

# Changes in Lipidemia during Chronic Care Treatment of Childhood Obesity

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## Abstract

**Background:** Childhood obesity and related co-morbidities are increasing. This intervention study assessed the associations between weight changes and lipidemia in obese children and adolescents.

**Methods:** A total of 240 obese children and adolescents (median age, 11.3 years; range, 3.9–20.9) were enrolled in a best-practice multidisciplinary chronic care treatment program. The concentrations of total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TGs) and anthropometric data comprising height and weight were collected at baseline and after up to 39 months of continuous treatment.

**Results:** The BMI standard deviation score (SDS) decreased in 51% of patients and maintained unchanged in 32% of patients during the treatment. At baseline, 65 (27.1%) of the patients exhibited dyslipidemia defined as increased concentrations of total cholesterol ( $>200$  mg/dL), LDL ( $>130$  mg/dL), or TGs ( $>150$  mg/dL), or decreased HDL concentration ( $<35$  mg/dL). Dyslipidemia improved with weight loss; the odds ratio (OR) was 0.37 per BMI SDS ( $p = 0.014$ ) after adjusting for age, sex, and baseline BMI SDS. Baseline TG concentration correlated positively and HDL concentration correlated negatively with baseline BMI SDS. Weight loss was associated with a decrease in the concentrations of total cholesterol ( $p = 0.0005$ ), LDL ( $p < 0.0001$ ), non-HDL ( $p < 0.0001$ ), and TGs ( $p < 0.0001$ ), and with an increase in HDL concentration ( $p < 0.0001$ ).

**Conclusion:** High lipid concentrations were associated with childhood obesity. The lipid profile improved during weight loss independently of the baseline BMI SDS and baseline lipid concentration.

## Introduction

The prevalence of childhood obesity is increasing,<sup>1</sup> and obese children and adolescents are more likely to become obese adults.<sup>2,3</sup> Consequently, the prevalence of obesity-related cardiovascular abnormalities, such as insulin resistance, diabetes, fatty liver disease, hypertension, and dyslipidemia, is expected to increase in adults in the future.<sup>4–8</sup> A medical focus on dyslipidemia is expected to be increasingly important.<sup>9</sup>

Atherosclerotic cardiovascular disease is the leading cause of death in the modernized parts of the world, and the first stages of atherosclerosis begin in childhood.<sup>8,10</sup> The severity of the atherosclerotic lesions correlate positively with BMI, blood pressure, and the concentrations of total cholesterol, low-density lipoprotein (LDL), and triglycerides (TGs).<sup>11</sup> Elevated cholesterol concentration in young adults is an independent predictor of later

cardiovascular morbidity and mortality,<sup>12,13</sup> and recently non-high-density lipoprotein (non-HDL) has been identified as an important factor predicting cardiovascular risk.<sup>14</sup> Low HDL concentrations in both adolescence and adulthood also predict cardiovascular disease. The risk is amplified by the presence of other independent risk factors, such as age, sex, and smoking.<sup>13,15</sup>

Metabolic risk factors are present in up to 50% of obese children, and dyslipidemia was found in 32% of overweight children<sup>16</sup> and in 20% of 12- to 19-year-old Americans in the National Health and Nutrition Examination Survey (NHANES) study, which included a representative population.<sup>17</sup> Because metabolic risk factors can be identified in childhood<sup>4</sup> and can track into adulthood,<sup>18</sup> it is important to identify and treat children at risk to reduce their future obesity-related morbidity and mortality.

In a recent study in our childhood obesity treatment clinic, we found that 63% of obese children and adoles-

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cents, followed for an average of 9 months, reduced their BMI standard deviation score (SDS) with a relatively high retention rate, irrespective of baseline adiposity, age, and socioeconomic class.<sup>19</sup>

In the present study, we investigated concomitant changes in the BMI SDS and lipid profile in obese children and adolescents during our multidisciplinary chronic care intervention program. We investigated whether a reduction in BMI SDS was associated with an improvement in lipid levels, indicating an improved risk profile.

## Patients and Methods

### Study Population

This study included 240 children and adolescents from The Children's Obesity Clinic, Department of Pediatrics, Copenhagen University Hospital Holbæk, Denmark. Patients were included from January 1, 2008, to April 30, 2011. The inclusion criteria were age 3–21 years and BMI above the 90<sup>th</sup> percentile according to age and sex. There were no other prior eligibility criteria for inclusion in the treatment.<sup>19</sup>

Anthropometric data and blood samples were obtained at baseline. The children/adolescents provided at least one additional blood sample during treatment. The characteristics of the children at baseline are shown in Table 1. Blood samples and anthropometric data were obtained after up to 39 months of continuous treatment (median 12.9 months).

Informed written consent was obtained from parents and from patients aged 18 years and older. The study received ethical approval by the ethics committee of Region Zealand, Denmark (ID no. SJ-104) and was performed in accordance with the Helsinki Declaration.

### Blood Samples

Venous blood samples were drawn from the antecubital vein between 7 a.m. and 9 a.m. after an overnight fast. If required, a local anesthetic cream was applied 1 hour before the blood sampling. The blood was analyzed immediately after venipuncture. Total cholesterol, HDL, and TG concentrations were measured by enzymatic colorimetric methods on a Cobas 6000® analyzer (Roche Diagnostics, Rotkreutz, Switzerland). LDL concentration was calculated using the values of total cholesterol, HDL, and TGs, and non-HDL using the values of total cholesterol and HDL.

### Reference Values for Lipids

In the present study, dyslipidemia was defined as a total cholesterol concentration >200 mg/dL, HDL concentration <35 mg/dL, LDL concentration >130 mg/dL, or TG concentration >150 mg/dL according to reference guidelines.<sup>20,21</sup>

### Anthropometry

Anthropometric measurements were obtained with the patient wearing light indoor clothing with empty pockets and without shoes. Weight was measured to the nearest

**Table 1. Characteristics of Obese Children and Adolescents Entering Childhood Obesity Treatment at Baseline and at the Latest Treatment Contact**

	Baseline			Latest Treatment Contact		
	Total Median (range)	Boys Median (range)	Girls Median (range)	Total Median (range)	Boys Median (range)	Girls Median (range)
N	240	113	127	240	113	127
Age (years)	11.3 (3.9–20.9)	11.5 (5.2–20.9)	11.1 (3.9–19.9)	12.6 (5.5–22.8)	12.5 (6.5–22.8)	12.6 (5.5–20.8)
Height (m)	1.51 (1.10–1.95)	1.51 (1.16–1.95)	1.50 (1.10–1.80)	1.58 (1.17–1.97)	1.59 (1.24–1.97)	1.58 (1.17–1.80)
Weight (kg)	58.1 (25.9–155.2)	60.4 (27.3–155.2)	56.7 (25.9–133.6)	64.1 (31.5–176.0)	65.8 (31.5–176.0)	63.2 (31.5–152.2)
BMI SDS	2.96 (1.17–5.54)	3.26 (1.39–5.54)	2.79 (1.17–4.51)	2.78 (0.73–5.36)	2.97 (0.73–5.36)	2.63 (1.05–4.20)
Total cholesterol (mg/dL)	162 (88–438)	158 (88–265)	165 (96–438)	159 (84–342)	157 (84–223)	161 (88–342)
LDL (mg/dL)	96 (38–354)	96 (38–188)	96 (38–353)	92 (34–269)	92 (34–146)	96 (38–269)
HDL (mg/dL)	46 (15–88)	46 (23–88)	46 (15–69)	46 (23–80)	46 (23–80)	46 (23–69)
Non-HDL (mg/dL)	115 (42–423)	111 (42–219)	115 (61–423)	112 (46–300)	111 (46–184)	111 (50–300)
TG (mg/dL)	88 (26–380)	79 (27–362)	97 (35–380)	79 (26–354)	79 (26–300)	88 (26–354)

BMI SDS, Body mass index standard deviation score; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglyceride.

0.1 kg on a Tanita Digital Medical Scale (WB-100 MA, Tanita Corp., Tokyo, Japan). Height was measured by stadiometer to the nearest 1 mm. BMI was calculated as weight in kilograms divided by height in meters squared ( $\text{kg/m}^2$ ). The BMI SDS was calculated by the least mean squares (LMS) method by transforming BMI into a normal distribution for each sex and age according to the Danish BMI charts.<sup>22</sup>

### Intervention

The Children's Obesity Clinic encompasses a full multidisciplinary best-practice tertiary team including pediatricians, nurses, dietitians, psychologists, research technicians, social workers, and secretaries.<sup>19</sup> The clinic tailors an individual treatment program for each child/adolescent and family that comprises 10–20 recommendations as part of a comprehensive advice strategy; these include items such as consideration of eating disturbances, sugar dependency, physical activity and inactivity, sources of nutrition, psychosocial functioning, and more.<sup>19</sup>

At each visit, the plan was modified according to the needs of, and in collaboration with, the individual child/adolescent and his/her family.<sup>19</sup> On average, consultations occurred 6.4 weeks apart, and 5.4 hours were invested in each patient per year.<sup>19</sup>

At baseline, interviews regarding activity and inactivity were conducted, and from these a physical activity score (PAS), including hours spent each week both on organized sports and unorganized activities such as trampoline jumping, walking and outdoor playing, and a physical inactivity score (PIS), including weekly hours spent in front of computer or television, was calculated. Activities considered to represent a lower physical activity level, *i.e.*, unorganized play and bowling, were reduced by 50% in calculation of the PAS.<sup>23</sup> The objective of the PAS and PIS was to test whether physical activity and inactivity influenced the lipid levels.

### Statistical Analysis

The lipid values were logarithmically transformed to achieve a normal distribution. Both at the baseline and at the latest treatment contact, the associations between BMI SDS, age, sex, and lipid values and the response to treatment were investigated using analysis of variance (ANOVA) comparing the groups decreasing, maintaining, or increasing BMI SDS during treatment. Dyslipidemia was analyzed using logistic regression. The relationships between BMI SDS and lipid concentrations at the baseline and again at the latest treatment contact were analyzed using linear regression adjusted for age and sex. The relationships between the changes in BMI SDS and changes in lipid values were analyzed using linear regression of the changes in the logarithmically transformed lipid values on the changes in BMI SDS adjusted for the baseline logarithmically transformed lipid values, baseline BMI SDS, age, sex, and time between the baseline and the latest treatment contact.

## Results

A total of 240 obese children and adolescents (127 girls) with a median age of 11.3 years (range, 3.9–20.9 years) were enrolled in the treatment and were evaluated at the baseline and after up to 39 months of continuous treatment (see Table 1). The total cumulative treatment period was 307.6 patient years, and the median treatment period was 12.9 months (1.08 years).

The children and adolescents were divided into three groups according to achieved changes in BMI SDS during the study: Group 1, decreasing BMI SDS more than 0.15 units; group 2, maintaining BMI SDS  $\pm$  0.15 units; and group 3, increasing BMI SDS more than 0.15 units. A total of 123 (51%) children decreased their BMI SDS, whereas 40 (17%) children increased their BMI SDS and 77 (32%) maintained a constant BMI SDS. The baseline BMI SDS was significantly higher in the groups maintaining and decreasing their BMI SDS during treatment ( $p = 0.03$ ). Age, sex, and lipid concentrations did not differ between the three groups and did not predict the changes in weight. The characteristics of the three groups at baseline are shown in Table 2.

The PIS at baseline was associated with 2.3% higher total cholesterol [95% confidence interval (CI) 0.2–4.5,  $p = 0.031$ ], 4.1% higher non-HDL cholesterol (95% CI 0.1–7.3,  $p = 0.010$ ), and 8.1% higher TG (95% CI 1.7–15.0,  $p = 0.013$ ) for each 10 points higher PIS adjusted for sex and BMI SDS. No significant association was found between PAS and lipid values, or between PIS and HDL or LDL.

### Dyslipidemia

At baseline, 65 (27.1%) of the children and adolescents exhibited dyslipidemia, defined as a high concentration of total cholesterol, LDL, or TG or low HDL concentration. At the latest treatment contact, 62 (25.8%) had dyslipidemia; 26 of these were new cases and 29 of the initial group no longer met the criteria for dyslipidemia. The children were on average 15 months older at their latest treatment contact. Both at the baseline and at the latest treatment contact, BMI SDS and the risk of dyslipidemia were positively associated. The odds ratio (OR) for dyslipidemia at baseline was 1.62 per unit of BMI SDS (95% CI 1.02–2.57,  $p = 0.04$ ), and the OR at the latest patient contact was 1.90 per unit of BMI SDS (95% CI 1.27–2.86,  $p = 0.002$ ). Weight loss was significantly associated with a reduced risk of dyslipidemia (OR = 0.37 per unit of BMI SDS lost; 95% CI 0.17–0.82,  $p = 0.014$ ) adjusted for sex, age, and baseline BMI SDS.

### Total Cholesterol Concentration

Twenty-six (10.8%; 12 boys/14 girls) had elevated levels of cholesterol at baseline. Total cholesterol concentration was not significantly related to levels of BMI SDS at baseline. However, at the latest treatment contact, total cholesterol concentration was 3.8% lower per unit

of BMI SDS lower (95% CI 0.6–7.0,  $p = 0.02$ ). During treatment, there was a positive association between the changes in total cholesterol concentration and BMI SDS. After adjusting for age, sex, and baseline total cholesterol concentration and BMI SDS, total cholesterol concentration decreased by 6.6% with each unit of BMI SDS lost (95% CI 2.8–10.4,  $p = 0.0005$ ). The association between the relative changes in total cholesterol concentration and changes in BMI SDS is illustrated in Figure 1. Total cholesterol was significantly lower at the latest treatment contact in the groups decreasing or maintaining their BMI SDS than in the group increasing their BMI SDS (see Table 3).

### LDL Concentration

At baseline 23 (9.5%; 11 boys/12 girls) children had elevated levels of LDL cholesterol (LDL-C). LDL-C concentration did not correlate significantly with the BMI SDS at baseline (0.5% higher LDL per unit of BMI SDS; 95% CI  $-0.8$ – $6.8$ ,  $p = 0.88$ ). However, at the latest treat-

ment contact, LDL concentration was on average 6.0% lower per unit of BMI SDS lower (95% CI 1.2–11.1,  $p = 0.014$ ). During treatment, a one-unit reduction in BMI SDS was associated with a 12.6% reduction in LDL concentration (95% CI 6.7–18.9,  $p < 0.0001$ ) after adjusting for age, sex, and baseline LDL concentration and BMI SDS. The association between the relative changes in LDL concentration and changes in BMI SDS is illustrated in Figure 2. The LDL concentration was significantly lower at the latest treatment contact in the group decreasing BMI SDS than in the group increasing BMI SDS (see Table 3).

### HDL Concentration

At baseline 15 (6.3%; 7 boys/8 girls) had reduced levels of HDL. HDL concentration and BMI SDS were inversely associated; HDL was 8.3% lower with each unit of BMI SDS higher (95% CI 3.5–13.0,  $p = 0.0005$ ). At the latest treatment contact, HDL concentration was on average 7.9% higher with each unit of BMI SDS lower (95%

**Table 2. Baseline Characteristics for Group 1 (BMI SDS Decreasing by More Than 0.15), Group 2 (Maintaining BMI SDS  $\pm$  0.15), and Group 3 (Increasing BMI SDS by More Than 0.15)**

	Group 1			Group 2			Group 3		
	Total Median (range)	Boys Median (range)	Girls Median (range)	Total Median (range)	Boys Median (range)	Girls Median (range)	Total Median (range)	Boys Median (range)	Girls Median (range)
N	123	68	55	77	31	46	40	14	26
Age (years)	11.3 (3.9–20.9)	11.5 (5.2–20.9)	10.7 (3.9–16.9)	11.1 (5.3–19.8)	11.0 (5.3–16.3)	11.4 (6.0–19.8)	12.3 (5.5–19.9)	10.9 (5.5–15.7)	14.0 (6.0–19.9)
Height (m)	1.51 (1.10–1.88)	1.52 (1.18–1.88)	1.48 (1.10–1.74)	1.49 (1.16–1.93)	1.48 (1.16–1.93)	1.54 (1.21–1.78)	1.52 (1.16–1.95)	1.48 (1.16–1.95)	1.57 (1.16–1.80)
Weight (kg)	56.7 (26.2–123.3)	59.3 (27.9–123.3)	56.0 (26.2–114.1)	61.3 (27.3–155.2)	61.7 (27.3–155.2)	60.1 (29.6–130.6)	60.9 (25.9–136.2)	58.8 (31.6–136.2)	61.7 (25.9–133.6)
BMI SDS	2.94* (1.58–5.54)	3.22 (1.58–5.54)	2.73** (1.96–4.51)	3.06* (1.39–4.31)	3.41 (1.39–4.31)	3.03** (1.72–4.25)	2.75* (1.17–5.12)	3.06 (2.18–5.12)	2.36** (1.17–3.72)
Total Cholesterol (mg/dL)	162 (96–438)	158 (104–238)	169 (96–438)	158 (88–265)	154 (88–265)	162 (100–231)	165 (104–262)	165 (131–262)	165 (104–253)
LDL (mg/dL)	96 (38–354)	94 (50–162)	96 (38–354)	96 (38–185)	96 (38–185)	96 (46–150)	101 (54–188)	104 (54–188)	100 (54–169)
HDL (mg/dL)	46 (15–73)	46 (23–73)	42 (15–62)	46 (23–88)	42 (27–88)	46 (23–69)	50 (27–73)	50 (34–73)	44 (27–69)
Non-HDL (mg/dL)	115 (62–423)	112 (62–181)	119 (62–423)	112 (42–212)	108 (42–212)	112 (65–188)	119 (62–219)	119 (69–219)	121 (62–212)
TG (mg/dL)	88 (27–363)	71 (27–363)	106 (35–354)	97 (27–336)	88 (27–327)	102 (35–336)	84 (35–381)	93 (62–212)	80 (35–380)
N	58	33	25	29	11	18	20	7	13
PAS	1.5 (0–10.0)	2.0 (0–10.0)	1.0 (0–4.0)	1.2 (0–10.0)	1.2 (0–5.0)	1.5 (0–10.0)	0.1 (0–4.0)	0.1 (0–3.6)	0 (0–4.0)
PIS	14.0 (0–63.0)	14.0 (0–63.0)	14.0 (0–42.0)	14.0 (0–49.0)	14.0 (0–49.0)	14.0 (0–42.0)	10.5 (0–63.0)	35.0 (0–63.0)	0 (0–42.0)

$p$  values describing analyses of variance.

\* $0.05 > p \geq 0.01$ . \*\* $0.01 > p \geq 0.001$ .

BMI SDS, Body mass index standard deviation score; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PAS, physical activity score; PIS, physical inactivity score; TG, triglyceride.

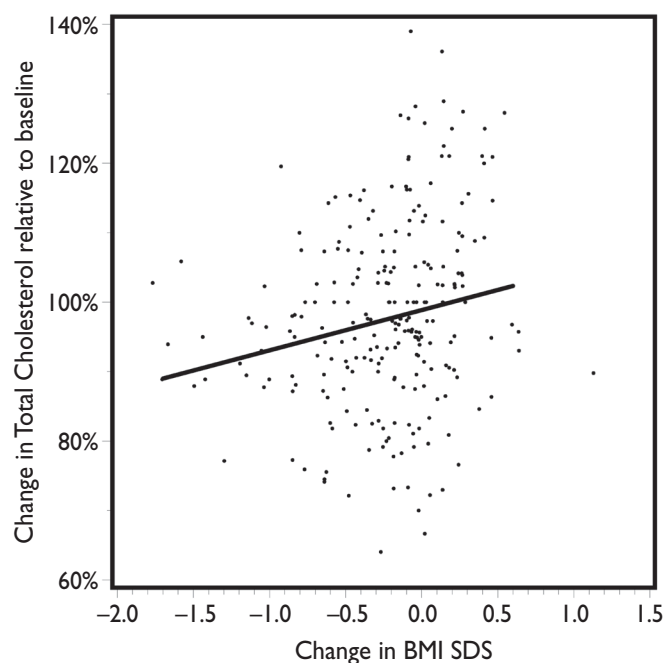


Figure 1. Relative changes in lipid concentrations and changes in BMI standard deviation score (SDS) during childhood obesity treatment. Total cholesterol concentration and BMI SDS.  $n = 240$ ,  $r^2 = 3.9\%$ ,  $p = 0.002$ .

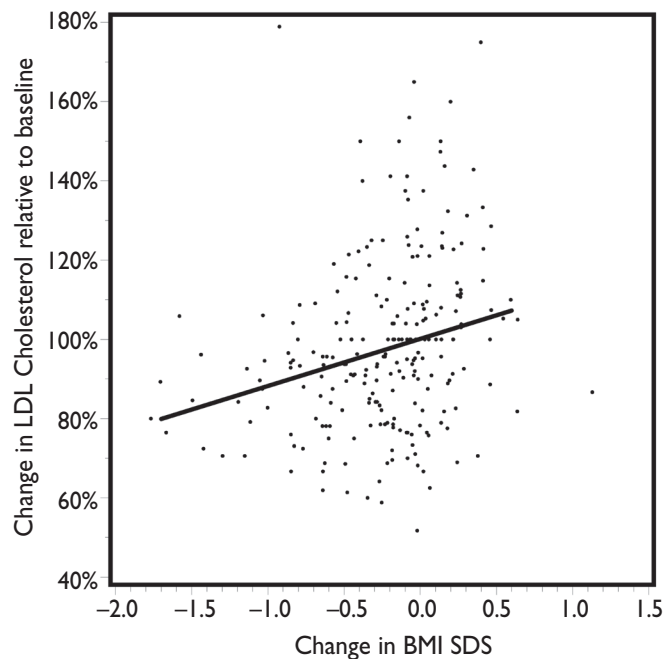


Figure 2. Relative changes in lipid concentrations and changes in BMI standard deviation score (SDS) during childhood obesity treatment. Low-density lipoprotein (LDL) concentration and BMI SDS.  $n = 240$ ,  $r^2 = 7.2\%$ ,  $p < 0.0001$ .

**Table 3. Characteristics at the Latest Treatment Contact for Group 1 (BMI SDS Decreasing by More Than 0.15), Group 2 (Maintaining BMI SDS  $\pm 0.15$ ), and Group 3 (Increasing BMI SDS by More Than 0.15)**

	Group 1			Group 2			Group 3		
	Total Median (range)	Boys Median (range)	Girls Median (range)	Total Median (range)	Boys Median (range)	Girls Median (range)	Total Median (range)	Boys Median (range)	Girls Median (range)
N	123	68	55	77	31	46	40	14	26
Age (years)	12.5 (5.5–22.8)	12.7 (7.2–22.8)	12.5 (5.5–18.6)	12.6 (6.6–20.8)	12.2 (6.6–18.2)	13.1 (7.0–20.8)	14.0 (6.5–20.8)	12.0 (6.5–17.8)	15.0 (6.9–20.8)
Height (m)	1.58 (1.17–1.88)	1.61 (1.30–1.88)	1.57 (1.17–1.76)	1.53 (1.25–1.94)	1.53 (1.25–1.94)	1.55 (1.28–1.80)	1.62 (1.24–1.97)	1.58 (1.24–1.97)	1.62 (1.30–1.80)
Weight (kg)	61.6 (31.5–119.4)	63.5 (31.5–119.4)	60.1 (31.5–102.8)	69.4 (32.8–163.3)	70.6 (32.8–163.3)	68.1 (36.8–137.6)	69.1 (36.4–176.0)	76.9 (40.6–176.0)	69.0 (36.4–152.2)
BMI SDS	2.37 (0.73–5.36)	2.71 (0.73–5.36)	2.28 (1.05–3.74)	3.04 (1.42–4.33)	3.34 (1.42–4.33)	2.99 (1.63–4.20)	3.07 (1.40–5.36)	3.44 (2.82–5.36)	2.76 (1.40–3.93)
Total cholesterol (mg/dL)	153 ** (88–342)	153 (100–219)	150 ** (88–342)	165** (84–223)	161 (84–223)	165** (96.2–219.2)	176** (111–265)	171 (142–211)	180** (111–265)
LDL (mg/dL)	88 ** (38–269)	92 (30–80)	84* (23–269)	92** (34–150)	88 (34–142)	96* (53–150)	103** (57–173)	101 (76–146)	103* (57–173)
HDL (mg/dL)	46 (23–80)	46* (30–80)	50 (23–65)	46 (23–69)	42* (23–65)	46 (26–69)	46 (26–65)	46* (26–57)	50 (30–65)
Non-HDL (mg/dL)	104 ** (50–300)	108* (54–185)	104 ** (50–300)	112 ** (46–173)	119* (46–169)	112 ** (62–173)	131 ** (73–215)	129 ** (88–181)	131* (73–215)
TG (mg/dL)	70 ** (26–283)	70* (26–283)	70* (26–274)	97** (35–354)	97* (35–300)	97* (35–354)	115** (44–336)	115* (53–221)	119* (44–336)

$p$  values describing analyses of variance.

\* $0.05 > p \geq 0.01$ . \*\* $0.01 > p \geq 0.001$ .

BMI SDS, Body mass index standard deviation score; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglyceride.

CI 4.3–11.6;  $p < 0.0001$ ). During treatment, the change in BMI SDS was associated with the change in HDL concentration; HDL concentration increased by 11.7% with each reduced unit of BMI SDS (95% CI 6.3–17.4,  $p < 0.0001$ ) after adjusting for age, sex, and baseline HDL concentration and BMI SDS. The association between the relative changes in HDL concentration and changes in BMI SDS is illustrated in Figure 3. There was no significant difference in the levels of HDL between the three groups at the latest treatment contact (see Table 3).

### Non-HDL Concentration

Non-HDL cholesterol concentration at the latest treatment contact was on average 9.3% lower per unit of BMI SDS lower (95% CI 4.7–14.2,  $p < 0.0001$ ). Non-HDL at baseline was not significantly related to baseline BMI SDS. During treatment, a one-unit reduction in BMI SDS was associated with a 15.1% reduction in non-HDL concentration (95% CI 10.1–20.3,  $p < 0.0001$ ) after adjusting for age, sex, and baseline values of non-HDL and BMI SDS. The association between the relative changes in non-HDL and BMI SDS is illustrated in Figure 4. Values of non-HDL were significantly lower at the latest treatment contact in the group decreasing BMI SDS than in the group increasing BMI SDS (see Table 3).

### TG Concentration

At baseline 42 (17.5%; 14 boys/28 girls) had elevated levels of TGs. The TG concentration at baseline was positively associated with BMI SDS; TG concentration on average was 22.0% higher per unit of BMI SDS (95%

CI 10.4–34.8;  $p = 0.0001$ ). At the latest treatment contact, TG concentration was 26.0% lower per unit of BMI SDS lower (95% CI 16.6–36.2,  $p < 0.0001$ ). During treatment, the TG concentration was reduced by 32.3% for each BMI SDS unit lost (95% CI 17.7–48.7,  $p < 0.0001$ ) after adjusting for age, sex, and baseline TG concentration and BMI SDS. The association between the relative changes in TG concentration and changes in BMI SDS is illustrated in Figure 5. The TG concentration at the latest treatment contact was significantly lower in the group decreasing the BMI SDS than in the group increasing the BMI SDS (see Table 3).

## Discussion

The present intervention study measured lipid concentrations in a cohort of 240 obese children and adolescents treated prospectively for up to 39 months in a multidisciplinary, best-practice, tertiary childhood obesity treatment program.<sup>19</sup> This study showed a prevalence of 27.1% for dyslipidemia, defined as an increased concentration of total cholesterol, LDL, or TG, or decreased HDL concentration in obese children and adolescents at baseline. This prevalence is similar to that reported in both the NHANES study<sup>17</sup> and the study by l'Allemand et al.<sup>24</sup>

In the present study, BMI SDS decreased in 51% of patients, and this reduction had a positive effect on the lipid profile, as shown by reductions in the concentrations of total cholesterol, LDL, non-HDL, and TG, and increased HDL concentration.

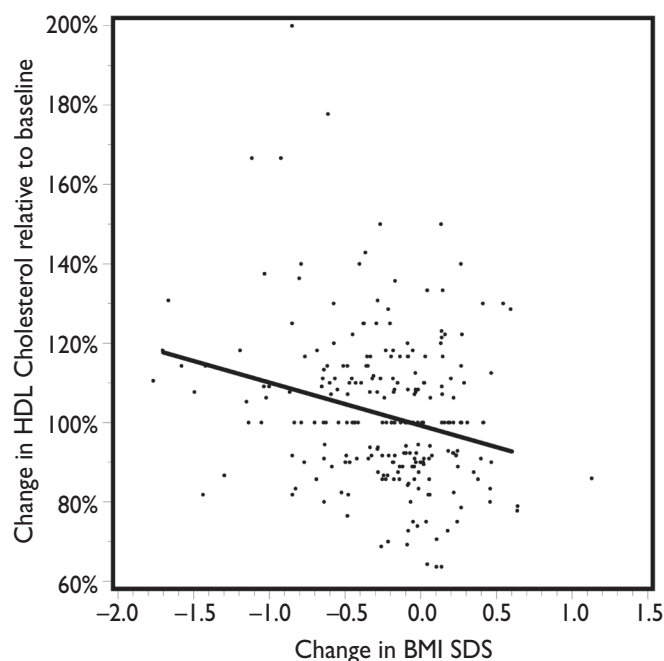


Figure 3. Relative changes in lipid concentrations and changes in BMI standard deviation score (SDS) during childhood obesity treatment. High-density lipoprotein (HDL) concentration and BMI SDS.  $n = 240$ ,  $r^2 = 6.8\%$ ,  $p < 0.0001$ .

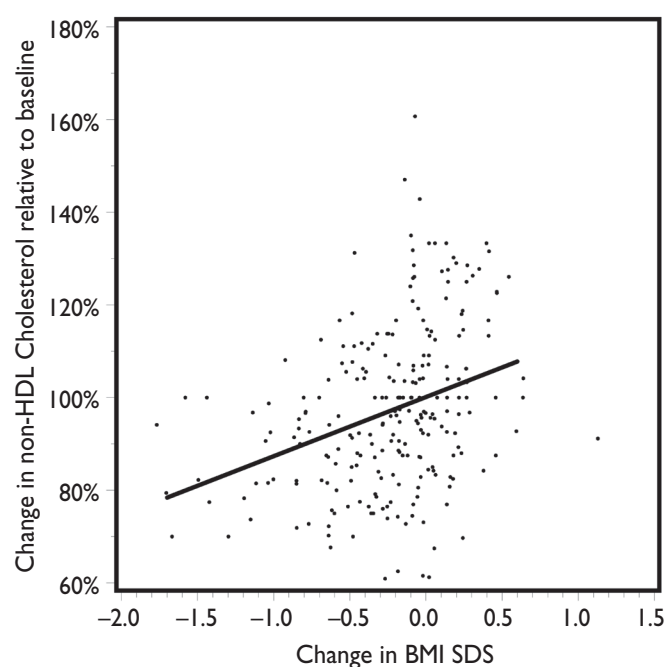


Figure 4. Relative changes in lipid concentrations and changes in BMI standard deviation score (SDS) during childhood obesity treatment. Non-high-density lipoprotein (HDL) concentration and BMI SDS.  $n = 240$ ,  $r^2 = 11.6\%$ ,  $p < 0.0001$ .

The patients were divided into three groups to ascertain whether weight loss was associated with the resultant lipid concentrations. The baseline lipid concentrations did not differ between the three groups. This suggests that obese children and adolescents derive benefits from chronic care treatment for obesity regardless of their baseline lipid concentrations. The most obese were less inclined to gain weight. At the latest treatment contact, the group with decreasing BMI SDS exhibited a healthier lipid status compared with both the group maintaining BMI SDS and the group increasing BMI SDS, indicating that response to treatment of childhood obesity was associated with an improved lipid status. The group maintaining their BMI SDS exhibited healthier lipid status compared to the group increasing their BMI SDS. Some of the children maintaining and increasing their BMI SDS even reduced their lipid levels, suggesting that improvements in lipid status precede improvements in BMI SDS. These results also suggest that this subgroup may have experienced a favorable change in body composition, possibly an increase in muscle mass, which would have increased the BMI SDS. However, this could not be confirmed because body composition was not measured in the present study.

At baseline, TG concentration and BMI SDS were positively associated, and HDL concentration and BMI SDS were inversely associated. These observations agree with those of the cross-sectional multicenter study of 26,008 overweight or obese European children by l'Allemand et al.<sup>24</sup> However, during treatment, the changes in BMI SDS were positively associated with the changes in concentra-

tions of total cholesterol, LDL, non-HDL, and TG, and negatively with the change in HDL concentration in the present study. In comparison, Reinehr et al. reported an improvement in LDL during a 1-year lifestyle intervention in 288 obese children aged 10–16 years with a mean BMI SDS of 2.48 despite no changes in TG or HDL concentrations.<sup>25</sup> The present study included fewer patients, but they had a higher mean BMI SDS, and we followed them for a longer treatment period, during which many patients lost weight, which may have caused the improvement in the lipid profile.

We found a positive association, both at baseline and at the latest treatment contact, between BMI SDS and the risk of dyslipidemia, which was independent of age and sex. Dyslipidemia improved during treatment after adjusting for baseline BMI SDS, age, and sex. Other studies have found that TG concentration increases with age, that total cholesterol and LDL concentrations increase after puberty, and that HDL concentration either remains stable or decreases during puberty.<sup>26,27</sup> Because the population in the present study was older at the latest treatment contact, our finding of improved lipid levels suggests a masked beneficial effect of the childhood obesity program.

We were unable to analyze the age-dependent distributions of lipids because this was not an epidemiological survey and we did not have normal weight controls to compare with. The effect of the age-dependent increase in the prevalence of dyslipidemia may also be suggested by the finding that half of those with dyslipidemia at the latest treatment contact comprised new cases and a similarly sized group no longer exhibited dyslipidemia in the present study. A limitation to the present study was that indices of puberty were not accounted for during childhood obesity treatment. This would have been informative regarding whether changes and the overall level in lipids over time were influenced by pubertal development. Normative data show that total cholesterol and LDL, especially for males, are anticipated to decrease from childhood to adolescence with a nadir around the age of 15 years and then increase again, and HDL is anticipated to decrease in males and remain stable in females.<sup>26</sup> Median age in this study was 11.9, making some of the observed effect of the decreased lipids (and increased HDL) prone to a natural pubertal development effect.

Magnussen et al. showed that lifestyle changes comprising exercise and healthier nutrition in childhood and adolescence have a positive effect on lipid levels in adulthood and thus seem to decrease the cardiovascular risk.<sup>28</sup> Unfortunately, we did not collect specific information about nutrition and exercise during the present study. However, at baseline we did estimate physical activity and inactivity as PAS and PIS. We did not find any association between our baseline values of lipids and PAS, but higher PIS was associated with higher total cholesterol, non-HDL, and TG, suggesting that inactivity does predispose to elevated lipid levels. We did not record these scores during treatment and therefore are not able to see

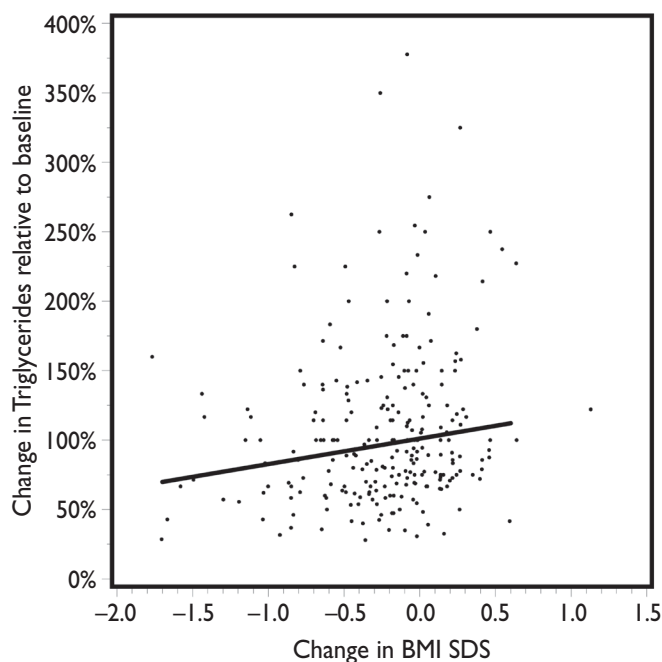


Figure 5. Relative changes in lipid concentrations and changes in BMI standard deviation score (SDS) during childhood obesity treatment. Triglyceride (TG) concentration and BMI SDS.  $n = 240$ ,  $r^2 = 3.6\%$ ,  $p = 0.0035$ .

which effect increasing activity or decreasing inactivity has on lipids independent of dietary adjustments, as these changes were commenced simultaneously.

There are several limitations. We believed it was unethical to initiate a control group of obese children who received no treatment. Instead, each child was used as his/her own control in the analysis of the changes in lipids during the intervention. Children and adolescents were included in the study if they had at least two blood samples taken, which filtered the effects of loss of subjects, because some dropped out prior to the second blood sample. Therefore, our results preclude any conclusions about how retention rate is associated with the effects of a childhood obesity intervention on the lipid profile. However, this was not the primary intention; instead, we sought to analyze how weight changes *per se* are associated with changes in lipid concentrations.

One study has found that waist circumference (WC) is a better predictor than BMI of cardiovascular risk factors,<sup>29</sup> whereas another study has found that BMI correlates more strongly than WC with dyslipidemia.<sup>30</sup> Other studies have shown a combined effect of both BMI and WC.<sup>31,32</sup> Including WC in our analyses may have improved our study, but our main objective was to evaluate the effect of response to childhood obesity treatment on the lipid profile. The primary strengths of the present study are that a relatively large number of patients were followed for 308 patient-years in an efficient childhood obesity treatment program that showed robust beneficial changes in lipid concentrations. Regression toward the mean may have influenced our results, but this is less likely because the baseline concentrations of lipids were compared with the changes in lipids and not just the later concentrations. In addition, those who responded to treatment exhibited larger changes in the lipid profile than did those who did not respond, suggesting a direct effect of weight loss induced by obesity treatment upon lipid levels rather than regression towards the mean. Improved lipid profiles attained during childhood obesity intervention may help reduce cardiovascular risk if a beneficial lipid profile is maintained over the long term.<sup>7</sup>

## Conclusion

High concentrations of lipids were reduced with weight loss during a multidisciplinary childhood obesity chronic care treatment program. Treatment strategies should focus on persistent weight loss to prevent hyperlipidemia in obese children and adolescents and thereby counter future cardiovascular disease.

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## Author Disclosure Statement

No competing financial interests exist.

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