Which amount of BMI-SDS reduction is necessary to improve cardiovascular risk factors in overweight children?

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Context: Knowing the changes of cardiovascular risk factors (CRF) in relation to weight loss would be helpful to advise overweight children and their parents and to decide whether drugs should be prescribed in addition to lifestyle intervention.

Objective: To determine the BMI-SDS reduction to improve CRFs in overweight children.

Design: Prospective observation study.

Setting: Specialized outpatient obesity clinic.

Patients: 1388 overweight children (mean BMI 27.9 ± 0.1, mean age 11.4 ± 0.1 years, 43.8% male, 45.5% prepubertal).


Main Outcome measures: We studied changes of blood pressure (BP), fasting HDL-, LDL-cholesterol, triglycerides, glucose, and insulin resistance index HOMA. Change of weight status was determined by delta BMI-SDS based on the recommended percentiles of the International Task Force of Obesity.

Results: BMI-SDS change was associated with a significant improvement of all CRFs except fasting glucose and LDL-cholesterol after adjusting for multiple confounders such as baseline CRF, age, gender, BMI, pubertal stage and its changes. BMI-SDS reduction ≥ 0.25–0.5 was related to a decrease of systolic BP (-3.2 ± 1.4 mmHg), diastolic BP (-2.2 ± 1.1 mmHg), triglycerides (-6.9 ± 5.8 mg/dl), HOMA (-0.5 ± 0.3), and triglyceride/HDL-cholesterol (-0.3 ± 0.2), while HDL-cholesterol increased (+1.3 ± 1.2 mg/dl). A reduction of >0.5 BMI-SDS led to more pronounced improvement (systolic BP -6.0 ± 1.3 mmHg, diastolic BP -5.1 ± 1.3 mmHg, triglycerides -16.4 ± 7.1 mg/dl, HDL-cholesterol +1.6 ± 1.5 mg/dl, HOMA -0.9 ± 0.3). Per 0.1 BMI-SDS reduction systolic BP (-1.0 mmHg), diastolic BP (-0.8 mmHg), triglycerides (-2.3 mg/dl), HOMA (-0.2), and triglyceride/HDL-cholesterol (-0.5) decreased significantly, while HDL-cholesterol (0.2 mg/dl) increased significantly in linear regression analyses accounted for multiple confounders.

Conclusions: A BMI-SDS reduction ≥ 0.25 improved significantly hypertension, hypertriglyceridemia and low HDL-cholesterol, while a BMI-SDS > 0.5 doubled the effect.

Abbreviations:
The prevalence of childhood obesity is stable at a high level in the U.S. and Europe, with up to one fifth of children affected (1, 2). Obesity negatively affects the quality of life (QOL) and social integration of children (3) and in the long term, obesity is associated with premature death (4). The reduced life span of children with obesity based on the increased risk for coronary heart disease (CHD) in adulthood (5) is primarily caused by associated comorbidities such as hypertension, dyslipidemia, and impaired glucose metabolism, which are commonly found in the Metabolic Syndrome (MetS) (6). Thus, these cardiovascular risk factors (CRF) have to be treated effectively to improve obesity-associated morbidity and mortality.

Lifestyle intervention is recommended as the treatment of choice for overweight children. However, the amount of overweight reduction to achieve improvements of CRFs is largely unknown. Usually the amount of overweight is expressed in childhood as standard deviation score (SDS) of body mass index (BMI), since BMI is both age and gender dependent (7, 8). We and others have previously shown that changes in pubertal stage also influence the CRF profile (14, 15), which has not been accounted for to date in deriving cut-off values to define successful BMI-SDS reduction in childhood.

Therefore, we analyzed nearly 1400 overweight children participating in the uniform lifestyle intervention “Obeldicks”, evaluating (a) which factors are predictive for changes of CRF profile and (b) at which cut-off for BMI-SDS reduction an improvement of CRFs can be expected. The advantages of analyzing overweight children participating at the lifestyle intervention “Obeldicks” are that all children attended a uniform intervention, which has been proven not only to reduce BMI-SDS compared to an untreated control group but also to improve the CRF profile compared to an untreated control group both in a randomized controlled trial and in non randomized trials (11, 16, 17). Additionally, to the best of our knowledge this is the first large longitudinal study using internationally accepted percentiles for overweight children (8).

**Materials and Methods**

The local ethics committee of the University of Witten/Herdecke approved this study. Written informed consent was obtained from all children and their parents prior to the study.

We included all overweight and obese children aged 5 to 17 years completing the “Obeldicks” intervention program at different treatment centers in North-West Germany (Datteln, Dortmund, Marl, Herne, and Gelsenkirchen) during the observation period between 2000 and 2015. Children with endocrine disorders or syndromal obesity were excluded from the study. Overweight was defined by Body Mass Index (BMI) > 90th and ≤ 97th percentile, obesity by BMI > 97th and ≤ 99.5th percentile, and extreme obesity by BMI > 99.5th percentile. We used the international accepted BMI percentiles recommended by the International Obesity Task Force (IOTF) (7, 8). The 90th percentile approaches nearly 25 kg/m² at the age of 18 years and the 97th percentile reaches BMI values of nearly 30 kg/m² at the age of 18 years.

**Intervention**

The lifestyle intervention “Obeldicks” has been described in detail elsewhere (11, 18). This intervention has to follow a published training manual and all personnel have to be trained during a one-week trainer seminar (18). Briefly, this outpatient intervention program is based on physical activity, nutrition education, and behavior therapy including the individual psychological care of the child and his or her family. An interdisciplinary team of pediatricians, nutrition counselors, psychologists, and exercise physiologists is responsible for the training. The children are separated into groups according to their sex and age. The exercise treatment consist of ball games, jogging, trampoline jumping, and instructions in physical exercise as part of everyday life and reducing the amount of time spent watching television. The nutritional course is based on the prevention concept of the “Optimized mixed diet”. Up-to-date scientific recommendations are translated into food-based dietary guidelines also considering the dietary habits of children and families in Germany (19). The children follow a “traffic-light system” when selecting their food. In this system, the foods and drinks available in Germany are separated according to their fat and sugar contents into “red = stop”, “orange = consider the amount”, and “green = o.k. when hungry or thirsty”. The attendance rate has to be > 90% for children and their parents otherwise the family was excluded from the intervention (18). Seventeen percent of the children dropped-out from the intervention (18).

**Measurements**

Degree of overweight was derived from BMI. Height was measured to the nearest centimeter using a rigid stadiometer. Weight was measured in underwear to the nearest 0.1 kg using a calibrated balance scale. We used the LMS method to calculate standard deviation scores (SDS) of BMI as a measurement for the degree of overweight (20). The LMS method summarizes the data in terms of three smooth age-specific curves called L (lambda), M (mu), and S (sigma) based on the data recommended by the International Obesity Task Force (IOTF) (7, 8).

Pubertal stage was determined by well-trained physicians according to Marshall and Tanner. Pubertal developmental stage was categorized into three groups based on breast and genital stages (prepubertal: boys with genital stage I, girls with breast stage I, early pubertal: boys with genital stage II-III; girls with breast stage II-III, late pubertal: boys with genital stage >III; girls with breast stage >III).

Blood pressure was measured using a validated protocol (21). Briefly, blood pressure (BP) was measured at the right arm after...
a 10-minute rest in the supine position with an oscillometric device (Omron M6). Two repeated recordings were made with 5 minutes in between and the lowest value of the 2 recordings of systolic BP (SBP) and diastolic BP (DBP) measurements was used. The cuff size was based on the length and circumference of the upper arm and was as large as possible without having the elbow skin crease obstructing the stethoscope (21).

Blood sampling was performed in the fasting state. All laboratory measurements were performed in one central lab. Serum insulin, triglyceride, HDL-cholesterol, LDL-cholesterol, and glucose concentrations were measured using commercially available test kits (LDL-C- and HDL-C-Plus™ Roche Diagnostics, Mannheim, Germany; Vitros™ analyzer Ortho Clinical Diagnostics, Neckargemünd, Germany; MEIA™, Abbott, Wiesbaden, Germany). Intra- and interassay variations for the concentrations (CV) of these variables were less than 5%. Insulin concentrations were measured by microparticle enhanced immunometric assay (MEIA™, Abbott, Wiesbaden, Germany).

Glucose levels were determined by colorimetric test using a Vitros™ analyzer (Ortho Clinical Diagnostics, Neckargemünd, Germany). Homeostasis model assessment (HOMA) was used to detect the degree of insulin resistance using the formula: resistance (HOMA) = (insulin [mU/l] x glucose [mmol/l]) / 22.5 (22). Additionally, the triglyceride to HDL-cholesterol ratio was calculated as an indirect parameter of insulin resistance.

**Definition of CRFs**

Impaired fasting glucose was defined by fasting glucose levels > 100 mg/dl (>5.60 mmol/l) (23). Hypertriglyceridemia was defined by triglycerides > 150 mg/dl (>1.65 mmol/l), increased LDL-cholesterol concentrations by > 130 mg/dl (>3.38 mmol/l) and low HDL-cholesterol levels < 40 mg/dl (<1.04 mmol/l) following German guidelines (24). Increased HOMA levels was defined by > 95th percentile according to gender and age based on the percentiles of Allard (25). Hypertension was defined by BP above the 95th percentile for height, age, and gender (21). Abnormal cardiovascular risk factors were defined by impaired fasting glucose, triglycerides > 150 mg/dl, LDL-cholesterol > 130 mg/dl, HDL-cholesterol < 40 mg/dl, hypertension or HOMA levels above the 95th percentile (24).

**Statistical Analysis**

Spearman’s rank correlation coefficient was used to calculate correlations between baseline CRFs, age, gender, pubertal stage, BMI-SDS, changes of BMI-SDS, changes of pubertal stage, and changes in CRFs during the intervention. Multivariable regression analysis was used to investigate the association between BMI-SDS decrease categories and changes in CRFs. In a first step, a baseline model was set up for all CRFs, respectively, with change in CRF as the dependent variable and BMI at baseline as the independent variables. Moreover, we adjusted for age at baseline, sex, baseline pubertal stage and change in pubertal stage. In case of significant correlation between baseline CRF and baseline BMI-SDS, we included an interaction term between both variables in the model. Since baseline pubertal stage and change in pubertal stage were strongly correlated, an interaction term between these variables was also included. We investigated the decrease in BMI-SDS necessary for a significant improvement of CRFs in a second model with the residuals of the baseline model as the dependent variable and BMI-SDS decrease as the independent variable. BMI-SDS decrease was included continuously as well as categorized into the model. BMI-SDS decrease categories were defined as a) stable or increase in BMI-SDS, b) BMI-SDS decrease < 0.125, c) BMI-SDS decrease ≥ 0.125 and < 0.25, d) BMI-SDS decrease ≥ 0.25 and ≤ 0.5, e) BMI-SDS decrease > 0.5. This division was used since in a previous study we observed improvements of CRFs like hypertension and dyslipidemia only if the BMI-SDS decreased by at least 0.5 over a 1-year period (10, 11). Furthermore, using these cut-offs resulted in a nearly equal distribution among the 4 groups with BMI-SDS reduction in our present study cohort (BMI-SDS decrease < 0.125: n = 217, BMI-SDS decrease ≥ 0.125 and < 0.25: n = 206, BMI-SDS decrease ≥ 0.25 and ≤ 0.5: n = 280, BMI-SDS decrease > 0.5: n = 205).

Changes of pubertal stage were set as 0 for remaining prepubertal or pubertal, 1 for entry into puberty, and −1 for changing from early to late puberty. This classification was used since entry into puberty is associated with a deterioration of CRFs, while changing from mid to late puberty is associated with an improvement of CRFs (14).

Data were presented as mean and 95% confidence interval (CI) in the adjusted models, mean and standard error of the mean in the unadjusted models or as median and interquartile range (IQR) if variables were not normally distributed.

A p-value < 0.05 was considered as statistically significant. Analyses were conducted using SAS statistical package (version 9.4; SAS Institute Inc, Cary, NC) and the Winstat® software package (R. Fitch Software, Bad Krozingen, Germany).

**Results**

A total of 1388 children were included in the study. The characteristics of the study population are shown in Table 1.

In univariate analyses, changes of systolic BP correlated significantly to baseline BMI-SDS (r = -0.07), baseline diastolic BP (r = -0.58), baseline pubertal stage (r = -0.05), changes of BMI-SDS (r = 0.24) and changes of pubertal stage (r = 0.05), but not to age or gender. Changes of diastolic BP were associated significantly with baseline BMI-SDS (r = -0.07), baseline systolic BP (r = -0.55), baseline pubertal stage (r = -0.05), changes of BMI-SDS (r = 0.28) and changes of pubertal stage (r = 0.05), but not with age, gender, pubertal stage or its changes. Changes of LDL-cholesterol correlated significantly to gender (r = 0.07), baseline LDL-cholesterol (r = -0.41), baseline pubertal stage (r = 0.08), changes of BMI-SDS (r = 0.11) and changes of pubertal stage (r = 0.06), but not to age or baseline BMI-SDS. Changes of HDL-cholesterol were associated significantly with gender (r = 0.10), baseline BMI-SDS (r = -0.12), baseline HDL-cholesterol (r = -0.38), baseline pubertal stage (r = -0.05), changes of BMI-SDS (r = 0.12) and changes of pubertal stage (r = -0.07), but not with age. Changes of triglycerides correlated significantly to baseline triglycerides (r = -0.43) and changes of BMI-SDS (r = 0.17) but not to age, gender, baseline BMI-SDS, pubertal stage or its changes. Changes of fasting glucose
The associations between changes of CRFs and changes of BMI-SDS in multiple linear regression analyses adjusted to baseline age, gender, pubertal stage, BMI-SDS, respective baseline CRFs, and changes of pubertal stage are shown in Table 2. In the entire study population, all changes of CRFs were significantly related to changes of BMI-SDS.

The effects of BMI-SDS changes categorized into 5 groups on CRFs are shown in figures 1-3. In the unadjusted models, a decrease of BMI-SDS ≥ 0.25 was associated with a significant improvement of all CRFs except fasting glucose. Furthermore, systolic BP also improved with a BMI-SDS reduction ≥ 0.125 BMI-SDS. LDL-cholesterol decreased significantly in any degree of BMI-SDS reduction. In the adjusted models a decrease of BMI-SDS ≥ 0.25 was associated with a significant improvement of all CRFs except LDL-cholesterol and fasting glucose.

The effects of BMI-SDS reduction in children with abnormal CRFs at baseline are shown in Table 3. A BMI-SDS reduction ≥ 0.125 was associated with an improvement of all CRFs. A reduction of BMI-SDS < 0.125 was also associated with a decrease of BP and LDL-cholesterol. The improvement of CRFs was at least threefold better in all BMI-SDS reduction categories in children with hypertension, dyslipidemia, or increased HOMA values > 95th percentile at baseline compared to children with normal CRFs at baseline (see Table 3 vs figures 1–3). The number of children with impaired fasting glucose (n = 40) was too small to separate into BMI-SDS reduction groups.

Discussion

This is the first large longitudinal study in overweight and obese children treated by an uniform one-year lifestyle intervention to derive cut-off values for defining successful overweight reduction based on internationally accepted BMI-SDS values (8). We observed that a decrease of BMI-SDS was associated with a decrease of BP and LDL-cholesterol. The improvement of CRFs was at least threefold better in all BMI-SDS reduction categories in children with hypertension, dyslipidemia, or increased HOMA values > 95th percentile at baseline compared to children with normal CRFs at baseline.

Table 1. Characteristics of study population consisting of 1388 children

<table>
<thead>
<tr>
<th>age [years]</th>
<th>11.4 ± 0.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>gender</td>
<td>43.8% male</td>
</tr>
<tr>
<td></td>
<td>45.5% prepubertal stage</td>
</tr>
<tr>
<td></td>
<td>30.9% early pubertal stage</td>
</tr>
<tr>
<td></td>
<td>23.6% late pubertal stage</td>
</tr>
<tr>
<td>BMI [kg/m²]</td>
<td>27.9 ± 0.1</td>
</tr>
<tr>
<td>BMI-SDS</td>
<td>2.59 ± 0.01</td>
</tr>
<tr>
<td>overweight</td>
<td>8.1%</td>
</tr>
<tr>
<td>obese</td>
<td>22.0%</td>
</tr>
<tr>
<td>extremely obese</td>
<td>69.9%</td>
</tr>
<tr>
<td>systolic blood pressure [mmHg]</td>
<td>116 ± 0.4</td>
</tr>
<tr>
<td>diastolic blood pressure [mmHg]</td>
<td>67 ± 0.3</td>
</tr>
<tr>
<td>hypertension</td>
<td>28.8%</td>
</tr>
<tr>
<td>LDL-cholesterol [mg/dl]</td>
<td>101 (83 – 121)</td>
</tr>
<tr>
<td>HDL-cholesterol [mg/dl]</td>
<td>49 (42 – 57)</td>
</tr>
<tr>
<td>HDL-cholesterol &lt;40 mg/dl</td>
<td>19.8%</td>
</tr>
<tr>
<td>triglycerides [mg/dl]</td>
<td>96 (86 – 141)</td>
</tr>
<tr>
<td>triglycerides &gt;150 mg/dl</td>
<td>21.4%</td>
</tr>
<tr>
<td>triglycerides / HDL-cholesterol</td>
<td>2.10 (1.34 – 3.44)</td>
</tr>
<tr>
<td>glucose [mg/dl]</td>
<td>86 ± 0.3</td>
</tr>
<tr>
<td>impaired fasting glucose</td>
<td>2.9%</td>
</tr>
<tr>
<td>HOMA</td>
<td>2.9 (1.9 – 4.5)</td>
</tr>
<tr>
<td>HOMA &gt; 95th percentile</td>
<td>24.9%</td>
</tr>
</tbody>
</table>

Data given as mean ± standard error of the mean or median and IQR if not normally distributed; variables were determined at the fasting status; converting factors cholesterol from mg/dl to mmol/liter × 0.026, triglycerides from mg/dl to mmol/liter × 0.011, glucose from mg/dl to mmol/liter: x 0.056

| were associated significantly with baseline glucose (r = -0.48) and changes of BMI-SDS (r = 0.10), but not with age, gender, baseline BMI-SDS, pubertal stage or its changes. Changes of HOMA correlated significantly to age (r = -0.11), baseline HOMA (r = -0.42), baseline pubertal stage (r = 0.11), changes of BMI-SDS (r = 0.24) and changes of pubertal stage (r = 0.08), but not to gender or baseline BMI-SDS. Changes of triglyceride/HDL-cholesterol ratio correlated significantly to baseline triglyceride/HDL-cholesterol ratio (r = -0.39) and changes of BMI-SDS (r = 0.18), but not to age, gender, baseline BMI-SDS, baseline pubertal stage or changes of pubertal stage. |

Table 2. Adjusted changes of cardiovascular risk factors per decrease of 0.1 BMI-SDS in the entire study group as well as stratified by pubertal status, degree of overweight, and abnormal cardiovascular risk factors at baseline

<table>
<thead>
<tr>
<th></th>
<th>entire study group</th>
<th>prepubertal children</th>
<th>pubertal children</th>
<th>overweight children</th>
<th>Obese children</th>
<th>extremely obese children</th>
<th>children with abnormal CRFs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δsystolic blood pressure [mmHg]</td>
<td>-1.04 (0.08)**</td>
<td>-1.10 (0.16)**</td>
<td>-0.90 (0.10)**</td>
<td>-1.22 (0.19)**</td>
<td>-0.77 (0.15)**</td>
<td>-0.81 (0.17)**</td>
<td>-0.84 (0.23)**</td>
</tr>
<tr>
<td>Δdiastolic blood pressure [mmHg]</td>
<td>-0.79 (0.07)**</td>
<td>-0.86 (0.13)**</td>
<td>-0.66 (0.09)**</td>
<td>-0.52 (0.22)*</td>
<td>-0.79 (0.12)**</td>
<td>-0.57 (0.81)**</td>
<td>-0.56 (0.22)**</td>
</tr>
<tr>
<td>ΔLDL cholesterol [mg/dl]</td>
<td>-0.70 (0.17)**</td>
<td>-0.36 (0.30)</td>
<td>-0.75 (0.21)**</td>
<td>-0.51 (0.46)</td>
<td>-0.66 (0.31)*</td>
<td>-0.56 (0.19)**</td>
<td>-0.28 (0.76)</td>
</tr>
<tr>
<td>ΔHDL cholesterol [mg/dl]</td>
<td>0.21 (0.06)**</td>
<td>0.32 (0.13)</td>
<td>0.20 (0.11)*</td>
<td>0.14 (0.21)</td>
<td>0.12 (0.16)</td>
<td>0.20 (0.09)*</td>
<td>0.44 (0.14)**</td>
</tr>
<tr>
<td>Δtriglycerides [mg/dl]</td>
<td>-2.3 (0.4)**</td>
<td>-2.2 (0.7)**</td>
<td>-2.1 (0.5)**</td>
<td>-0.56 (0.3)</td>
<td>-2.4 (0.7)**</td>
<td>-2.0 (0.4)**</td>
<td>-6.9 (2.5)**</td>
</tr>
<tr>
<td>Δfasting glucose [mg/dl]</td>
<td>-0.24 (0.07)**</td>
<td>-0.25 (0.09)**</td>
<td>-0.17 (0.10)</td>
<td>-0.26 (0.17)</td>
<td>-0.25 (0.10)**</td>
<td>-0.15 (0.06)*</td>
<td>-0.36 (0.17)*</td>
</tr>
<tr>
<td>ΔHOMA</td>
<td>-0.16 (0.02)**</td>
<td>-0.11 (0.03)**</td>
<td>-0.20 (0.03)**</td>
<td>-0.04 (0.05)</td>
<td>-0.13 (0.03)**</td>
<td>-0.18 (0.03)**</td>
<td>-0.36 (0.17)*</td>
</tr>
</tbody>
</table>
| Δtriglyceride/HDL-cholesterol | -0.05 (0.01)** | -0.07 (0.02)** | -0.05 (0.02)** | -0.01 (0.03) | -0.05 (0.02)** | -0.05 (0.01)** | -

Data given as b-coefficient and standard error in brackets, values derived from linear regression analyses adjusted for baseline age, gender, pubertal stage, BMI-SDS, baseline respective CRF and changes of pubertal changes; *: P < 0.05; **: P < 0.01; ***: P < 0.001; &: number of children with impaired fasting glucose too low for calculation; converting factors cholesterol from mg/dl to mmol/liter × 0.026, triglycerides from mg/dl to mmol/liter × 0.011, glucose from mg/dl to mmol/liter: x 0.056.
SDS was significantly associated with improvements of CRFs. These findings are in line with previous smaller studies (9–11, 13). However, the univariate associations were only weak to moderate (r = 0.10–0.28) suggesting that other important confounders influence the relationship between change of BMI-SDS and change of CRF.

The most important factor influencing the changes of CRFs was the baseline value of the respective CRF (r = 0.38–0.58). This finding is of clinical importance since in children with hypertension, dyslipidemia or insulin resistance at baseline even smaller amounts of BMI-SDS reduction were associated with a significant improvement of their CRFs. Furthermore, the effect of BMI-SDS reduction on CRFs was much better in children with hypertension or dyslipidemia.

Another factor influencing the changes of CRFs was the degree of overweight at baseline. However, the observed effects were only weak (r < 0.13). We found no impact of age on change of CRFs except a weak correlation to HOMA. There was a small influence of gender on improvements of lipids while all other changes of CRFs were not related to gender. These findings are in line with previous studies (9–11, 13). Change of pubertal stage was associated with change of CRF profile in our study as reported in previous studies (14). However, the impact was weak (r < 0.08).

In our study, a BMI-SDS reduction of ≥ 0.25 in one year (which is approximately a BMI reduction of 0.5 kg/m² in a 7 year old child and a BMI reduction of 1.0 kg/m² in a 13 year old adolescent) was associated with an improvement of all CRFs except fasting blood glucose and LDL-cholesterol even after adjusting for the above mentioned confounders. This amount of BMI-SDS reduction to achieve significant improvements of CRFs was lower compared to most previous studies reporting a significant improvement in BMI-SDS reduction > 0.5 (9–11, 13). Based on the IOTF percentiles, a BMI-SDS reduction of 0.5 represents approximately a weight loss of 5 kg in a male adolescent with 1 cm growth per year or a stable weight in children growing ≥ 5 cm per year.

An explanation for the observed difference might be the lack of power in the other studies to detect significant changes of CRF. Moreover, in children with hypertension or dyslipidemia at baseline, already a BMI-SDS reduction > 0.125 lead to an improvement of these CRFs suggesting that already minimal BMI-SDS reduction is sufficient to improve CRFs in these children. Weiss and colleagues have shown that BMI z-score reduction ≥ 0.09 was associated with increased HDL-cholesterol levels, decreased fasting glucose levels and triglycerides (26).

Improving the key factors of MetS (hypertension, hypertriglyceridemia, low HDL-cholesterol and insulin resistance) has likely a clinical impact since MetS determines the morbidity and mortality in obesity (6). The influence of CRFs on vascular changes is already detectable in childhood as shown by measurements of carotid intima-media thickness (27). The mean reduction of triglycerides and the increase of HDL-cholesterol in the children with BMI-SDS reduction ≥ 0.25 BMI-SDS in the adjusted models were comparable to the effect of medical therapy, while the effect of > 0.5 BMI-SDS reduction was better than drug treatment (28, 29). Also the mean reduction of systolic and
diastolic BP in BMI-SDS reduction \( \geq 0.25 \) BMI-SDS in the adjusted model was similar to the effects of medical therapies like captopril in adults, while the effect of \( > 0.5 \) BMI-SDS reduction was superior (30). In summary, the improvements of the lipid profile and BP in BMI-SDS reduction \( \geq 0.25 \) were at least as clinically relevant as achievements by drug treatment, but without concerns about possible side-effects.

Of interest, the changes of LDL-cholesterol and fasting blood glucose over time were only weakly related to the degree of BMI-SDS reduction in the unadjusted models and not related in the adjusted models. Probably the change of dietary behavior may be more important for LDL-cholesterol levels than the degree of BMI-SDS reduction. Furthermore, LDL-cholesterol levels are determined predominately by the genetic background and not by weight status (31). Since fasting glucose was normal in the great majority of our children at baseline (\( > 97\% \)) this finding might explain the lack of significant association between blood glucose and BMI-SDS reduction. One could not expect an improvement of fasting glucose if this CRF is already normal at baseline.

**Methodological considerations**

Our study has some potential limitations. First, data from clinical samples may not be representative for general populations and selection and referral bias may have influenced our results. However, the distribution of lipids, glucose, and BP values in our study were similar to those reported from larger population-based studies or studies including different ethnicities (32, 33). Second, different ethnicities have to be studied separately, since CRFs also depend on race (34). Third, we had no untreated control group. This is of importance, since the phenomenon “regression to the mean” should be accounted for especially in those children with pathological CRFs at baseline. Accordingly, a study reported a normalization of lipids over time in children with hypercholesterolemia without any intervention (35). Therefore, our findings may overestimate the effect of BMI-SDS reduction on CRFs in children with hyperten-
sion or dyslipidemia. However, we have previously shown that children participating in the intervention “Obeldicks” were able to reduce their BMI-SDS and to improve their CRFs profile in contrast to an untreated control group both in a randomized controlled trail and in non randomized trials (11, 16, 17). Third, the observed changes of CRFs represented the effects of reduced caloric and fat intake as well as increased physical activity, which have been shown in an earlier study by the participants of the “Obeldicks” intervention (18). Since physical exercise, behavior therapy and nutritional education were performed together in the intervention group, we cannot distinguish the impact of each of them on the components of the MetS. Furthermore, the effects of dieting and increased physical activity probably strengthened each other. Physical activity and dieting improve dyslipidemia, BP, and insulin resistance (36).

Fourth, the HOMA model is only an indirect assessment of insulin resistance and clamp studies are the gold standard to analyze insulin resistance. Since the HOMA model correlated to clamp studies, it seems to be a suitable method to study insulin resistance in field studies even if HOMA values have no therapeutic value on the individual level (37). Additionally, we presented the triglyceride to HDL-cholesterol levels as an approximation of insulin resistance. Fifth, we have no data concerning the impact of BMI-SDS reduction on glucose tolerance in an oral glucose tolerance test (OGTT). Weiss and colleagues have recently reported that changes of weight were tightly related to change of glucose effectiveness measured in oGTT (38). Finally, defining success in lifestyle intervention should not only depend on improvement of CRFs but also on other factors such as improvement of health behavior as well as QOL. Interestingly, QOL improved in obese children participating in lifestyle interventions independent of the degree of BMI-SDS reduction (39, 40).

In summary, we observed that a BMI-SDS reduction ≥ 0.25 based on internationally accepted BMI-SDS values...
improved the CRFs summarized in the MetS. The effect of BMI-SDS reduction on CRFs was more pronounced in BMI-SDS reduction \(>0.5\) or in children with hypertension or dyslipidemia at baseline. The observed effect of BMI-SDS reduction on CRFs as shown in Table 2 and 3 might be useful to decide whether additional drug treatment besides lifestyle intervention is needed for a given CRFs to reach treatment goals.

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### References


