ABSTRACT
Background: Conjugated linoleic acid (CLA) is a supplemental dietary fatty acid that decreases fat mass accretion in young animals.

Objective: The aim of this study was to determine CLA’s efficacy with regard to change in fat and body mass index (BMI; in kg/m²) in children.

Design: We conducted a 7 ± 0.5-mo randomized, double-blind, placebo-controlled trial of CLA in 62 prepubertal children aged 6–10 y who were overweight or obese but otherwise healthy. The subjects were randomly assigned to receive 3 g/d of 80% CLA (50:50 cis-9,trans-11 and trans-10,cis-12 isomers) or placebo in chocolate milk.

Results: Fifty-three subjects completed the trial (n = 28 in the CLA group, n = 25 in the placebo group). CLA attenuated the increase in BMI (0.5 ± 0.8) compared with placebo (1.1 ± 1.1) (P = 0.05). The percentage change in body fat measured by dual-energy X-ray absorptiometry was smaller (P = 0.001) in the CLA group (−0.5 ± 2.1%) than in the placebo group (1.3 ± 1.8%). The change in abdominal body fat as a percentage of total body weight was smaller (P = 0.02) in the CLA group (−0.09 ± 0.9%) than in the placebo group (0.43 ± 0.6%). There were no significant changes in plasma glucose, insulin, or LDL cholesterol between groups. Plasma HDL cholesterol decreased significantly more (P = 0.05) in the CLA group (−5.1 ± 7.3 mg/dL) than in the placebo group (−0.7 ± 8 mg/dL). Bone mineral accretion was lower (P = 0.04) in the CLA group (0.05 ± 0.03 kg) than in the placebo group (0.07 ± 0.03 kg). Reported gastrointestinal symptoms did not differ significantly between groups.

Conclusions: CLA supplementation for 7 ± 0.5 mo decreased body fatness in 6–10-y-old children who were overweight or obese but did not improve plasma lipids or glucose and decreased HDL more than in the placebo group. Long-term investigation of the safety and efficacy of CLA supplementation in children is recommended. Am J Clin Nutr 2010;91:1157–64.

INTRODUCTION
Childhood obesity rates in the United States have been on the rise since 1960. In 2003–2006, 17% of all 6–11-y-old children in the United States were considered obese, an increase from 15% in 1999–2000 (1). Obesity during childhood is associated with a high probability of obesity in adulthood (1–4) and is also associated with a large array of health problems later in life, including an increased risk of coronary heart disease (5), hypertension, and diabetes (6). Whereas much research is being performed to identify the numerous factors that contribute to childhood as well as adult obesity, a great deal is also being done to try to reverse the increasing trends of weight gain and obesity. Of these is the use of conjugated linoleic acid (CLA) as an oral supplement and food ingredient. As recently reviewed, CLA supplementation has shown a beneficial effect on percentage body fat in healthy adults (7). The meta-analysis of the large number of adult studies found that the weight reduction observed during CLA supplementation consisted largely of fat and was dose dependent. The total weight loss was also relatively modest, reaching a group average of slightly more than 2 kg after treatments of ≥1 y (7).

CLA is a naturally occurring polyunsaturated 18-carbon compound most commonly present in dairy and beef products, but it is also found in other ruminant and nonruminant sources. It is naturally synthesized from linoleic acid by ruminant animals (8); however, human dietary intake from these sources is estimated at 0.1–1.1% of ruminant animal fat leading to possible total intakes of 130–440 mg/d (9). For larger doses, CLA can be commercially prepared from plant oils containing high amounts of linoleic acid. There are many CLA isomers. The most common naturally occurring in dairy fat and meat from ruminant animals is the cis-9, trans-11c9,r11 isomer (9). The cis-9, trans-11 and trans-10, cis-12 (t10,c12) can also be commercially synthesized from linoleic acid–rich oils such as sunflower and safflower oil (10). These are considered the most physiologically active isomers, and the 50:50 mixture has been shown to be the most effective for weight management or body fat reduction (11). The first studies to identify the antiadiposity characteristics of CLA were performed in laboratory animals (12). The t10,c12 isomer was found to be more effective as an antiadiposity agent, but this isomer caused a slight increase in insulin resistance (13), which

1 From the Department of Nutritional Sciences, University of Wisconsin–Madison, Madison, WI (NMR, ACW, ARO, and DAS); the School of Medicine and Public Health, University of Wisconsin–Madison, Madison, WI (ALC, DBA, JM, and RRC); and Lipid Nutrition, BV Wormerveer, Netherlands (CES and MO).

2 Supported by a grant from Lipid Nutrition BV, Wormerveer, Netherlands, and the NIH-supported Clinical and Translational Research Core at the University of Wisconsin Hospital (RR025011). CLA and placebo were provided by Lipid Nutrition.

3 Address correspondence to DA Schoeller, 1415 Linden Drive, Madison, WI 53706. E-mail: dschoell@nutrisci.wisc.edu.

generally was not observed when both the $c_9, t_{11}$ and $t_{10}, c_{12}$ isomers were given together (14).

Not only did the studies in laboratory animals show the efficacy of CLA for fat loss, they also showed that the antiadiposity characteristics of CLA were stronger in young animals during growth than in mature animals (15, 16). Because of this, it is important to perform similar efficacy trials in children.

The hypothesis of the current study was that a 50–50 mixture of $c_9, t_{11}$ and $t_{10}, c_{12}$ CLA supplementation would improve measures of body mass index (BMI) and body composition in overweight and obese children in a randomized placebo-controlled trial. The aims of this study also included assessment of safety, including blood chemistry tests, and generalized well-being.

SUBJECTS AND METHODS

Subjects

Subjects were recruited from the Madison metropolitan area largely through recruitment flyers. Eligible participants were 6–10-y-old children with a BMI at or above the 85th percentile (17) at the time of screening. The exclusion criteria included Tanner stage 2 and beyond, any history of metabolic disease, excessive fear of a blood draw, claustrophobia, and an extreme dislike of the taste of the treatment delivery beverage. Subjects were also excluded if their fasting blood chemistry values at screening exceeded the following: glucose $>110$ mg/dL, insulin $>45$ μIU/mL, LDL $>160$ mg/dL, total cholesterol $>240$ mg/dL, triglycerides $>200$ mg/dL, aspartate aminotransferase (AST) $>40$ U/L and $>50$ U/L (males age 10 y), alanine aminotransferase (ALT) $>65$ U/L, and $\gamma$-glutamyl transferase (GGT) $>30$ U/L. The study was approved by the Health Sciences Institutional Review Board of the University of Wisconsin–Madison. The parents or guardians signed an informed consent form, and the subjects signed a minor assent form before screening.

The parents of 92 subjects indicated a willingness to participate, and the children were screened for eligibility. Of the 92 screened subjects, 72 were eligible to participate. Of these, 62 (36 boys and 26 girls) agreed to participate and were randomly assigned to receive CLA or placebo (sunflower oil) (Figure 1). Randomized was achieved by using a stratified design according to sex (male or female), BMI percentile (<95th or $\geq$95th percentile), and then age (< 9.5 or $\geq$9.5 y) (Table 1). Criteria for completion included consumption of 75% of the milk provided and return for outcome measures scheduled at follow-up.

Protocol

All procedures followed were in accordance with the ethical standards of the University of Wisconsin Health Sciences Institutional Review Board. During screening, BMI was calculated to determine eligibility. The subjects’ parents or guardians provided a medical history, and subjects underwent a physical examination during a meeting with a University of Wisconsin Hospital pediatric endocrinologist, including the assessment of Tanner stage. A short nutrition education session was held with a registered dietitian. This session included describing a food guide pyramid, making healthy choices, trying new foods, and presenting ideas to parents on including children in the preparation of healthy meals.

The subjects were then seen at the Exercise Science Laboratory of the University of Wisconsin FitKids Clinic at Sports Medicine for body-composition measurements within 2 wk of passing

![FIGURE 1. Flow chart of subject enrollment and completion. CLA, conjugated linoleic acid.](https://academic.oup.com/ajcn/article-abstract/91/5/1157/4597181)
Females (n) BMI. CLA, conjugated linoleic acid. Clarinol contains 80% CLA manufactured from safflower oil and Nutrition BV, Wormerveer, Netherlands) added per serving. kcal/serving. The CLA treatment milk had 3 g Clarinol (Lipid
Wisconsin Hospital for a follow-up fasting blood draw. The parents
compliance and were provided with an additional 3-mo supply. At 6 mo,
parents reported the amount of milk remaining to monitor com-
pliance and were provided with an additional 3-mo supply. At 6 mo,
the parents reported the amount of milk remaining and were
scheduled for follow-up body-composition testing and survey
collection and were instructed to return to the University of
Wisconsin Hospital for a follow-up fasting blood draw. The parents
were provided with enough milk for the child to consume until both
body composition and the blood draw were completed. The parents
were later contacted to again report the amount of milk remaining.
Both the CLA and placebo were added to skim milk to produce
a 250-g chocolate milk beverage containing 1.4% fat and 183
kcal/serving. The CLA treatment milk had 3 g Clarinol (Lipid
Nutrition BV, Wormerveer, Netherlands) added per serving. Clarinol contains 80% CLA manufactured from safflower oil and consists of a 50:50 mix of c9,t11 and t10,c12 isomers in tri-
glyceride form, which resulted in 2.4 g active CLA per serving.
The remaining 20% (0.6 g) consists of 14% linoleic acid, 4% palmitic acid, and 1% stearic acid. The placebo milk had 3 g
sunflower oil added per serving, provided by Lipid Nutrition. The milk was packaged by Tetra Pak, Inc (Denton, TX). Fatty acid
profiles were determined by the International Organization for
Standardization method 15304 for determination of trans fatty
acid isomers in animal and vegetable fats and oils. This method
uses fatty acid methyl esterification followed by gas chromat-
ography and is approved by the American Oil Chemists’ Society.

Weight, height, and body composition

Weight, height, and body composition were measured within
2 wk of screening for pretreatment testing and at ≈7 mo for
posttreatment testing while the subjects were still consuming the
treatment. All measurements were made under standardized
conditions by the same investigators. All participants were asked
to void and defecate before beginning the procedures. Height
used in the statistical analysis was measured with a wall-mounted
stadiometer to the nearest 0.5 cm. Weight used for the DXA scan
calculations and statistical analysis was measured with a cali-
ibrated beam balance platform scale to the nearest 0.1 kg while
the subjects were wearing only a swim suit or T-shirt and gym
shorts.

Body composition was measured with a Norland XR-36 Bone
Densitometer (Norland Corporation, Fort Atkinson, WI), and
tissue masses were analyzed by using host software version 3.7.4/2.1.0. On the basis of 18 scans in 6 subjects made by using XR-36
whole-body procedures, the total-body CVs were as follows: soft
tissue mass, 0.2%; total body mass, 0.2%; lean body mass, 1.0%;
fat mass (FM), 2.5%; percentage fat, 2.4%; and total BMC, 0.9%.
The XR-36 uses the following calibration standards for mea-
surings bone, fat, and lean mass from X-ray attenuation: bone,
hydroxyapatite; fat, stearic acid; and lean mass, 0.6% NaCl in
water. All body regions (head, trunk, abdomen, arms, and legs)
were set manually after completion of the scan by the same
trained investigator using predetermined bone landmarks for each
subject. All subjects were scanned in the supine position.
The subjects removed metal objects or clothing containing metal
components and wore only a swim suit or gym shorts and a T-shirt
for the scan procedure. The DXA-derived body density was
converted to percentage body fat by using the Lohman equation.
This calculation accounts for the physiologic differences in the
water component of fat-free mass (FFM) in children, which
changes with age and differs between sexes (18). This was
calculated by using body density as measured by DXA and an
adjustment on constants defined by Lohman (18). These con-
stants are based on age (in y), and, because some of the subjects
had birthdays between the baseline and follow-up measures, the
constant that would apply to them changed. This approach creates
a stepwise, nonlinear change with age, which is physiologically
unlikely. To account for this, we used the linear relation between
age and Lohman’s constants and interpolated them to find the
constant for follow-up measures based on their age at baseline
and time elapsed by the time of follow-up. Percentage FFM was
calculated as 100 minus percentage body fat. Fat and FFM were
calculated as the percentages/100 multiplied by body weight.
Abdominal and peripheral fat percentages were calculated as
measured FM for those regions divided by total body mass
multiplied by 100. DXA was also used to assess bone mineral
content (BMC).

Safety

Fasting blood samples were collected within 1 wk of the first
body-composition visit (before treatment began) and within 1 wk
of the follow-up body-composition visit (during treatment). Fasting
glucose and insulin, LDL cholesterol, HDL cholesterol, total cho-
lesterol, triglycerides, AST, ALT, and GGT were measured in
the samples. A pediatric endocrinologist reviewed all of the laboratory
results and compared them with acceptable ranges as listed above.

Symptoms

The subjects’ parents or guardians were asked to complete a
health symptoms survey at the first body-composition visit and
at the follow-up body-composition visit, which described their
child’s gastrointestinal and general health symptoms. They were
asked to describe the incidence and intensity of their child’s
nausea, stomach pain, vomiting, diarrhea, constipation, heart-
burn, bloating, loss or increase of appetite, cold or flu, and any
other health symptom over the previous 2 mo.
Statistics
The primary outcome variable was the change in percentage body fat as measured by DXA. A power analysis assuming an effect size of 2.3% fat, an SD of 4.4% fat, and a dropout rate of 25% indicated that 56 subjects completing the trial would provide a power of 80% and an α of 5%. Data from noncompliant participants were removed. All variables were tested for normality by using the Shapiro-Wilk test in Number Crunching Statistical System 2007 software, and none were different from a normal distribution. Next, the change scores for all variables were tested for outliers (measures beyond 3 SDs from the mean), which were removed from further analysis: BMC, head excluded (CLA, n = 4; placebo, n = 2), percentage peripheral fat (CLA, n = 1), and percentage abdominal fat (placebo, n = 2). Then, the between-group change was tested with a 2-tailed t test for comparison of intervention differences in BMI (in kg/m²), BMI z score, body-composition variables, and blood chemistry values; within-group changes were tested with a paired t test. This study was designed with an outcome analysis to be performed for subjects completing the trial with ≥75% milk compliance. Because of difficulties scheduling around the holidays and family schedules, treatment duration varied (average: 7.0 ± 0.6 y; placebo: 8.1 ± 0.8 y; P = 0.01; Table 3). When taken as a percentage of total body weight, percentage body fat in the CLA group (0.5 ± 0.1% decrease) was smaller than that in the placebo group (1.1 ± 1.1; P = 0.05; Table 3). When expressed as BMI z score, the value trended numerically downward in the CLA group (−0.03 ± 0.16) but was not statistically different from that of the placebo group (0.05 ± 0.23; P = 0.2; Table 3).

The increase in body FM, as measured by DXA, was smaller in the CLA group (0.8 ± 1.4 kg) than in the placebo group (1.8 ± 1.3 kg) (P = 0.01; Table 3). When taken as a percentage of total body weight, percentage body fat in the CLA group (−0.5 ± 2.1%) decreased numerically from baseline and differed significantly from that in the placebo (1.3 ± 1.8%; P = 0.001; Table 3; Figure 2). Abdominal body fat as a percentage of total body weight decreased numerically from baseline in the CLA group (−0.1 ± 0.9%) and differed significantly from that in the placebo group (0.4 ± 0.6%; P = 0.02; Table 3; Figure 2). Peripheral fat (including arms and legs) as a percentage of total body weight decreased from baseline in the CLA group (−1.2 ± 1.0%) and differed significantly from that in the placebo group (0.5 ± 1.2%; P = 0.01; Table 3; Figure 2). There was a difference in change in BMC, excluding the head, during treatment as measured by DXA between the CLA (0.05 ± 0.03 kg) and placebo (0.07 ± 0.03 kg) groups (P = 0.04; Table 3). There was a trend, although not statistically significant, toward smaller increases in height-adjusted BMC (infected bone strength) as measured by BMC/height in the CLA group (0.01 ± 0.09 g/mm) compared with placebo (0.04 ± 0.03 g/mm) (P = 0.09) (20).

RESULTS
Subjects
There were 55 subjects who completed the study, 53 of whom are included in this data analysis (n = 28 CLA, n = 25 placebo). The 2 subjects who were not included in the data analysis did not meet the compliance rate of 75% treatment consumption. The 7 subjects who did not complete this study included 3 who grew to dislike the milk delivery vehicle, 1 who did not consume 75% of the milk in the first 3 mo, 1 who had gastrointestinal problems, 1 who left the study because of self-esteem issues, and 1 who could no longer be contacted (Figure 1).

Anthropometric measures and body composition
Baseline subject characteristics are presented in Table 2. In females, height was significantly different between groups at baseline (CLA: 136 ± 7 cm; placebo: 130 ± 3 cm; P = 0.01); however, when indexed with weight as BMI, there were no significant differences. In males, there were no significant differences in height or BMI between groups at baseline. In addition, there were no differences between either sex at baseline in weight, BMI percentile, or BMI z score. Females in the CLA group tended to be older (CLA: 8.6 ± 0.8 y; placebo: 8.1 ± 0.6 y; P = 0.09). There were no significant differences in body composition at baseline between groups for either sex, and there were no significant differences between treatment groups for any characteristics when sexes were combined.

The increase in height from baseline to follow-up did not differ between the CLA (3 ± 1 cm) and placebo (3 ± 2 cm) (P = 0.3, Table 3) groups, nor did body weight gain (CLA: 3.2 ± 1.9 kg, placebo: 3.7 ± 2.3 kg; P = 0.4; Table 3). The increase in BMI in the CLA group (0.5 ± 0.8) was smaller than that in the placebo group (1.1 ± 1.1; P = 0.05; Table 3). When expressed as BMI z score, the value trended numerically downward in the CLA group (−0.03 ± 0.16) but was not statistically different from that of the placebo group (0.05 ± 0.23) (P = 0.2; Table 3).

The increase in body FM, as measured by DXA, was smaller in the CLA group (0.8 ± 1.4 kg) than in the placebo group (1.8 ± 1.3 kg) (P = 0.01; Table 3). When taken as a percentage of total body weight, percentage body fat in the CLA group (−0.5 ± 2.1%) decreased numerically from baseline and differed significantly from that in the placebo (1.3 ± 1.8%; P = 0.001; Table 3; Figure 2). Abdominal body fat as a percentage of total body weight decreased numerically from baseline in the CLA group (−0.1 ± 0.9%) and differed significantly from that in the placebo group (0.4 ± 0.6%; P = 0.02; Table 3; Figure 2). Peripheral fat (including arms and legs) as a percentage of total body weight decreased from baseline in the CLA group (−1.2 ± 1.0%) and differed significantly from that in the placebo group (0.5 ± 1.2%; P = 0.01; Table 3; Figure 2). There was a difference in change in BMC, excluding the head, during treatment as measured by DXA between the CLA (0.05 ± 0.03 kg) and placebo (0.07 ± 0.03 kg) groups (P = 0.04; Table 3). There was a trend, although not statistically significant, toward smaller increases in height-adjusted BMC (infected bone strength) as measured by BMC/height in the CLA group (0.01 ± 0.09 g/mm) compared with placebo (0.04 ± 0.03 g/mm) (P = 0.09) (20).

Safety
There were no significant differences between groups in any of the blood chemistry variables at baseline (Table 4). After

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Baseline characteristics of the subjects at entry</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CLA</td>
</tr>
<tr>
<td>Race-ethnicity (n)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>12</td>
</tr>
<tr>
<td>Black</td>
<td>2</td>
</tr>
<tr>
<td>Asian</td>
<td>1</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1</td>
</tr>
<tr>
<td>No. of subjects</td>
<td>16</td>
</tr>
<tr>
<td>Age (y)</td>
<td>8.8 ± 1.3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>45.6 ± 16.5</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>139 ± 8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.0 ± 5.7</td>
</tr>
<tr>
<td>BMI (%)*</td>
<td>95.1 ± 3.4</td>
</tr>
<tr>
<td>BMI z score</td>
<td>1.7 ± 0.5</td>
</tr>
</tbody>
</table>

*CLA, conjugated linoleic acid.

1 Mean ± SD (all such values).

2 Significantly different from placebo within the same sex, P < 0.05.

3 BMI percentile based on Centers for Disease Control and Prevention growth charts (19).
TABLE 3
Changes in anthropometric and body-composition measures from baseline to follow-up

<table>
<thead>
<tr>
<th></th>
<th>CLA (n = 28)</th>
<th>Placebo (n = 25)</th>
<th>P for between-group change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Month 0</td>
<td>Follow-up</td>
<td>Change</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>138 ± 8</td>
<td>141 ± 8</td>
<td>3 ± 1.2 ^2</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>45 ± 14</td>
<td>48 ± 14</td>
<td>3.2 ± 1.9 ^2</td>
</tr>
<tr>
<td>BMI (kg/m^2)</td>
<td>23.3 ± 4.6</td>
<td>23.8 ± 4.7</td>
<td>0.5 ± 0.8 ^2</td>
</tr>
<tr>
<td>BMI z score</td>
<td>1.83 ± 0.48</td>
<td>1.81 ± 0.49</td>
<td>−0.03 ± 0.16</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>15.1 ± 7.0</td>
<td>16.0 ± 7.3</td>
<td>0.8 ± 1.4 ^2</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>32.7 ± 5.0</td>
<td>32.2 ± 5.0</td>
<td>−0.5 ± 2.1</td>
</tr>
<tr>
<td>Fat-free mass (kg)</td>
<td>29.7 ± 6.9</td>
<td>32.1 ± 7.1</td>
<td>2.4 ± 1.2 ^2</td>
</tr>
<tr>
<td>Fat-free mass (%)</td>
<td>67.3 ± 5.0</td>
<td>67.8 ± 5.0</td>
<td>0.5 ± 2.1</td>
</tr>
<tr>
<td>Peripheral fat (%)</td>
<td>22.8 ± 2.3</td>
<td>21.8 ± 2.6</td>
<td>−1.2 ± 1.0 ^2</td>
</tr>
<tr>
<td>Abdominal fat (%)</td>
<td>9.1 ± 1.4</td>
<td>9.1 ± 1.4</td>
<td>−0.0 ± 0.9</td>
</tr>
<tr>
<td>BMC, head excluded (kg)</td>
<td>1.24 ± 0.23</td>
<td>1.28 ± 0.25</td>
<td>0.05 ± 0.03</td>
</tr>
</tbody>
</table>

1 All values are means ± SDs. Subjects are those who completed follow-up measures with outliers beyond 3 SD from the mean removed. CLA, conjugated linoleic acid; BMC, bone mineral content.
2,3,4 Significance within-group change comparison: ^2P ≤ 0.05, ^3P ≤ 0.01.

Our results indicate that CLA supplementation has an effect on fat gain during prepubertal growth. Compared with placebo, CLA significantly reduced total body fat gain in a 7-mo trial and regionally reduced the percentage of abdominal fat and peripheral fat as a percentage of total body weight. BMI increased less than control during the supplementation period, although the BMI z score did not.

**Intent-to-treat analysis**

The above analyses were completed by using inclusion criteria; however, the differences were also analyzed by intent-to-treat with the last measure carried forward. Thus, there was zero change for those who did not return for the 6-mo measurements. The CLA treatment outcomes that remained significant based on intent-to-treat were FM (P = 0.02) and percentage body fat (P = 0.002)

**DISCUSSION**

Our results indicate that CLA supplementation has an effect on fat gain during prepubertal growth. Compared with placebo, CLA significantly reduced total body fat gain in a 7-mo trial and regionally reduced the percentage of abdominal fat and peripheral fat as a percentage of total body weight. BMI increased less than control during the supplementation period, although the BMI z score did not.

![Changes in Body Composition](https://example.com/changes-body-composition.png)

**FIGURE 2.** Mean (±SE) changes in body composition after 7 mo of treatment with 3 g/d of an 80% conjugated linoleic acid (CLA) 50:50 mixture of cis-9,trans-11 and trans-10,cis-12 isomers in triglyceride form compared with a sunflower-oil placebo. Results are expressed as the percentage of body weight, and the differences were determined by a 2-tailed t test. Includes subjects who completed follow-up measures with outliers beyond 3 SD from the mean removed. n = 27–28 in the CLA group, and n = 23–25 in the placebo group. Excluded outliers are indicated as data points above or below the bars. ^2Significant between-group comparison: ^2P ≤ 0.001, ^3P ≤ 0.05.
In the current study, as indicated above, CLA was associated with a smaller rate of increase in BMI than was placebo. The change in BMI observed, however, was still numerically greater than the BMI value of 0.3 expected in 7 mo for both groups based on the 50th percentile of the 2001 National Center for Health Statistics growth charts (19), but was numerically less than the 95th percentile increase of 0.7 in 7 mo for the CLA group. Weight changes were not different between treatments, but both were similar to the 3- and 4-kg gains expected for the 95th percentile of this age group of boys and girls, respectively. This is still greater than the 2–2.5 kg expected at the 50th percentile (19). Thus, although CLA had a positive effect on the increase in BMI, the rates of increase did not appear to return to the 50th percentile averages for age. Results from individual studies of CLA supplementation in adults have been mixed with respect to whether or not CLA causes fat loss. Our recent meta-analysis, however, found that when taken as 50–50 mixture of c9,t11 and t10,c12 isomers, CLA decreased FM by 0.09 g/wk compared with placebo (7). A net FM loss, however, may not be an expectation in children of this age because, unlike adults, they are still growing. For example, in growing animals, CLA treatment has produced dramatic results, not in terms of loss of FM, but rather in terms of decreased accretion of FM. In the rat model, treatment with CLA as 2% of daily feed for 42 d resulted in a final body fat thickness of 18% less compared with placebo (21). Infant pigs supplemented with 1% CLA had a decrease in body fat accretion compared with no supplementation when given in either a low-fat (−3%) or a high-fat (25%) diet (16). Growing pigs had a dose-dependent lower back-fat thickness after 3 wk of supplementation (15). For dose comparison, we estimated the CLA treatment as 0.6% of daily matter in the current study based on prescribing 3 g/d of 80% CLA oil to children and assuming an intake of ~2300 kcal/d from the estimated energy requirement prediction equations developed by the Institute of Medicine (22) and typical US macronutrient composition. It is not known whether the initiation of CLA treatment in younger children before excess weight gain and continuing throughout childhood would have the same effects on adiposity, as in animal models, or whether the effect would asymptotically approach a modest 2-kg effect as reported in adults (7). On the basis of the greater increase in FFM observed in our current pediatric study than observed in adults, it would appear that the effects of CLA on pediatric body composition may differ from those observed in adults (23). Longer-term studies, however, are needed in children to test this.

On the basis of the outcomes of many human studies, CLA was recently granted generally recognized as safe (GRAS) status in the United States (GRN no. 232; www.cfsan.fda.gov). During clinical trials, no severe adverse events have been reported. In some trials, a small incidence in minor gastrointestinal distress has been reported. Some of the shorter clinical studies using single isomer supplementation found increases in insulin resistance (13, 24). Several have reported a decrease in HDL cholesterol (13, 25–27).

CLA supplementation was relatively well tolerated in this study, which agrees with the study by Moya (28). One subject stopped taking the CLA supplement because of gastrointestinal distress; however, it was reported that this subject concurrently had influenza. Similar to this only other CLA trial in children (28), we found no change in fasting glucose, insulin, or homeostasis model assessment of insulin resistance (13, 24). One subject had a diagnosis of type 2 diabetes.

We did find that subjects taking CLA had a decrease from baseline in HDL, which was also significantly different from the change in subjects taking placebo. This negative finding is the only such report in children, but other studies in adults also reported a greater decrease in HDL cholesterol in the treatment group than in the placebo group (13, 25–27). Conversely, other studies found no decreases in HDL cholesterol with CLA supplementation (24, 29–31). The increases in insulin, LDL cholesterol, and total cholesterol in the CLA group at follow-up, although not statistically significant, were a little surprising in children who already had a diagnosis of type 2 diabetes.

Table 4 Changes in blood chemistry values from baseline to follow-up

| Variable                  | Month 0 | 6-mo Follow-up | Change | Month 0 | 6-mo Follow-up | Change | P
|---------------------------|---------|----------------|--------|---------|----------------|--------|---
| Glucose (mg/dL)           | 90.3 ± 5.7 | 92.0 ± 5.2 | 1.8 ± 5.2 | 90.2 ± 4.63 | 90.6 ± 5.0 | 0.4 ± 3.9 | 0.3
| Insulin (µU/mL)           | 8.9 ± 7.1 | 9.5 ± 5.4 | 0.6 ± 4.4 | 9.4 ± 4.4 | 9.2 ± 4.8 | 0.04 ± 6.7 | 0.6
| LDL cholesterol (mg/dL)   | 54.1 ± 11.6 | 49.0 ± 9.2 | −5.1 ± 7.3 | 53.6 ± 13.9 | 53.0 ± 13.2 | −0.7 ± 8.2 | 0.05
| HDL cholesterol (mg/dL)   | 164.7 ± 29.7 | 170.0 ± 34.1 | 5.3 ± 23 | 164.1 ± 26.7 | 164.8 ± 28.4 | 0.7 ± 18.2 | 0.7
| Total cholesterol (mg/dL) | 26.8 ± 4.2 | 27.4 ± 7.3 | 0.2 ± 7.6 | 25.5 ± 3.63 | 25.0 ± 4.6 | −0.4 ± 2.7 | 0.8
| Triglycerides (mg/dL)     | 35.0 ± 4.1 | 37.3 ± 15.2 | 2.4 ± 16 | 34.2 ± 5.12 | 35.6 ± 8.0 | 1.4 ± 5.8 | 0.9
| AST (U/L)                 | 16.3 ± 3.2 | 18.3 ± 4.4 | 2.1 ± 3.9 | 18.2 ± 4.0 | 19.0 ± 4.8 | 0.8 ± 4.2 | 0.3
| HOMA-IR                   | 2.0 ± 1.6 | 2.1 ± 1.2 | 0.2 ± 0.9 | 2.2 ± 1.0 | 2.1 ± 1.1 | −0.02 ± 2 | 0.4

1 All values are means ± SDs. One subject did not complete the follow-up laboratory tests; one subject in the conjugated linoleic acid (CLA) group did not have results for follow-up glucose or aspartate aminotransferase (AST) because of lysed cells. ALT, alanine aminotransferase; GGT, γ-glutamyltranspeptidase; HOMA-IR, homeostasis model assessment of insulin resistance.

2 Significant between-group change comparison, P ≤ 0.05.
similar to those reported in many adult studies (33). Any longer-term studies of the efficacy of CLA in children conducted in the future should include more frequent measures of fasting glucose and insulin, liver function enzymes, lipid variables, BMC, BMI, and body composition.

Last, we found a slight trend toward a lower BMC accrual in the CLA group. This increase in BMC of 51 g in 7 ± 0.5 mo for the CLA treatment group is still typical for children of this age (34). The lesser rate of BMC increase in the CLA group is surprising and has not been seen in other studies, which tend to show no effect or small positive effects in animal studies (35). Studies in adults have also generally shown no effect of CLA on variables of bone or bone markers (36). We suggest that BMC be monitored in any future pediatric studies of CLA to resolve this issue.

Our study design had some limitations. For example, we recruited only overweight and obese children and thus did not obtain any data on the prevention of obesity in an average population. Consequently, we could not test a hypothesis of obesity prevention that has been shown in growing animal models. Because we did not determine Tanner stage at follow-up, we could not determine whether puberty-related changes in body composition might have influenced our results. An intent-to-treat analysis may have unusual effects in a pediatric study in terms of body composition compared with adults. In a group of adults, a follow-up measure of BMI, weight, height, and FM could reasonably result in zero change; however, in a group of growing children, it is reasonable to expect that any of these measures increase with time, and thus an intent-to-treat analysis in children is not as conservative an analysis as it is in adults. Specifically, the extrapolation of zero change for the intent-to-treat analysis may result in an unintended beneficial effect in a pediatric trial. In this regard, however, of the 8 subjects who did not complete follow-up, half were from the CLA group and the other half were from the placebo group, which should have minimized any possible dropout effect on the intent-to-treat outcome. In a similar vein, after randomization, the CLA group started with greater adiposity and thus, some of the changes we observed could have been a result of a regression toward the mean. Finally, whereas the changes we observed were statistically significant, the question regarding clinical significance still remains. Because of this, a longer trial needs to be done to determine the maximal effect of CLA on body composition (7) and to further investigate the safety of its long-term use as a food ingredient or supplement as well as the long-term effects of CLA treatment on body weight and composition in children.

In conclusion, the CLA supplement was well tolerated, and no serious adverse events were reported; however, there was an adverse decrease in HDL and a small lowering of the accretion rate of BMC associated with CLA. Thus, safety and longer-term efficacy remain to be determined. Supplementation with 80% pure CLA containing equal amounts of cis9,t11 and t10,c12 CLA was effective at reducing body fat accretion and percentage body fat in the first placebo-controlled trial of prepubescent overweight and obese children.

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The authors’ responsibilities were as follows—DAS and MO: conceived the study; DAS, MO, ACW, ALC, and DBA: participated in the study design; NMR, ACW, and ARO: participated in subject recruitment; NMR, ACW, ARO, and RRC: participated in data collection; JJM, ALC, and DBA: provided medical evaluation; DAS and NMR: participated in data analysis; NMR: wrote the first draft of the manuscript; and DAS, ACW, ALC, DBA, JIM, RRC, ARO, MO, and CES: revised the manuscript. MO and CES are employees of Lipid Nutrition, BV, Wormerveer, Netherlands, the manufacturer of the CLA used in this study. DAS has been named on a use patent application for CLA submitted by Lipid Nutrition. DAS, NMR, ACW, ALC, DBA, JIM, RRC, and ARO have had a portion of their salaries paid from the grant provided by Lipid Nutrition in proportion to the amount of effort each put toward designing, conducting, and documenting this study.

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