International Obesity Task Force (12).

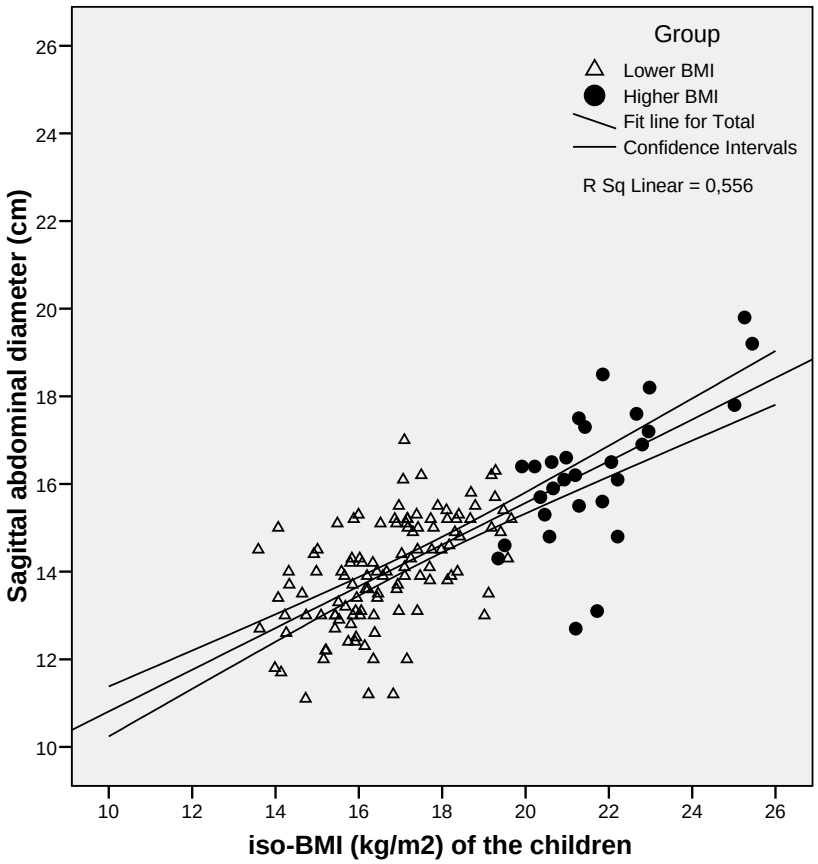

Figure 2 Correlation between body mass index (BMI) and sagittal abdominal diameter in 10-y-old children (n=144) with either lower BMI (114 normal weight and 1 underweight child) or higher BMI (29 overweight and 1 obese child). Pearson correlation coefficient R=0.745 (P<0.05).

$R^2 = 0.556$

Appendix 1

Scatter matrixes of correlations between children's BMI and anthropometry, blood pressure and blood values of children and their parents.

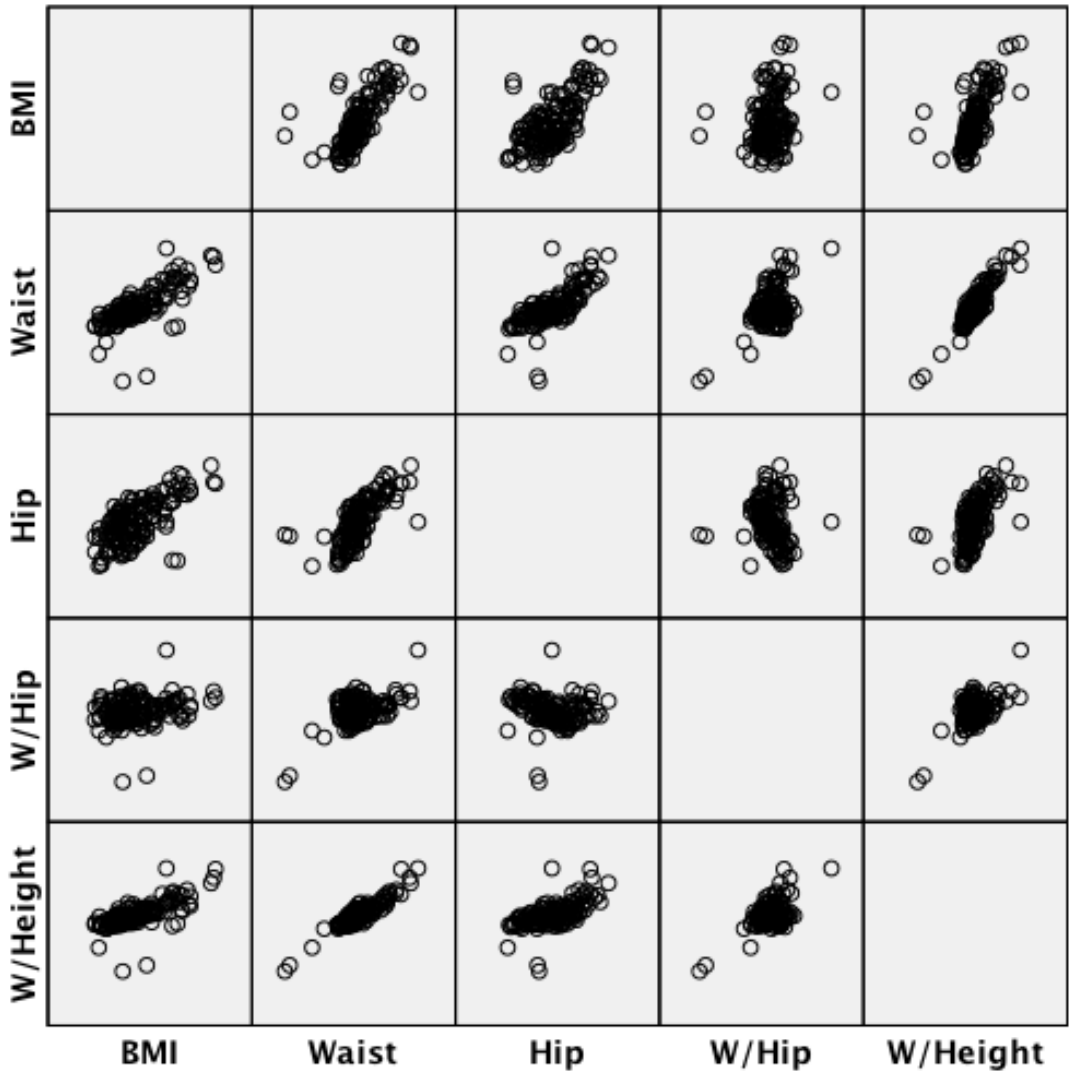

Figure 1 Scatter matrix of children's body mass index (BMI), waist circumference (Waist), hip circumference (Hip), waist/hip ratio (W/Hip) and waist/height ratio (W/Height).

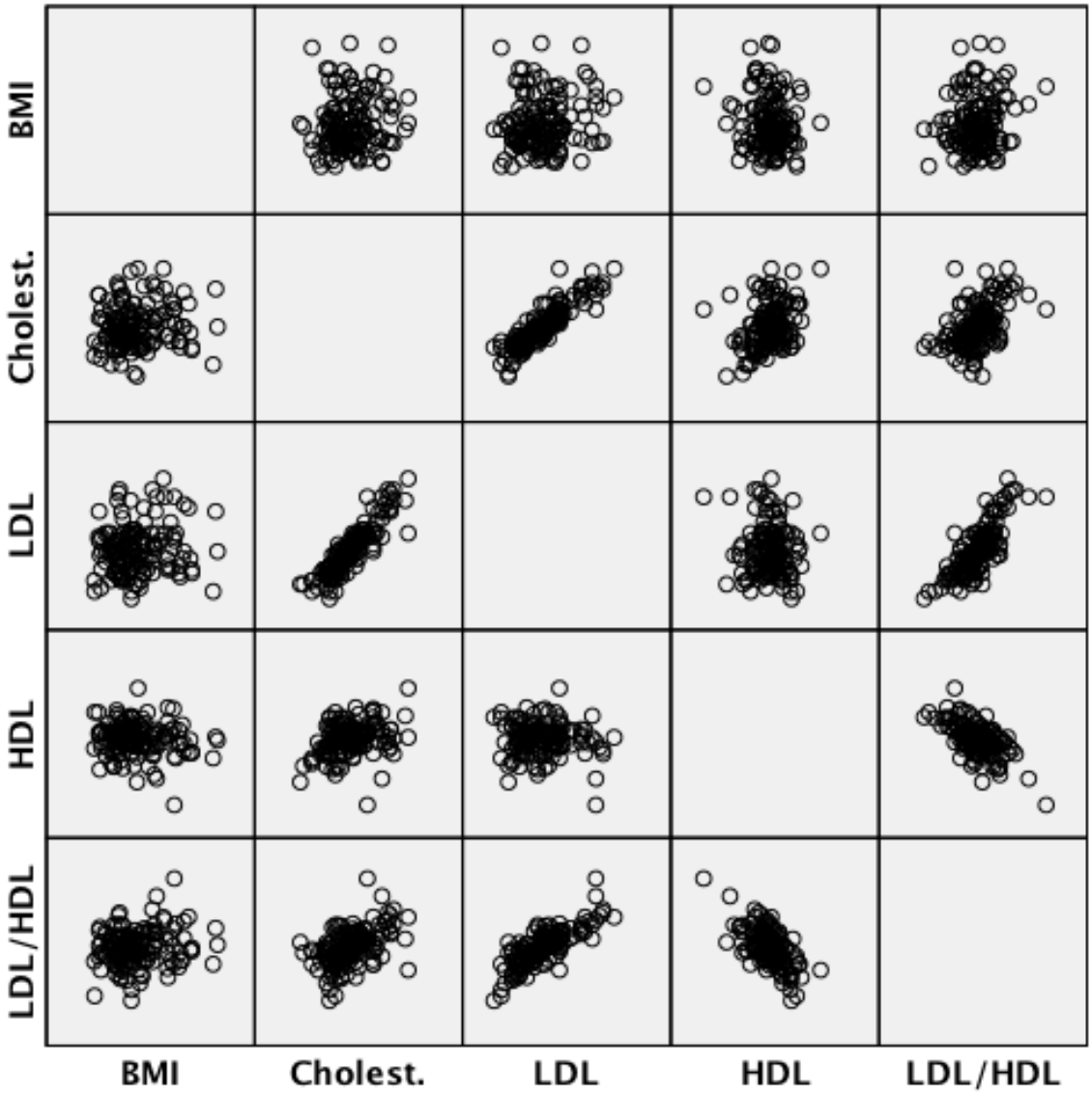

Figure 2 Scatter matrix of children's body mass index (BMI), total cholesterol (Cholest.), LDL cholesterol (LDL), ln HDL cholesterol (HDL) and ln LDL/HDL ratio (LDL/HDL).

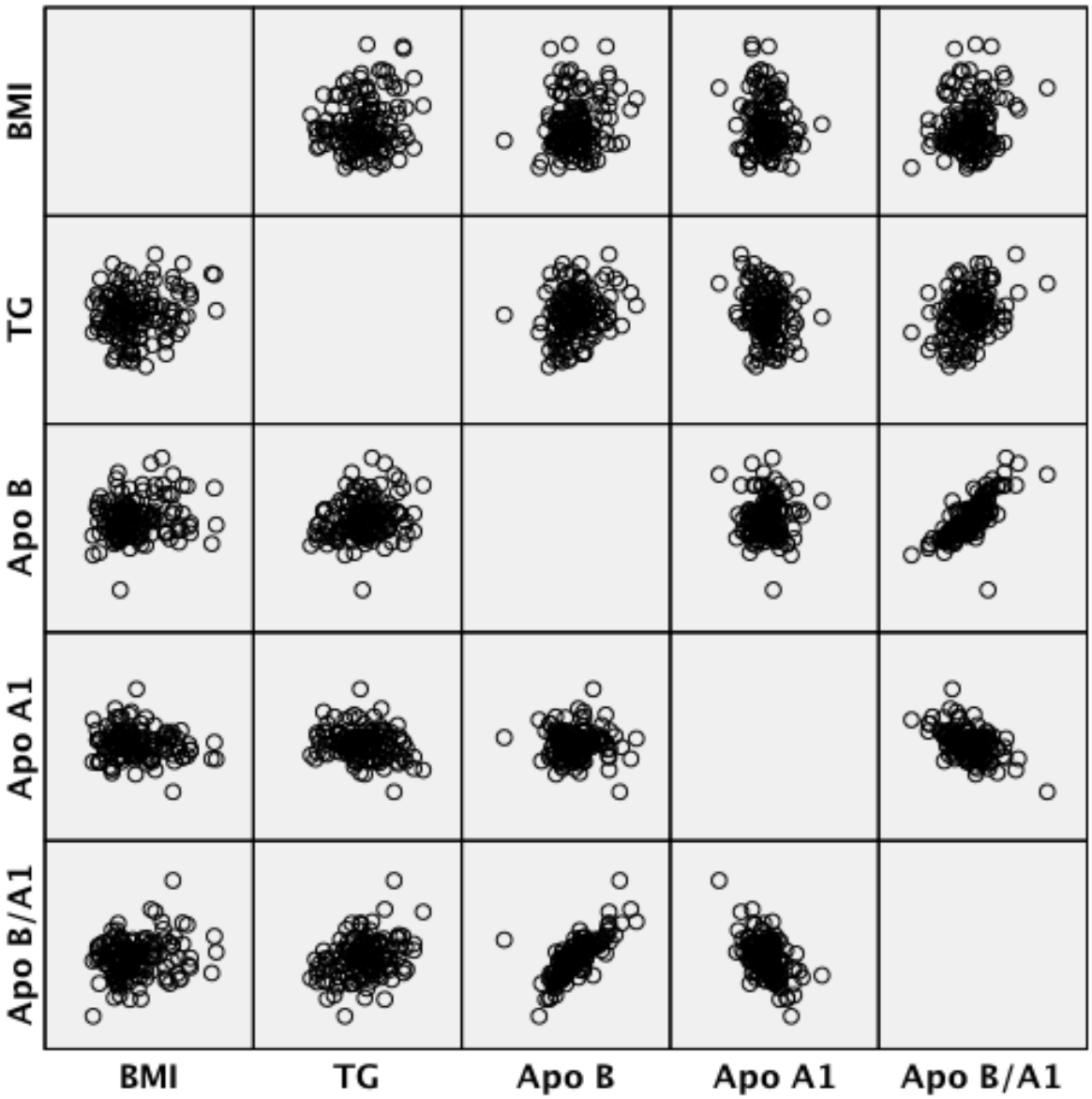

Figure 3 Scatter matrix of children's body mass index (BMI), ln S-triglycerides (TG), S-apolipoprotein B (Apo B), S-apolipoprotein A_1 (Apo A1) and ln apolipoprotein B/A_1 ratio (Apo B/A_1).

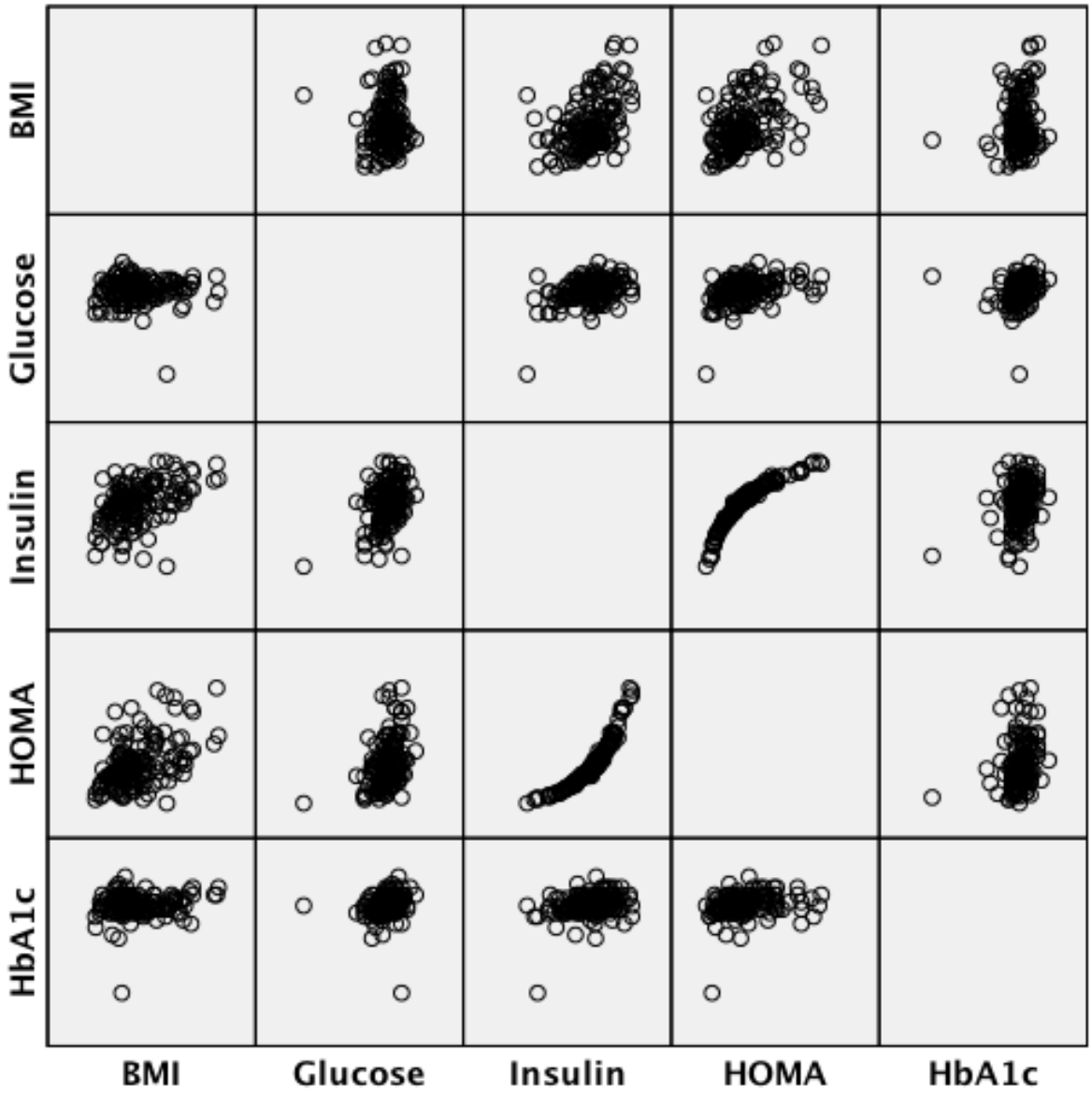

Figure 4 Scatter matrix of children's body mass index (BMI), ln P-glucose (Glucose), ln S-insulin (Insulin), HOMA index (HOMA) and HbA1c.

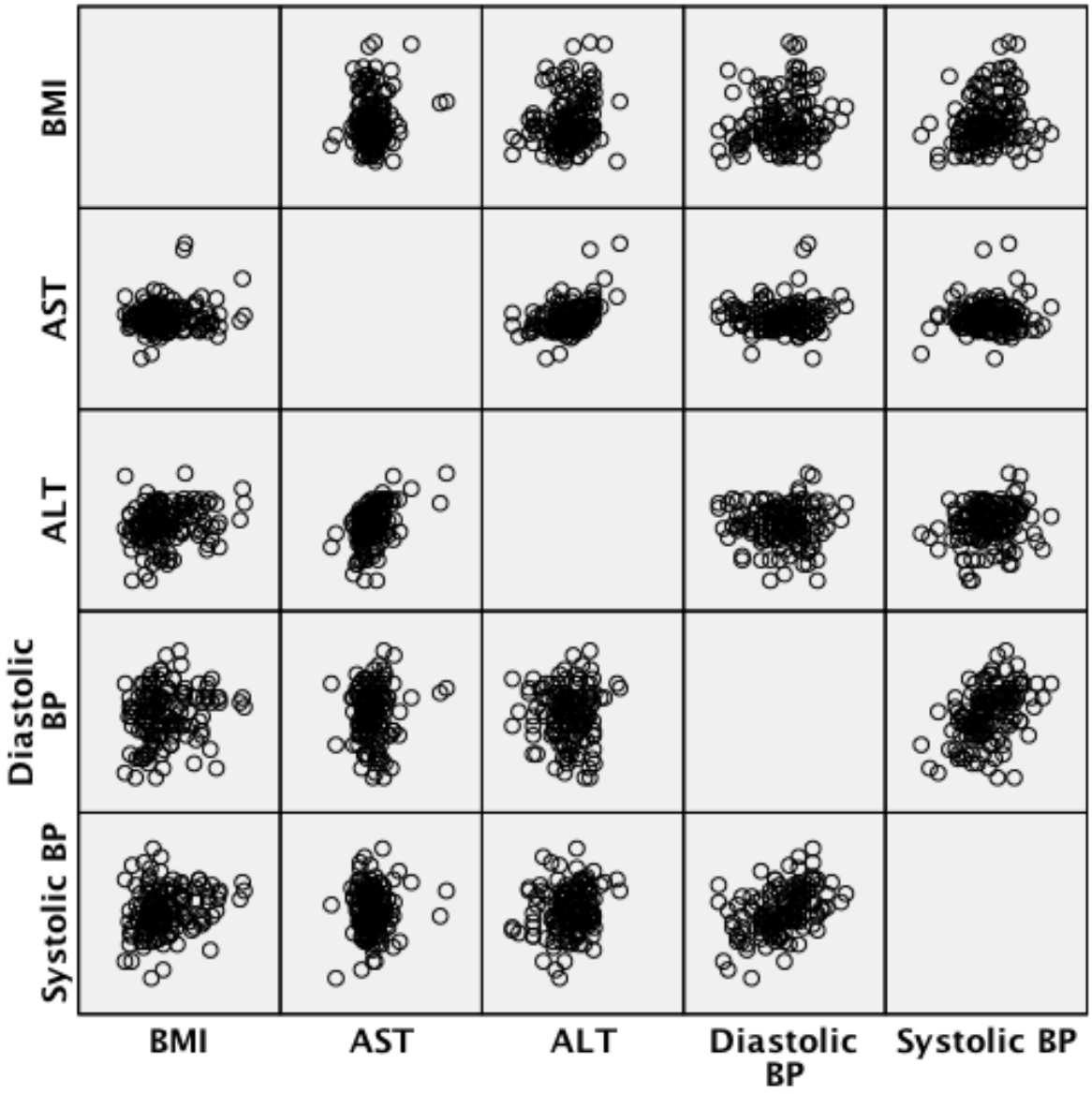

Figure 5 Scatter matrix of children's body mass index (BMI), ln S-AST (AST), ln S-ALT (ALT), diastolic blood pressure (Diastolic BP) and systolic blood pressure (Systolic BP).

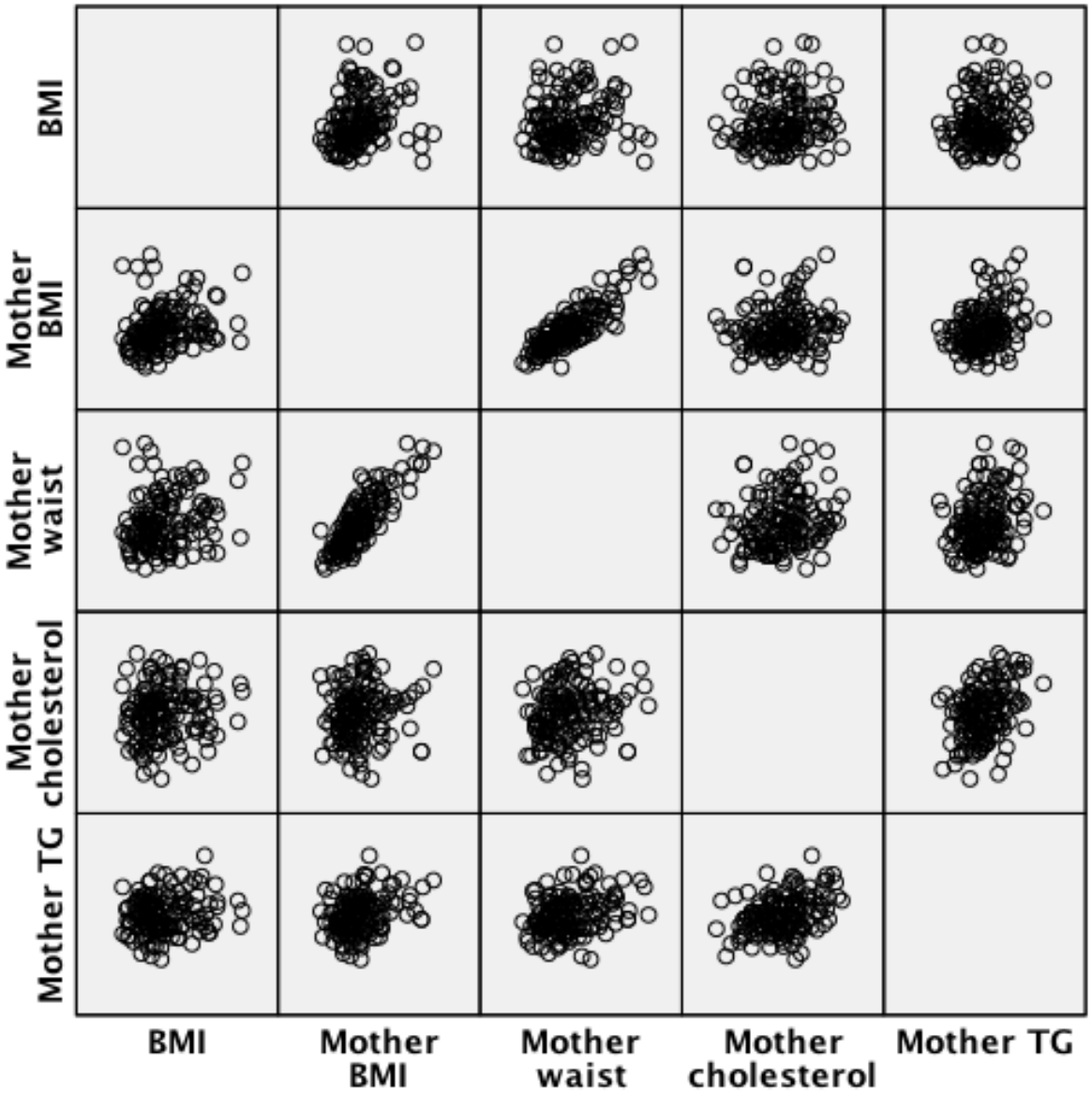

Figure 6 Scatter matrix of children's body mass index (BMI) and their mothers' body mass index (Mother BMI), waist circumference (Mother waist), ln total cholesterol (Mother cholesterol), and ln S-triglycerides (Mother TG).

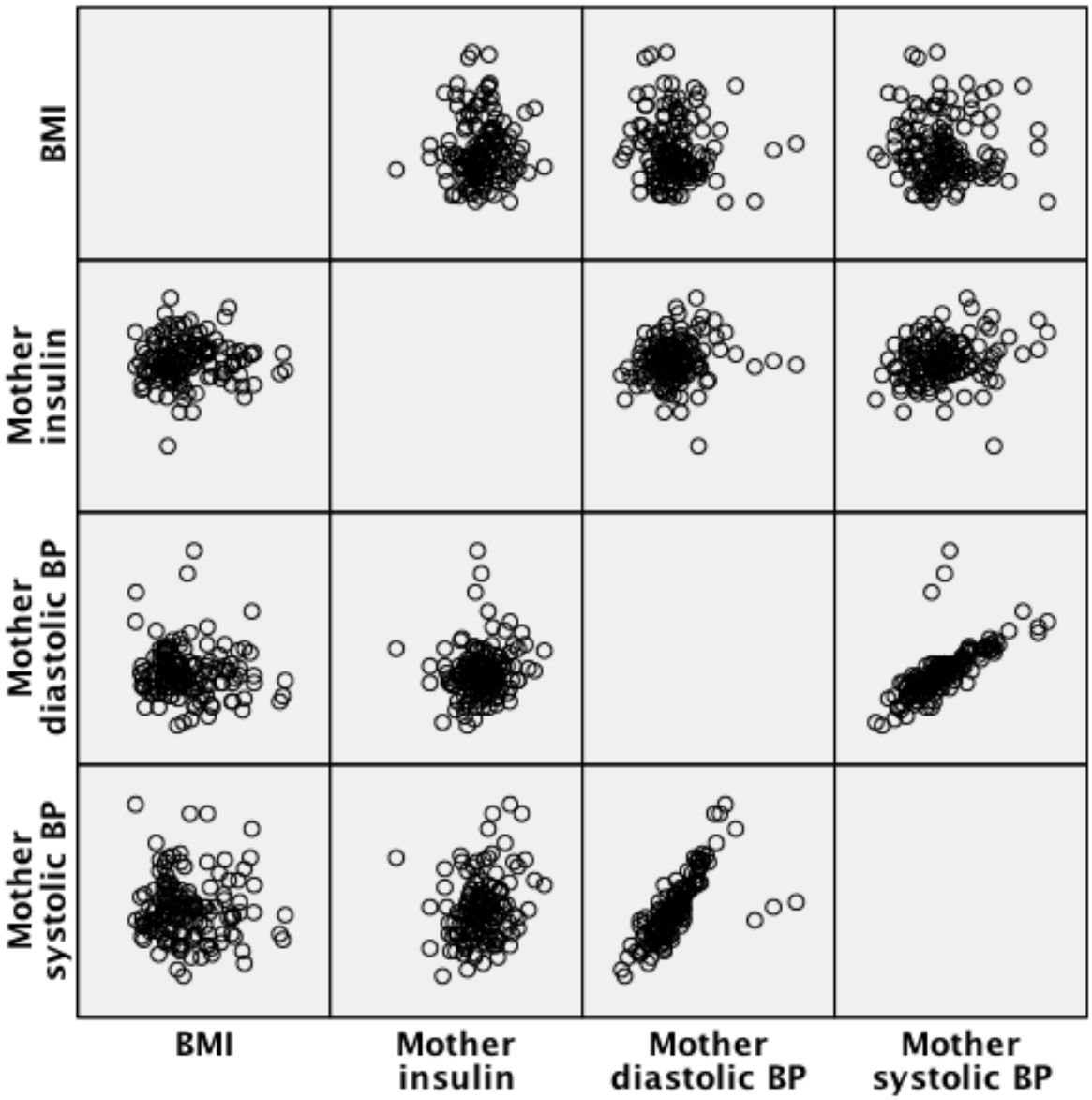

Figure 7 Scatter matrix of children's body mass index (BMI) and their mothers' ln S-insulin (Mother insulin), ln diastolic blood pressure (Mother diastolic BP) and in systolic blood pressure (Mother systolic BP).

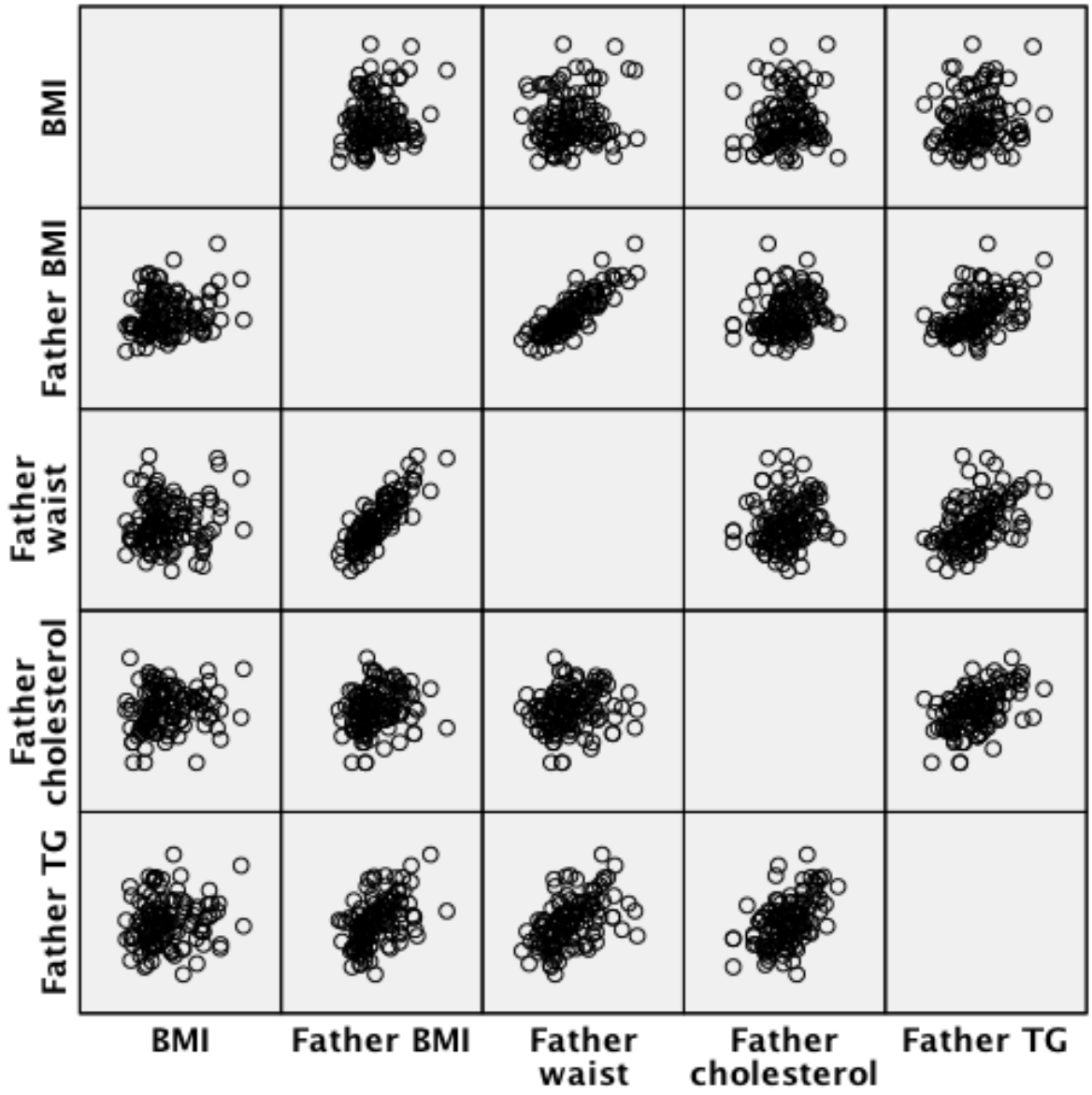

Figure 8 Scatter matrix of children's body mass index (BMI) and their fathers' body mass index (Father BMI), waist circumference (Father waist), ln total cholesterol (Father cholesterol), and ln S-triglycerides (Father TG).

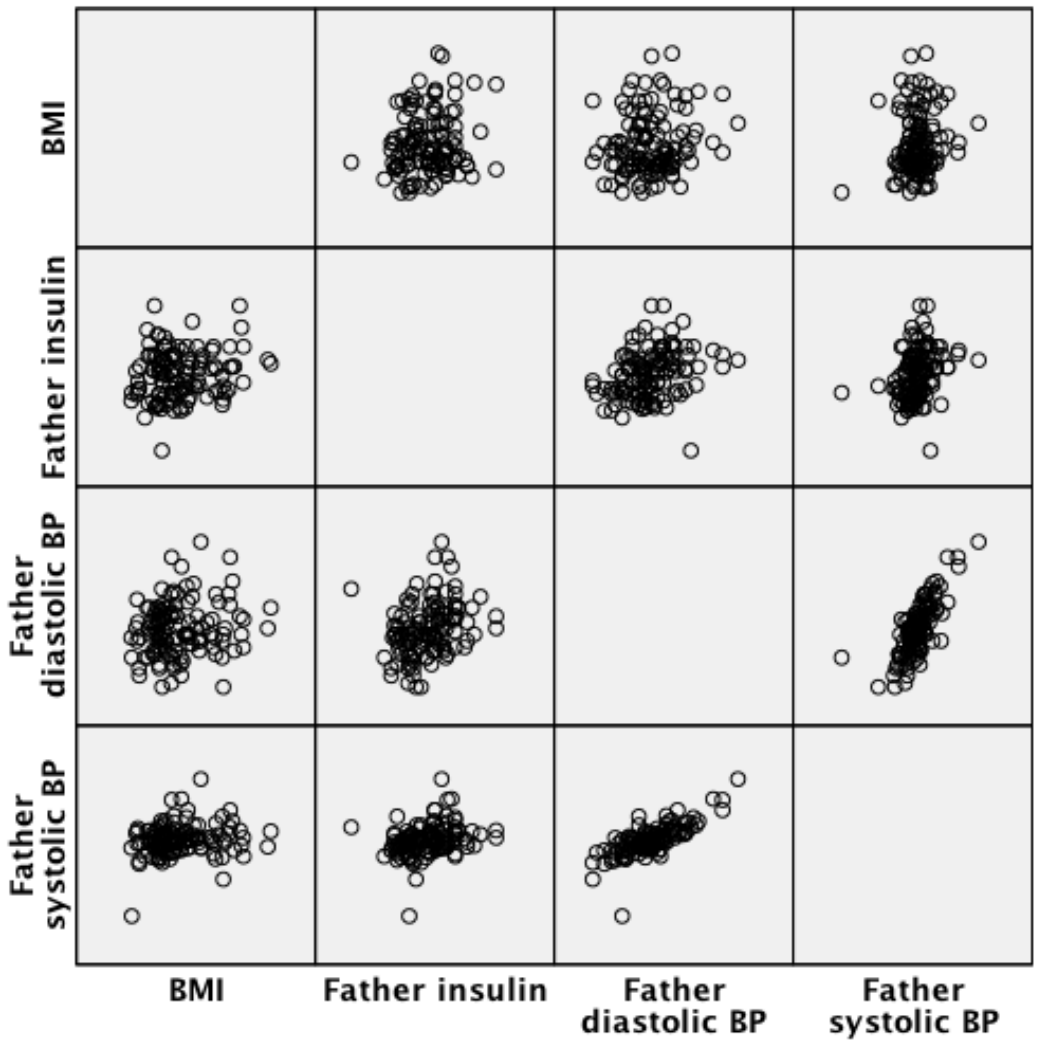

Figure 9 Scatter matrix of children's body mass index (BMI) and their fathers' ln S-insulin (Father insulin), ln diastolic blood pressure (Father diastolic BP) and in systolic blood pressure (Father systolic BP).