Spillover Effects of a Family-Based Childhood Weight Management Intervention on Parental Nutrient Biomarkers and Cardiometabolic Risk Factors

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Abbreviations used: BMI, body mass index; CLA, conjugated linolenic acid; CMRF, cardiometabolic risk factor; CV, coefficient of variation; D5D, delta-5-desaturase; D6D, delta-6-desaturase; DNL, de novo lipogenesis; EP, enhanced program; GC, gas chromatography; HDL-C, high-density lipoprotein-cholesterol; HPLC, high performance liquid chromatography; hsCRP, high sensitive C-reactive protein; IL-6, interleukin-6; LDL-C, low-density lipoprotein-cholesterol; mol%, molar percentage; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; RBC, red blood cell; SC, standard care; SCD, stearoyl co-A desaturase; SFA, saturated fatty acid; sICAM, soluble intercellular adhesion molecule; TC, total cholesterol; TG, triglyceride; TNFα, tumor necrosis factor alpha.

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ABSTRACT

Background: Parental involvement has been shown to favorably affect childhood weight management interventions, but whether these interventions influence parental diet and cardiometabolic health outcomes is unclear.

Objective: To evaluate whether a 1-year family-based childhood weight management intervention altered parental nutrient biomarker concentrations and cardiometabolic risk factors (CMRF).

Methods: Secondary analysis from a randomized-controlled, parallel-arm clinical trial (NCT00851201). Families were recruited from a largely Hispanic population and assigned to either Standard Care (SC; American Academy of Pediatrics overweight/obesity recommendations), or Standard Care + Enhanced Program (SC+EP; targeted diet/physical activity strategies, skill building and monthly support sessions). Nutrient biomarkers (plasma carotenoids and fat-soluble vitamins, RBC fatty acid profiles) and CMRF (BMI, blood pressure, glucose, insulin, lipoprotein profile, inflammatory and endothelial dysfunction markers, adipokines) were measured in archived samples collected from parents of participating children at baseline and end of the 1-year intervention.

Results: Parents in both groups (SC=106 and SC+EP=99) had significant reductions in trans fatty acid (-14%), and increases in MUFA (2%), PUFA-n6 (2%), PUFA-n3 (7%) and beta-carotene (20%) concentrations, indicative of lower partially-hydrogenated fat and higher vegetable oil, fish, and fruit/vegetable intake, respectively. Significant reductions in hsCRP (-21%) TNFα (-19%), IL-6 (-19%) and triglycerides (-6%) were also observed in both groups. An additional significant improvement in serum insulin
concentrations (-6%) was observed in the SC+EP parents. However, no major reductions in BMI or blood pressure, and significant unfavorable trajectories in LDL-cholesterol and endothelial dysfunction markers (P-selectin, sICAM, thrombomodulin) were observed. Higher carotenoid, MUFA, PUFA (n-6 and n-3), and lower SFA and trans fatty acid concentrations were associated with improvements in circulating glucose and lipid measures, inflammatory markers, and adipokines.

**Conclusions:** The benefits of a family-based childhood weight management intervention can spill over to parents, resulting in apparent healthier dietary shifts that are associated with modest improvements in some CMRF.

**Keywords:** childhood obesity, parent spill-over, family-based intervention, fatty acids, carotenoids, nutrient biomarkers, cardiometabolic risk factors

**LAY SUMMARY**
The benefits of a family-based lifestyle intervention focused on children with overweight and obesity can spill-over to parents, improving diet quality and some cardiometabolic risk factors.
INTRODUCTION

Childhood overweight/obesity is a major public health problem in the United States, and is associated with adverse health outcomes throughout the lifespan (1). Current recommended strategies to prevent/treat excess weight gain during childhood include a combination of dietary modification, increased physical activity, and behavioral therapy (2-5). The majority of childhood weight management interventions have been implemented in school and community settings with modest success (6-9). More recently, focus has shifted to the family/home environment, since parental involvement has been shown to be a key mediator in the effectiveness of childhood obesity interventions, especially in young children (10-16). These family-based interventions have sought to involve parents in various ways, ranging from solely targeting them as “agents of change” in their child’s weight loss (17, 18) to participating in educational modules that support fostering a home environment that promotes healthy dietary habits, increases physical activity and reduces sedentary behaviors (19-31).

Using the latter approach, we have documented that providing targeted family-based behavioral counseling as part of standard care (American Academy of Pediatrics overweight/obesity recommendations) (31) can help children with overweight/obesity adopt healthier eating patterns that are associated with modest improvements in BMIz and several CMRF (30). The majority of parents who participated in this intervention were female (94% mothers) and nearly all of them (92%) had a BMI that classified them as being in the overweight or obese categories. This is consistent with the observation that children with BMIz scores over the 85% percentile tend to have home environments
where either one or both parents are overweight/obese (23). Interestingly, maternal rather than paternal weight status (23) and nutrient intake (27) are stronger predictors of their child’s dietary intake and weight status. This finding suggests that overall family lifestyle is predominantly driven by maternal outcomes (32, 33). Yet, very few family-oriented interventions (13, 19, 20, 22, 25, 27, 28, 34) have measured parental diet and their relation to health outcomes. Given the high prevalence of children as well as adults with obesity, a family centered weight management intervention that has beneficial effects for both the children and parents could have a significant public health impact (35, 36). Thus, the goal of the present study was to investigate whether a family-based weight management intervention influenced parental nutrient intake patterns as well as cardiometabolic risk factors (CMRF). We hypothesized that adoption of the lifestyle recommendations by the parents of the participating children would be reflected in circulating nutrient biomarker concentrations and lead to an improvement in their CMRF profile.

METHODS

Study Subjects and Design: Detailed descriptions of the family-based management trial (NCT00851201 registered on clinicaltrials.gov) including design, intervention and primary outcomes in the children have been previously published (30, 31). This study is focused on the parents (n=205) of participating children (aged 7-12 years with baseline BMI z-score ≥85th percentile) who had an archived fasting plasma, serum and red blood cell (RBC) sample at both baseline and end of the 1-year intervention. All study procedures were approved by the Institutional Review Board of the Albert Einstein
College of Medicine. Approval to analyze de-identified samples and data was obtained from Tufts University/Tufts Medical Center Institutional Review Board.

Briefly, the study was a two-arm randomized, controlled, parallel-group trial comparing Standard Care Alone (SC) to Standard Care + Enhanced Program (SC+EP), and was conducted in a pediatric primary clinical care urban setting in Jacobi Medical Center (Bronx, New York, United States). The SC intervention was based on the American Academy of Pediatrics evidence-based recommendations (37) and included an initial comprehensive visit to assess weight-related issues and to engage both the children and parents/guardians in developing intervention goals collaboratively. The pediatricians utilized the 35-item Pediatric Symptom Checklist to screen for emotional and behavioral dysfunction (38, 39); the 5-item Habits questionnaire to assess dietary, physical activity and sedentary behaviors (40) and made referrals to a registered dietitian. The Habits questionnaire addressed meals (e.g., eating as a family and avoid eating while watching TV), fruit and vegetable intake (e.g., increasing serving, excluding juices), beverage intake (e.g., decreasing sugar-sweetened beverages, choosing 1% fat milk and water), fast food (e.g., decreasing frequency, avoiding super-sizing and choosing healthier options), and physical activity/sedentary behavior (e.g., increasing moderate and vigorous physical activity and decreasing screen time). Families also received a dietary booklet targeting behaviors associated with excess body weight (soda, sugary beverages, junk food, fast foods) as well as the federal 2005 Dietary Guidelines, recipes, physical activity booklet (listing recreational facilities, tips to reduce TV viewing and do 60 to 90 minutes of vigorous activity per day), and a monthly
newsletter (tips for healthy living). During the quarterly follow-up pediatrician visits, the collaborative goals identified at the initial visit were reviewed and re-iterated. The pediatricians who provided the SC to both study groups were blinded to treatment allocation.

The Enhanced Program added a behavioral change component (eight weekly skill-building core sessions, each 1.5 to 2 hours in duration), and subsequent monthly post-core support sessions focused on improving dietary behaviors and increasing engagement in physical activities) provided by bilingual multidisciplinary staff. As described previously (31), the skill-building core sessions included alternating in-person groups and parent phone consultations. The in-person core group sessions consisted of food preparation or other skill activity for parents and children, followed by a physical activity session for the children and discussion session for parents to enhance parenting and problem-solving skills related to the themes covered in the joint family sessions. The monthly post-core support sessions consisted of engagement activities that were designed to provide on-going support to parents/guardians and children during the intervention program. A group “meet up” approach was used to provide families with the opportunity to “check in” with Enhanced Program multidisciplinary staff. Post-core session themes included “boot camp” circuit training, holiday themes with active games and outing/field trips to a local park or within the campus grounds. Development of the Enhanced Program components was guided by evidence-based recommendations and interventions, and clinical experience in the target communities. Motivational enhancement based on Motivation Interviewing (MI) principles was used to engage both parent and child to evoke “their” reasons for changing unhealthy lifestyle behaviors. All
intervention components were available in Spanish and English. The newsletter (provided to both groups) included healthful versions of Latinx recipes and featured information regarding popular Latin American fruits and vegetables sold in the local farmers’ market sponsored by the health system. Likewise, the physical activity sessions included popular Latin American dance steps.

Outcome Variables and Assessment

**Nutrient Biomarkers:** Both dietary and endogenous metabolism biomarkers were measured in fasting plasma and RBC samples collected from the parents both pre and post intervention. Dietary biomarkers included plasma carotenoid concentrations (pigmented fruit and vegetable intake) (41), fat soluble vitamins A, D, E and K (animal foods, fortified foods, supplements and/or vegetable oils) (42), and red blood cell (RBC) fatty acid profiles including 18:2n-6 and 18:3n-3 (vegetable oils) (43), 20:5n-3, 22:5n-3 and 22:6n-3 (fish) (44), 15:0 (products containing dairy fat) (45), and *trans* fatty acids (ruminant/partially-hydrogenated fat) (46). Endogenously synthesized saturated fatty acid (SFA), monounsaturated fatty acid (MUFA) and polyunsaturated (PUFA) omega 6 profiles were also measured, and desaturase enzyme indices estimated to reflect *de novo* lipogenesis (DNL) (47).

High-performance liquid chromatography was used to determine plasma carotenoid (lutein, zeaxanthin, cryptoxanthin, β-carotene, and lycopene) including vitamin A and vitamin E, (48) as well as vitamin K concentrations (49), as previously described. Vitamin D (25-hydroxyvitamin D) was measured using a commercially available kit.
(DiaSorin, Stillwater, MN). The respective intra-assay and inter-assay CVs were 4% and 3.9% for carotenoids, and 9% and 10% for vitamin D. For vitamin K, two pooled plasma samples were run as low (CV:12%) and high (CV:8%) controls with every batch. RBC fatty acid profiles were quantified using an established gas chromatography method (50-52). The inter-assay CVs ranged from 0.5-4.3% for fatty acids present at levels >5%, 1.8-7.1% for fatty acids present at levels between 1-5 mol%, and 2.8-11.1% for fatty acids present at levels <1 mol%. Desaturase Enzyme Activities were calculated as product to precursor ratios of individual fatty acids and included: stearoyl-CoA-desaturase (SCD1-16:1n-7/16:0 and SCD2-18:1n-9/18:0), delta-6-desaturase (D6D:20:3n-6/18:2n-6) and delta-5-desaturase (D5D:20:4n-6/20:3n-6) (47).

**Cardiometabolic Risk Factors:** Available CMRF data for the parents from the primary clinical trial (31) and ancillary study (30) were divided into 7 broad categories: BMI, blood pressure (systolic and diastolic), glucose metabolism (fasting glucose and insulin), lipid profile (total cholesterol [TC], low density lipoprotein-cholesterol [LDL-C], high density lipoprotein cholesterol [HDL-C] triglycerides [TG]), markers of inflammation (high sensitive C-reactive protein [hsCRP], tumor necrosis factor alpha [TNFα], interleukin-6 [IL-6]), vascular adhesion (E-selectin, P-selectin, soluble intercellular adhesion molecule [sICAM]) and coagulation (thrombomodulin), and adipokines (leptin and adiponectin).

Fasting TG, LDL-C, HDL-C, TG, insulin and glucose were assessed using standard methods, as described for the primary study (31). Serum TNFα, IL-6, E-selectin, P-
selectin, sICAM, thrombomodulin, leptin and adiponectin concentrations were measured using commercially available multiplex assays (electro-chemiluminescence detection sandwich immunoassay: V-PLEX Human Cytokine Assays; V-PLEX Human Biomarker Assays; Human Metabolic Assays) from Meso Scale Discovery (MDS, Rockville, MD) using a Meso Scale Discovery SECTOR Imager 2400. Serum hsCRP was measured by solid-phase, two-site chemiluminescent immunometric assay using the IMMULITE 2000, (Siemens Healthcare Diagnostics, Los Angeles, CA). All CMRFs were measured in the fasted state.

**Study sample:** Sample size estimates for the primary clinical trial which provided the samples for the present study have been reported previously (31). For the 321 children in the primary trial, there were 287 parents after accounting for siblings, with 205 parents having an archived blood sample to perform the nutrient biomarker and CMRFs reported in the present study. With this given sample size of 106 in SC and 99 in SC+EP groups, there was 80% power to detect between-group differences of 0.39 standard deviations (SD) with a two-sided type I error rate of 5%. Additionally, to account for multiple comparisons, with a type I error rate=0.005 under a conservative Bonferroni adjustment with 80% power, the minimum detectable standardized effect size was 0.52 SD.

**Statistical analysis:** The analysis was based on an intention-to-treat approach. Data from each parent was analyzed as per their initial assignment in the primary clinical trial to the SC or SC+EP group. Only parents with nutrient biomarkers and CMRF data at
both baseline and 1-year were included in the analysis. Data was checked to identify and resolve reasons for missing values, inconsistencies, and out-of-range values.

Descriptive analyses of baseline characteristics of the SC and SC+EP groups were summarized using median (interquartile range) or proportions. Nutrient biomarkers and CMRF data at baseline and 1-year were summarized for each group using geometric means and SD estimated from log-transformed values.

Differences in nutrient biomarker and CMRF, as dependent variables, were assessed using a mixed-effects random intercept linear model with group, time, and group*time interaction as fixed-effects. Participant was included as a random effect within the model and p values presented from the corresponding F-test for each fixed effect. Robust standard errors were used to account for possible model misspecification. Dependent variables were log-transformed to facilitate reporting differences as mean percent difference [95% confidence intervals] and were calculated from back transformed model-based least square means as \(2.72\times[\text{LSMEANS}(1 \text{ year} - \text{baseline})] – 1\)\)*100%. Additionally, given the lack of intervention effect, least square means for 1-year change in outcomes was reported from the mixed-effects model to represent pooled results across all parents among combined groups.

Spearman rho correlation between 1-year change of CMRF with 1-year change in nutrient biomarkers was presented for each outcome pair. Correlation estimates were adjusted for sex, age, group, and baseline CMRF (and additionally adjusted for baseline
BMI for correlations not with BMI). Sex differences were not presented due to the small number of fathers in the sample (7 males in SC and 6 males in SC+EP). All statistical analyses were performed with SAS software (version 9.4; SAS Institute Inc., Cary, NC). Significance level was set at $p<0.05$.

**RESULTS**

**Baseline Characteristics:** The baseline characteristics of the parents are listed in Table 1. Their age ranged between 23 and 68 years and 93% were women (mothers). The mean BMI was $33.0 \text{ kg/m}^2$ with 7% being classified as normal weight, 27% in the overweight category and 66% in the obese category. The majority of the parents in both groups had normal fasting glucose concentrations (85%) and blood pressure (67%), but about 20% met either the stage 1 or 2 hypertension classification (53). Approximately 70% of the parents self-identified as Hispanic/Latino, approximately 50% had less than a high-school education, and over 70% reported an annual income less than $30,000.

**Nutrient Biomarkers:** No significant effect of the intervention (group effect) was observed between parents in either the SC or SC+EP groups (Table 2). However, significant differences were observed in several nutrient biomarkers at the end of the 1-year intervention (time effect) in both groups. Thus, nutrient biomarker data from parents in both groups were combined and the pooled change over 1-year is summarized in Figure 1. Results indicate a significant increase in plasma concentrations of beta-carotene (20%) (predominately yellow/orange fruits and vegetables) and lycopene (7%) (predominately tomatoes and derived products). There
was a significant decrease in vitamin D (-7%) and vitamin E (-14%) concentrations. No significant changes were observed in plasma vitamin A or K concentrations. Among the fatty acids, total SFA was significantly decreased in both groups (-3%), primarily due to lower proportions of 16:0 (-9%), with compensatory higher proportions of the minor SFA (2% to 20% for 14:0, 18:0, 20:0 and 24:0). MUFA significantly increased, especially those in the DNL pathway (6% to18% for 16:1n-7, 16:1n-9, 20:1n-9 and 24:1n-9). Total PUFAn-6, 18:3n-6, 20:2n-6, 20:3n-6, 20:4n-6, and 22:4n-6 were significantly increased (2% to 13%), with the exception of 22:5n-6 which was significantly decreased (-18%). All PUFAn-3 including 18:3n-3 (15%) from vegetable oils and 20:5n-3, 22:5n-3 and 22:6n-3 (6% to 11%) from fish and seafood, were significantly increased in the parents. Conversely, all trans fatty acids, indicators of ruminant fat (16:1n-7t, 16:1n-9t, 18:1n-7t, 18:2t, 18:2CLA), and partially hydrogenated fat typically found in traditional margarines, commercially prepared fried foods and savory snacks (18:1n-9t, 18:1n-10 to12t) were significantly decreased (-10% to -18%). Desaturase enzyme activity indices, SCD1 (8%) and D6D (12%) were significantly increased, while SCD2 (-2%) and D5D (-9%) were significantly decreased.

**Cardiometabolic Risk Factors**: At the end of the 1-year intervention period, parents in both groups had significant decreases in circulating markers of inflammation (hsCRP, TNFα, and IL-6) and increases in LDL-cholesterol, P-selectin, sICAM and thrombomodulin concentrations (**Table 3**). Parents in the SC+EP group had additional significant decreases in insulin concentrations, compared to parents in the SC group. No significant changes were observed in BMI, blood pressure, or glucose, total and
HDL-cholesterol, and adipokine concentrations. When both groups of parents were combined (Figure 2), significant improvements in triglyceride (-6%), hsCRP (-21%), TNFα (-19%) and IL-6 (-19%) concentrations were observed. However, significant unfavorable increases in LDL-cholesterol (3%), P-selectin (21%), sICAM (20%) and thrombomodulin (-8%) were also observed.

**Correlation between Nutrient Biomarkers and Cardiometabolic Risk Factors:** A heat map of Spearman correlation between the change in nutrient biomarkers and change in CMRF over the 1-year intervention period is presented in Figure 3.

**Carotenoids** – The changes in plasma carotenoid concentrations (adjusted by triglyceride concentrations) were generally associated with an improvement in CMRF including an inverse association with BMI (lutein), insulin (lutein), triglycerides (all), TNFα (zeaxanthin, cryptoxanthin and beta-carotene), and IL-6 (beta-carotene), and a positive association with HDL-cholesterol concentrations (lutein and zeaxanthin). An exception was lycopene (found in tomatoes and derived products) which was positively associated with LDL-cholesterol concentrations.

**Fat Soluble Vitamins** – Positive associations were observed between the fat-soluble vitamins and glucose (vitamin K), total cholesterol (all), LDL-cholesterol (vitamins A and D), HDL-cholesterol (vitamin A), and triglyceride (vitamins E and K) concentrations. Vitamin E also showed a positive association with inflammatory (IL-6), vascular
adhesion (E-selectin, P-selectin, sICAM) and coagulation (thrombomodulin) markers. In contrast, vitamin A was negatively associated with hsCRP and TNFα concentrations.

**RBC Fatty Acids** – Among the SFA, associations with CMRF varied by fatty acid type. Total SFA, 12:0, 14:0 and 16:0 were positively associated with insulin, total cholesterol, triglyceride, hsCRP, IL-6, P-selectin, sICAM, thrombomodulin and adiponectin concentrations. Longer chain SFA (18:0 to 24:0) were generally inversely associated with BMI (20:0), total and HDL-cholesterol (18:0), hsCRP (20:0 and 22:0), IL-6 (20:0), E-selectin (20:0), P-selectin (20:0, 22:0 and 24:0), sICAM (20:0), and thrombomodulin (20:0). Leptin concentrations were negatively associated with 18:0 but positively associated with 22:0. The odd chain fatty acid, 15:0 (biomarker of dairy fat) was inversely associated with hsCRP.

Among the MUFA, 16:1n-7, 16:1n-9 and 18:1n-7 which are synthesized from carbohydrates via the DNL pathway were positively associated with BMI, total cholesterol, triglyceride and P-selectin concentrations. Conversely, the omega-9 fatty acid concentrations were negatively associated with BMI (22:1n-9 and 24:1n-9), diastolic blood pressure (22:1n-9), glucose (22:1n-9), insulin and leptin (20:1n-9, 22:1n-9 and 24:1n-9), hsCRP (20:1n-9, 22:1n-9), IL-6 and P-selectin (20:1n-9, 24:1n-9), sICAM and thrombomodulin (18:1n-9, 20:1n-9). Total MUFA, predominantly driven by 24:1n-9 was positively associated with adiponectin concentrations.

Among the omega-6 class of fatty acids, total PUFAn-6, 20:2n-6, 20:4n-6, 22:4n-6 and 22:6n-6 were negatively associated with several CMRF including BMI, glucose, insulin, total cholesterol, triglyceride, IL-6, P-selectin, sICAM, thrombomodulin and leptin.
Interestingly, 22:2n-6 (DHA) was positively associated with sICAM, thrombomodulin and adiponectin. Positive associations were also observed between 18:2n-6 and 18:3n-6 and BMI, insulin, total and LDL-cholesterol, triglyceride and leptin concentrations.

The plant derived omega-3 PUFA (18:3n-3) were positively associated with total cholesterol, triglyceride, adiponectin and negatively associated with TNFα, sICAM and thrombomodulin. Among the marine derived PUFAs, 22:6n-6 (DHA) and 22:5n-3 (DPA) but not 20:5n-3 (EPA) were negatively associated with insulin, P-selectin and leptin.

Majority of the trans fatty acids were positively associated with inflammatory, vascular adhesion and coagulation markers, as well as leptin. Surprisingly they were negatively associated with blood pressure. CLA was the only TFA that showed a weak but significant positive association with BMI.

**Desaturase Enzyme Indices** – SCD1 was positively associated with BMI, total cholesterol, and triglyceride concentration. SCD2 was also positively associated with total cholesterol, triglyceride and adiponectin but negatively associated with sICAM and thrombomodulin concentrations. D6D positive with HDL-cholesterol and negative with P-selectin. Conversely, D5D was associated negatively with the lipid profile and positively with P-selectin.

**DISCUSSION**

To our knowledge, this study is the first to evaluate whether a 1-year family-based childhood weight management intervention influenced parental nutrient patterns and cardiometabolic health outcomes. Results suggest an improvement in diet quality, as
indicated by an increase in biomarkers of fruits and vegetables (carotenoids), dairy (15:0), vegetable oils (18:3n-3), and fish (20:5n-3, 22:5n-3, 22:6n-3), and a decrease in biomarkers of ruminant and partially hydrogenated fat (trans fatty acids). Additionally, there were modest yet significant favorable improvements in 4 (triglycerides, hsCRP, TNFα and IL-6) of the 18 CMRFs measured at the end of the 1-year intervention. These improvements were weakly to moderately correlated with the shifts in nutrient patterns. However, we did not observe a significant reduction in BMI. Furthermore, the intervention did not slow the unfavorable trajectories observed in LDL-cholesterol and markers of endothelial dysfunction (P-selectin, sICAM and thrombomodulin). For the most part, changes in nutrient biomarkers and CMRF in the parents were independent of the intervention group, suggesting limited added benefit of the enhanced program component. Nonetheless, these results document that standard care alone, based on the American Academy of Pediatrics evidence-based recommendations that target lifestyle behaviors associated with excess body weight in children can result in beneficial dietary and cardiometabolic health benefits in their parents when implemented within the context of a family-based clinical setting.

There is limited research on change in parental diet quality as part of family-based weight management interventions (13). This is partly due to the challenges and inherent limitations associated with capturing dietary intake using subjective assessment tools (24-hour recall, food frequency questionnaires, food diaries) (54). To overcome this, we choose to objectively measure selected nutrients that reflected some of the dietary components of the intervention. We observed higher β-carotene and lycopene.
concentrations in the parents at the end of the intervention. This suggests increased consumption of foods such as carrots, tomato-based dishes and fresh or canned fruits (apples, cherries, oranges). Of note, assessment of the dietary intake of the children in this study highlighted a “pizza and pasta” based pattern, that was associated with their parents/guardian being born in mainland USA and having a higher educational level (55). This highlights the important of parental acculturation in influencing dietary behaviors of the family. The lower concentrations of the predominantly diet derived trans fatty acids observed, suggests that the parents in our study adhered to the lower fried foods/savory snack recommendations. Also noted were lower proportions of total SFA and higher production of fatty acids in the DNL pathway. The lower SFA is most likely due to a combination of lower intake of 16:0 which is the major dietary SFA in the diet, as well as increased endogenous desaturation to 16:1 and conversion to downstream MUFA metabolites, as supported by the observation of higher SCD1 and lower SCD2 activities. The higher PUFA n-6 downstream metabolites observed reflect endogenous synthesis from 18:2n-6 via D6D. Additionally, the increase in diet derived long chain PUFA n-3 intake from both plant (18:3n-3) and marine (20:5n-3,22:5n-3, 22:6n-3) sources could account for the lower D5D activities, given the competition between PUFA n-6 and n-3 for D5D (47).

While it is difficult to contextualize our nutrient data given the dearth of comparable research, we identified a few studies that assessed dietary components using self-administered tools in parents participating in family-based intervention programs. Two studies, the High 5 for Preschool Kids (H5-KIDS) program, a home-based intervention
to teach parents how to ensure a positive fruit-vegetable environment for their preschool child (25), and the Stoplight/Traffic-light Diet Treatment (20), both reported increases in fruit-vegetable servings in participating parents, which in the latter study was at the expense of a high-fat/high-sugar foods. Among the 3 studies that reported dietary total fat intake of participating parents, one study (28) achieved significant reductions in total fat intake and to a smaller extent for sugar and complex carbohydrate intake following family dietary coaching to improve nutritional intake and weight control, while the other (19) observed a significant decrease in total fat and sodium intake, but only in non-Hispanic and not in Mexican American families who participated in a family-based CVD risk reduction intervention. The third study (56), explored the efficacy of a 12-week culturally specific obesity prevention program in low-income, inner-city African American girls and their mothers and showed significant differences between the treatment and control mothers for daily SFA intake and percentage of calories from fat. These data, including the present results, suggest that parent involvement in family-based interventions with a specific dietary component, whether indirect (targeting their child’s dietary intake) or direct (targeting both parent and child), can result in modest shifts in their dietary behaviors.

An unexpected finding in this study was the decrease in concentrations of fat-soluble vitamins, most notably for Vitamin D and E. These vitamins are transported in circulation via triglyceride rich particles, however, similar results were still observed after correcting for triglyceride concentrations. It is possible that an overall decrease in intake of fortified foods such as cereals, and fried foods prepared with vegetable oils, major
dietary sources of vitamins D and E, respectively, could account for this observation. Alternately, evidence also suggest that, in the presence of obesity, there is a tendency for higher incorporation and storage of fat soluble vitamins, especially in adipose tissue, which results in lower circulating concentrations (57).

Most family-based studies are designed to assess whether parent involvement enhanced the effectiveness of interventions that aimed to change their child’s weight, with a few studies (20, 26, 29, 34, 58) also targeting parental weight. However, these latter studies have had mixed results. Some studies (20, 26) that targeted weight loss as an outcome in both parents and children reported better success in parents. However, another family-based exploratory community study in low-income Latino mothers and daughters, did not show any significant differences in BMI in mother daughter dyads in the experimental versus control group, after adjusting for baseline BMI as a covariate (34). Among school-and community-based childhood weight management programs, one study observed a spill over intervention effect on parents resulting in a significant decrease in BMI (58), while the other study did not (29). We also did not observe a significant reduction in parental BMI, although there was a downward trend after adjustment for baseline variables. Nevertheless, we observed improvements in several obesity related CMRF, notably systemic inflammation markers, insulin and triglycerides concentrations. Additionally, these favorable changes in CMRF were associated with the changes in nutrient profiles. Whereas inverse associations between carotenoids and CMRF (57) and positive associations between fatty acids, including trans, and inflammation/endothelial dysfunction (59-61) have been previously
documented in overweight and obese adults, our findings provide preliminary evidence that the shifts toward heather eating patterns can extend beyond changes in BMI and improve cardiometabolic health outcomes, within a family-based childhood obesity intervention.

Excess body weight has also been associated with lower adiponectin and higher leptin concentrations (62). The absolute levels of these adipokines were not significantly altered by the intervention, and this is most likely due to the lack on an effect on BMI, as their levels tend to correlate with fat mass. However, the positive associations observed between both adipokines and several of the endogenously synthesized SFA, MUFA and PUFA n-6 fatty acids at the end of the 1-year intervention, suggests a potential modulatory effect that warrants further investigation (63).

Of note, there were unfavorable increases in LDL-C concentrations at the end of the study. This could reflect increase transfer of triglycerides from VLDL to LDL, as supported by the concomitant lowering of triglyceride concentrations observed. Also observed were increases in concentrations of P-selectin, sICAM and thrombomodulin, suggestive of endothelial injury (64) that may already be present in this group of parents with overweight and obesity that the dietary components targeted in our intervention was unable to slow or reverse these trajectories.

Strengths of this study include the randomized design, drawing on the social-ecological framework to develop intervention components and the principles of social cognitive
theory and social marketing to address the interaction of behavioral, environmental, and personal factors, collaborative goal-setting to empower families, and an expanded dataset of overweight and obesity related CMRF variables, in an underserved, high obesity risk group of largely Hispanic mothers who participated in their child’s weight management intervention. Given the extremely low participation of fathers in our study, we were limited in our ability to analyze intervention effect on paternal diet. Second, the clinical trial was not designed to address parental adherence with the lifestyle intervention per se. Consequently, the parental dietary and physical activity assessments were limited. We chose to utilize an objective biomarker approach, focusing on selected nutrients, since self-report dietary intake especially in populations with overweight and obesity has been associated with under- and over-reporting of certain food groups (65, 66). However, there are limited number of validated nutrients of dietary intake and none that capture total energy intake/balance, sugar sweetened beverage intake or quantity of the food consumed. Third, the possibility cannot be ruled out that the changes observed in CMRF could potentially be mediated by increased physical activity levels of the parents and not solely related to modification of dietary behaviors. Finally, majority of the changes in nutrient concentrations and CMRF were observed in both groups of parents, which was contrary to our original hypothesis, and suggest limited added benefit of the enhanced module. While this could be because the dietary guidance/tools were provided to all participating families as part of standard care and reinforced during the quarterly visits by the highly specialized study pediatricians and research staff, it is possible that other components, such as intensity of contacts,
adherence, and/or resource sharing between groups may have contributed to these observations.

In conclusion, this study documents a beneficial outcome of a family-based childhood weight management intervention delivered within a primary care setting on parental nutrient patterns which were associated with favorable changes in selected CMRF, despite non-significant changes in BMI. These findings have significant public health implications since improving diet quality and health outcomes in a parent with overweight or obesity using the same guidelines that targeted their child could potentially result in a major cost-benefit of family-based interventions, and merits further investigation.

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Authors’ Contributions to the Manuscript

N.R.M., A.H.L., and J.W.-R., contributed to designing and conducting the present study; J.W.-R., A.E.G-P., P.M.D., M.G., and Y. M-R., contributed to designing and conducting the primary intervention. X.X. and K.B. assumed responsibility for data analysis. The
manuscript was written by N.R.M. with editing from A.H.L., J.W.R., A.E.G.-P., P.M.D., X.X., Q.G., K.B., M.G and Y. M.-R. All authors read and approved the final manuscript.

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**FIGURE 1. Pooled 1-year Change in Nutrient Biomarker Concentrations and Desaturase Enzyme Activities.** For each individual nutrient biomarker, the mean percent difference is plotted as the symbol and the 95% confidence intervals displayed as the bars. The mean percent difference value and 95% confidence intervals were
derived from least square means calculated from a mixed-effects random intercept model with time (baseline or 1-year) as a fixed effect and a random intercept for subject correlations. A separate model was fitted for each log-transformed outcome. N=205 and included parents in the SC and SC+EP groups with both a baseline and 1-year nutrient biomarker value.

FIGURE 2. Pooled 1-year Change in Cardiometabolic Risk Factors. For each individual CMRF, the mean percent difference is plotted as the symbol and the 95% confidence intervals displayed as the bars. The mean percent difference value and 95% confidence intervals are derived from least square means calculated from a mixed-effects random intercept model with time (baseline or 1-year) as a fixed effect and a random intercept for subject correlations. A separate model is fitted for each log-transformed outcome. Number of parents in the SC and SC+EP group with both a baseline and 1-year values was as follows: BMI (n=193), blood pressure (n=194),
glucose metabolism (n=205), lipid profile (n=205), inflammatory, vascular adhesion, coagulation markers and adipokines (n=192).

| BIOMARKERS | BM | BLOOD PRESSURE | GLUCOSE METABOLISM | LIPOID PROFILE | INFLAMMATION | VASCULAR ADHESION AND COAGULATION | ADIPOKINES |
|------------|----|----------------|-------------------|---------------|-------------|-----------------------------------|-----------|
| Leptin     | -0.15 | 0.08 | 0.30 | -0.09 | -0.15 | -0.10 | 0.14 | 0.14 | -0.05 | -0.11 | -0.25 | -0.01 | 0.63 | 0.30 | -0.06 | -0.13 | -0.12 |
| Z Kıne     | 0.11 | 0.08 | 0.11 | -0.10 | -0.06 | 0.09 | 0.12 | 0.19 | 0.24 | -0.09 | 0.15 | -0.26 | 0.01 | 0.92 | 0.01 | -0.08 | 0.12 |
| Alkaline   | 0.16 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 |
| Cytokines  | -0.11 | -0.05 | 0.04 | -0.12 | -0.07 | -0.13 | 0.04 | 0.04 | 0.07 | -0.13 | -0.30 | -0.26 | 0.04 | 0.67 | -0.12 | -0.13 | -0.03 |
| Leptin A   | 0.24 | 0.12 | 0.24 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 | 0.12 |
| Leptin B   | 0.15 | 0.07 | 0.04 | 0.07 | 0.06 | 0.24 | 0.17 | 0.17 | 0.13 | -0.18 | -0.16 | 0.05 | 0.62 | 0.07 | -0.04 | -0.07 | -0.09 |
| Leptin C   | 0.15 | 0.07 | 0.04 | 0.07 | 0.06 | 0.24 | 0.17 | 0.17 | 0.13 | -0.18 | -0.16 | 0.05 | 0.62 | 0.07 | -0.04 | -0.07 | -0.09 |
| Leptin D   | -0.11 | -0.05 | 0.04 | -0.12 | -0.07 | -0.13 | 0.04 | 0.04 | 0.07 | -0.13 | -0.30 | -0.26 | 0.04 | 0.67 | -0.12 | -0.13 | -0.03 |
| Leptin E   | 0.15 | 0.07 | 0.04 | 0.07 | 0.06 | 0.24 | 0.17 | 0.17 | 0.13 | -0.18 | -0.16 | 0.05 | 0.62 | 0.07 | -0.04 | -0.07 | -0.09 |
| Leptin F   | -0.11 | -0.05 | 0.04 | -0.12 | -0.07 | -0.13 | 0.04 | 0.04 | 0.07 | -0.13 | -0.30 | -0.26 | 0.04 | 0.67 | -0.12 | -0.13 | -0.03 |

**FIGURE 3.** Heat Map of the Correlation between Nutrient Biomarkers, Desaturase Enzyme Activities and Cardiometabolic Risk Factors. The correlation between 1-year change of CMRF with 1-year change in nutrient biomarkers for each outcome pair was estimated using Spearman rho correlation, adjusted for sex, age, group, and baseline CMRF (and additionally adjusted for baseline BMI for correlations not with BMI). Blue indicates a negative association, while red indicates a positive association, with darkness of each color corresponding to the magnitude of the “r” value, with significant values (p<0.05) in bold. Number of parents included ranged from193 to 205.
TABLE 1 Characteristics of Parents at Baseline

| Variables                        | Standard Care [SC; n=106] | Standard Care+ Enhanced Program [SC+EP; n=99] |
|----------------------------------|---------------------------|-----------------------------------------------|
| Age (years)                      | 37 (32-42)                | 38 (33-43)                                    |
| Sex (Females/Males)              | 99/7                      | 93/6                                          |
| BMI (kg/m^2)                     | 33.5 (6.9)                | 32.5 (7.0)                                    |
| **BMI Classification, n (%)**    |                           |                                               |
| Normal weight (<25 kg/m^2)       | 2 (2%)                    | 10 (10%)                                      |
| Overweight (≥25 to <30 kg/m^2)   | 25 (24%)                  | 30 (30%)                                      |
| Obesity (≥30 kg/m^2)             | 76 (74%)                  | 59 (60%)                                      |
| **Blood Pressure Classification, n (%)** |           |                                               |
| Normal (<120/<80 mmHg)           | 63 (61%)                  | 71 (72%)                                      |
| Elevated (120-129/<80 mmHg)      | 20 (19%)                  | 11 (11%)                                      |
| Stage 1 Hypertension (130-139/ 80-80 mmHg) | 9 (9%)               | 9 (9%)                                        |
| Stage 2 Hypertension (≥140/≥90 mm Hg) | 12 (11%)             | 8 (8%)                                        |
| **Fasting Plasma Glucose n (%)** |                           |                                               |
| <100 mg/dL                       | 64 (60%)                  | 69 (70%)                                      |
| 100-125 mg/dL                    | 24 (23%)                  | 19 (19%)                                      |
| ≥125 mg/dL                       | 18 (17%)                  | 11 (11%)                                      |
| **Education (%)**                |                           |                                               |
| No Formal Schooling              | 1.8%                      | 1.0%                                          |
| Grades 1-11                      | 50.0%                     | 54.5%                                         |
| High School/GED                  | 29.3%                     | 20.2%                                         |
| Some college/Tech school certificate | 9.5%                | 15.2%                                         |
| Associate’s/Bachelor’s degree    | 9.4%                      | 9.1%                                          |
| **Race/Ethnicity (%)**           |                           |                                               |
| Hispanic/Latino                  | 70.8%                     | 78.8%                                         |
| Non-Hispanic Black               | 20.7%                     | 14.1%                                         |
| White, Asian and Multi-racial    | 8.5%                      | 7.1%                                          |
| **Occupation (%)**               |                           |                                               |
| Homemaker                        | 56.6%                     | 52.5%                                         |
| Employed full time               | 12.3%                     | 12.1%                                         |
| Employed part time               | 20.8%                     | 21.2%                                         |
| Unemployed/ Retired              | 10.3%                     | 14.1%                                         |
| **Income (%)**                   |                           |                                               |
| 0-9,999                          | 39.6%                     | 37.4%                                         |
| Income Range         | 10,000-29,999 | 30,000 or above | Prefer not to answer |
|----------------------|---------------|-----------------|----------------------|
|                      | 34.9%         | 5.6%            | 19.8%                |
|                      | 35.4%         | 10.1%           | 17.2%                |

**Marital Status (%)**

| Marital Status          | Married/Living as married | Widowed | Divorced/ Separated | Never married | Prefer not to answer |
|-------------------------|---------------------------|---------|---------------------|---------------|----------------------|
|                         | 59.4%                     | 2.8%    | 18.9%               | 15.1%         | 3.8%                 |
|                         | 54.6%                     | 1.0%    | 14.2%               | 24.2%         | 6.1%                 |

1. Median (IQR)
2. Mean (SD)
| BIOMARKERS                      | Standard Care (SC) | Standard Care + Enhanced Program | P-value<sup>2</sup> |
|--------------------------------|--------------------|---------------------------------|---------------------|
|                                | Baseline<sup>4</sup> | 1 Year<sup>4</sup> | Mean Percent Difference<sup>4</sup> | Baseline<sup>4</sup> | 1 Year<sup>4</sup> | Mean Percent Difference<sup>4</sup> | Group | Time | Group * Time |
| Carotenoids (ug/dL)            |                    |                                |                     |
| Lutein                         | 10.0 (5.6)         | 10.3 (5.7)                     | 2.8 [-4.0, 10.0]    | 11.1 (6.4)         | 10.4 (5.9)         | -6.7 [-13.8, 0.8]     | 0.319 | 0.427 | 0.069       |
| Zeaxanthin                     | 3.4 (2.1)          | 3.5 (2.03)                     | 4.5 [-2.9, 12.5]    | 3.7 (2.40)         | 3.7 (2.2)          | -0.1 [-7.5, 6.3]      | 0.319 | 0.412 | 0.426       |
| Cryptoxanthin                  | 9.1 (12.7)         | 10.3 (14.0)                    | 12.8 [1.6, 25.4]    | 10.8 (15.5)        | 10.2 (16.0)        | -5.9 [-16.2, 5.7]     | 0.483 | 0.448 | 0.023       |
| Beta-Carotene                  | 15.3 (25.8)        | 19.3 (32.7)                    | 26.3 [12.9, 41.3]   | 16.6 (18.8)        | 19.6 (22.6)        | 17.8 [3.4, 34.1]      | 0.652 | <0.001 | 0.422       |
| Trans-Lycopene                 | 17.6 (11.3)        | 18.7 (13.7)                    | 6.4 [-3.4, 17.2]    | 20.4 (11.3)        | 19.6 (11.8)        | -4.2 [-13.8, 6.4]     | 0.114 | 0.792 | 0.148       |
| Fat Soluble Vitamins           |                    |                                |                     |
| Vitamin A (ug/dL)              | 48.4 (14.9)        | 47.2 (12.7)                    | -2.5 [-6.0, 1.1]    | 46.5 (12.0)        | 44.8 (11.5)        | -3.5 [-8.5, 1.8]      | 0.154 | 0.064 | 0.757       |
| Vitamin D (ng/mL)              | 17.9 (8.9)         | 17.2 (7.2)                     | -4.8 [-11.9, 2.9]   | 18.5 (9.61)        | 16.9 (7.05)        | -1.6 [-5.1, -0.8]     | 0.915 | 0.017 | 0.513       |
| Vitamin E (ug/dL)              | 184 (120)          | 168 (122)                      | -8.8 [-17.1, 0.3]   | 188 (128)          | 158 (121)          | -26.3 [-48.4, -8.8]   | 0.783 | <0.001 | 0.241       |
| Vitamin K (nM/L)               | 0.54 (0.69)        | 0.55 (0.63)                    | 0.8 [-13.7, 17.7]   | 0.54 (0.58)        | 0.49 (0.52)        | -0.8 [-22.1, 8.5]     | 0.533 | 0.508 | 0.424       |
| Fatty Acids (mol %)            |                    |                                |                     |
| SFA                            | 41.1 (1.88)        | 39.8 (2.03)                    | -3.3 [-4.4, -2.2]   | 41.1 (2.08)        | 39.8 (1.69)        | -3.4 [-4.5, -2.2]     | 0.934 | <0.001 | 0.938       |
| 12:0                           | 0.13 (0.12)        | 0.12 (0.14)                    | -0.1 [-2.1, 1.8]    | 0.14 (0.13)        | 0.12 (0.12)        | -0.1 [-2.5, 2.6]      | 0.415 | 0.266 | 0.569       |
| 14:0                           | 0.43 (0.16)        | 0.53 (0.20)                    | 24.0 [14.5, 34.3]   | 0.48 (0.18)        | 0.56 (0.19)        | 21.7 [12.3, 31.9]     | 0.138 | <0.001 | 0.746       |
| 15:0                           | 0.35 (0.08)        | 0.38 (0.11)                    | 10.8 [3.5, 18.6]    | 0.36 (0.09)        | 0.38 (0.14)        | 7.1 [-1.3, 16.2]      | 0.750 | 0.002 | 0.529       |
| 16:0                           | 22.2 (2.15)        | 20.1 (1.85)                    | -9.2 [-11.1, -7.2]  | 22.1 (2.26)        | 20.1 (1.63)        | -9.8 [-10.8, -7.0]    | 0.732 | <0.001 | 0.86        |
| 18:0                           | 16.2 (1.11)        | 16.6 (1.15)                    | 2.4 [1.0, 3.8]      | 16.2 (1.25)        | 16.6 (1.09)        | 2.4 [1.0, 3.8]        | 0.873 | <0.001 | 0.965       |
| 20:0                           | 0.16 (0.03)        | 0.19 (0.05)                    | 20.1 [14.5, 25.9]   | 0.17 (0.03)        | 0.20 (0.05)        | 18.8 [12.8, 25.2]     | 0.245 | <0.001 | 0.772       |
| 22:0                           | 0.46 (0.09)        | 0.49 (0.11)                    | 3.3 [3.1, 13.7]     | 0.46 (0.10)        | 0.49 (0.11)        | 5.3 [-0.3, 11.2]      | 0.956 | <0.001 | 0.453       |
| 24:0                           | 1.07 (0.23)        | 1.13 (0.31)                    | 6.6 [-0.1, 11.7]    | 1.09 (0.24)        | 1.15 (0.30)        | 4.9 [-1.0, 11.1]      | 0.398 | 0.012 | 0.869       |
| MUFA                           | 16.3 (1.56)        | 16.48 (1.5)                    | 1.5 [-0.3, 3.3]     | 16.2 (1.51)        | 16.5 (1.44)        | 1.9 [0.1, 3.7]        | 0.868 | 0.010 | 0.748       |
| 16:1n-7                        | 0.49 (0.21)        | 0.55 (0.21)                    | 11.9 [5.6, 18.5]    | 0.50 (0.21)        | 0.57 (0.28)        | 13.3 [5.8, 21.4]      | 0.54  | <0.001 | 0.772       |
| 16:1n-9                        | 0.1 (0.03)         | 0.12 (0.03)                    | 19.5 [12.5, 26.8]   | 0.11 (0.03)        | 0.13 (0.03)        | 19.2 [11.9, 26.9]     | 0.389 | <0.001 | 0.955       |
| 18:1n-7                        | 1.72 (0.66)        | 1.81 (0.77)                    | 5.5 [-3.4, 15.2]    | 1.77 (0.73)        | 1.71 (0.71)        | -3.4 [-12.7, 6.8]     | 0.736 | 0.784 | 0.192       |

<sup>1</sup> Mean Differences were calculated using ANOVA and Tukey’s HSD test. <sup>2</sup> P-values for group differences were calculated using ANOVA and Tukey’s HSD test.

This analysis examines the changes in nutrient biomarkers and desaturase enzyme activities at baseline and end of the 1-year intervention by study group.
|        | SC1 (16:1-7/16:0) | SC2 (16:1-9/18:0) | D6D (20:3n-6/18:2n-6) | D5D (20:4n-6/20:3n-6) |
|--------|------------------|------------------|-------------------|-------------------|
| 18:1n-9 | 12.39 (1.27)     | 12.32 (1.07)     | -0.5 [-2.2, 1.2]  | 12.2 (1.32)       |
| 20:1n-9 | 0.21 (0.05)      | 0.24 (0.06)      | 16.4 [11.3, 21.7] | 14.9 [10.7, 19.3] |
| 22:1n-9 | 0.046 (0.02)     | 0.049 (0.02)     | 5.4 [-3.9, 15.7]  | 3.5 [-5.9, 13.9]  |
| 24:1n-9 | 1.12 (0.23)      | 1.19 (0.28)      | 6.2 [0.8, 11.9]   | 5.8 [0.0, 12.0]   |
| PUFA n-6 |                   |                  |                   |                   |
| 18:2n-6 | 13.7 (1.59)      | 13.7 (1.70)      | -0.1 [-1.7, 1.7]  | 14.1 (2.20)       |
| 18:3n-6 | 0.07 (0.04)      | 0.08 (0.04)      | 6.8 [-2.2, 16.6]  | 17.8 [5.9, 31.0]  |
| 20:2n-6 | 0.33 (0.08)      | 0.38 (0.08)      | 14.1 [11.1, 17.2] | 12.6 [9.3, 16.0]  |
| 20:3n-6 | 1.86 (0.57)      | 2.08 (0.58)      | 12.0 [7.8, 16.4]  | 11.5 [7.1, 16.0]  |
| 20:4n-6 | 14.5 (1.27)      | 14.8 (1.52)      | 1.8 [0.1, 3.6]    | 14.3 (1.69)       |
| 22:2n-6 | 0.072 (0.03)     | 0.073 (0.04)     | 1.9 [-10.1, 15.5] | 0.08 (0.04)       |
| 22:4n-6 | 3.17 (0.69)      | 3.54 (0.77)      | 11.4 [8.2, 14.8]  | 10.9 [7.3, 14.6]  |
| 22:5n-6 | 0.97 (0.33)      | 0.79 (0.29)      | -18.6 [-24.5, -12.3] | 0.92 (0.34)  |
| PUFA n-3 |                   |                  |                   |                   |
| 18:3n-3 | 0.19 (0.06)      | 0.22 (0.07)      | 18.0 [10.5, 25.9] | 15.2 [8.2, 22.7]  |
| 20:5n-3 | 0.41 (0.21)      | 0.43 (0.26)      | 7.1 [0.3, 14.5]   | 15.8 [8.0, 24.2]  |
| 22:5n-3 | 2.03 (0.33)      | 2.17 (0.41)      | 6.9 [3.5, 10.4]   | 8.3 [4.0, 12.7]   |
| 22:6n-3 | 3.59 (1.17)      | 3.79 (1.3)       | 5.7 [19.9, 9.6]   | 6.1 [17.1, 10.7]  |
| Trans  | 0.99 (0.25)      | 0.88 (0.27)      | -11.7 [-16.4, -6.7] | 1.00 (0.29)  |
| 16:1n-7f | 0.084 (0.03)     | 0.076 (0.02)     | -8.9 [-13.6, -4.0] | 0.08 (0.02)     |
| 16:1n-9f | 0.03 (0.01)      | 0.02 (0.01)      | -13.7 [-19.6, -7.4] | 0.03 (0.01)  |
| 18:1n-7f | 0.16 (0.06)      | 0.15 (0.07)      | -7.3 [-15.0, 1.0]  | 0.18 (0.06)     |
| 18:1n-9f | 0.3 (0.11)       | 0.26 (0.10)      | -14.0 [-18.7, -9.1] | 0.31 (0.12)  |
| 18:1n-10-12f | 0.20 (0.08) | 0.17 (0.08)      | -14.2 [-21.6, -6.1] | 0.20 (0.09)   |
| 18:2f  | 0.11 (0.06)      | 0.10 (0.05)      | -11.3 [-21.3, -1.1] | 0.11 (0.05)   |
| 18:2CLA | 0.07 (0.03)      | 0.07 (0.03)      | -9.9 [-16.9, -3.4] | 0.08 (0.03)   |
| Desaturase Activity6 | SC1 (16:1-7/16:0) | SC2 (16:1-9/18:0) | D6D (20:3n-6/18:2n-6) | D5D (20:4n-6/20:3n-6) |
| SCD1 (16:1-7/16:0) | 0.02 (0.01)      | 0.02 (0.01)      | 7.1 [11.1, 13.4]  | 0.02 (0.01)     |
| SCD2 (16:1-9/18:0) | 0.77 (0.11)      | 0.74 (0.09)      | -2.9 [-5.2, -0.5] | 0.76 (0.12)     |
| D6D (20:3n-6/18:2n-6) | 0.14 (0.04)      | 0.15 (0.04)      | 12.1 [7.4, 16.9]  | 0.13 (0.03)     |
| D5D (20:4n-6/20:3n-6) | 7.80 (2.62)      | 7.09 (2.13)      | -9.1 [-12.7, -5.4] | 7.66 (2.63)    |

Desaturase Activity6

SCD1 (16:1-7/16:0) 0.02 (0.01) 0.02 (0.01) 7.1 [11.1, 13.4] 0.02 (0.01) 0.02 (0.01) 8.8 [19.9, 16.3] 0.513 <0.001 0.713
SCD2 (16:1-9/18:0) 0.77 (0.11) 0.74 (0.09) -2.9 [-5.2, -0.5] 0.76 (0.12) 0.75 (0.10) -1.0 [-3.6, 1.6] 0.817 0.03 0.299
D6D (20:3n-6/18:2n-6) 0.14 (0.04) 0.15 (0.04) 12.1 [7.4, 16.9] 0.13 (0.03) 0.15 (0.03) 12.6 [7.5, 17.9] 0.414 <0.001 0.876
D5D (20:4n-6/20:3n-6) 7.80 (2.62) 7.09 (2.13) -9.1 [-12.7, -5.4] 7.66 (2.63) 7.11 (2.27) -7.2 [-11.0, -3.2] 0.832 <0.001 0.473


1 Number of parents with both baseline and 1-y values: Carotenoids (106 in SC and 99 in SC+EP); Fat-soluble vitamins (91-106 in SC and 95-99 in SC+EP); Fatty acids and desaturase activity (106 in SC and 99 in SC+EP).

2 F-tests on fixed effects of study group, time, and group by time interaction from a mixed-effects random intercept linear model.

3 Values are geometric means (STD); STD was estimated from log-transformed values and based on equations described in Quan et al.

4 Values are % mean difference [95% CI], calculated from model-based least square means as \{2.72^{\text{LSMEANS}(1 \text{ year } - \text{baseline})} \} – 1\*100

5 Values are calculated as fatty acid product: precursor ratios

SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; n-6, omega 6; n-3, omega 3; trans, trans fatty acids; CLA, conjugated linolenic acid; SCD1, stearoyl co-A desaturase; SCD2, stearoyl co-A desaturase 2; D5D, delta-5-desaturase; D6D, delta-6-desaturase.

### TABLE 3 Cardiometabolic Risk Factors at Baseline and End of the 1-year Intervention by Study Group

| CARDIOMETABOLIC RISK FACTORS | Standard Care (SC) | Standard Care + Enhanced Program (SC + EP) | P-value |
|-----------------------------|-------------------|-----------------------------------|---------|
| **BMI (kg/m²)**             | Baseline³ 1 Year³ | Mean Percent Difference⁴ Baseline³ 1 Year³ | Group  Time Group * Time |
| 33.0 (6.2)                  | 32.9 (6.0)        | -0.4 [-1.7, 0.9]                 | 31.8 (6.5) 31.6 (6.8) -0.7 [-2.1, 0.7] | 0.176 0.233 0.738 |
| **Blood Pressure (mmHg)**  |                   |                                   |         |
| Diastolic                   | 67.3 (8.8)        | 66.8 (8.9) -0.8 [-2.9, 1.3]     | 66.5 (8.8) 66.6 (8.4) -1.2 [-3.5, 1.1] | 0.158 0.200 0.786 |
| Systolic                    | 115.7 (14.9)      | 114.9 (13.2) -0.7 [-2.6, 1.2]  | 114.6 (16.4) 113.2 (14.2) -1.1 [-3.3, 1.1] | 0.170 0.206 0.779 |
| **Glucose Metabolism**      |                   |                                   |         |
| glucose (mg/dL)             | 103.4 (31.7)      | 103.8 (46.3) 0.3 [-5.7, 6.8]   | 98.8 (26.6) 101.1 (27.3) 2.3 [-1.0, 5.7] | 0.348 0.469 0.593 |
| insulin (uU/mL)             | 19.19 (9.91)      | 19.23 (10.3) 0.2 [-8.0, 9.1]   | 17.5 (9.39) 16.5 (9.68) 5.5 [-12.8, 2.4] | 0.030 0.357 0.328 |
| **Lipid Metabolism (mg/dL)**|                   |                                   |         |
| Total Cholesterol           | 179.2 (39.1)      | 181.4 (35.2) 1.2 [-1.8, 4.4]   | 184.0 (39.8) 184.2 (34.2) 0.2 [-2.6, 3.1] | 0.472 0.499 0.636 |
| LDL-Cholesterol             | 104.0 (35.1)      | 106.9 (32.1) 2.9 [-14.7, 9.5]  | 107.0 (32.0) 111.1 (28.9) 3.7 [0.0, 7.6] | 0.270 0.024 0.801 |
| HDL-Cholesterol             | 48.6 (10.7)       | 48.4 (11.3) 0.5 [-3.1, 2.2]    | 48.9 (11.8) 47.4 (10.4) -3.1 [-5.7, 0.4] | 0.781 0.062 0.168 |
| Triglycerides               | 115.2 (81.9)      | 108.5 (70.0) -5.8 [-12.8, 1.8] | 113.6 (87.4) 107.7 (73.4) 4.9 [-12.0, 2.9] | 0.776 0.051 0.862 |
| **Inflammatory Markers**    |                   |                                   |         |
| hsCRP (mg/L)                | 4.06 (20.4)       | 3.64 (18.9) -10.3 [-22.0, 3.2] | 3.86 (10.2) 2.82 (9.41) -26.9 [-37.0, -15.2] | 0.343 <0.001 0.049 |
| TNFa (pg/mL)                | 4.82 (1.52)       | 3.85 (1.44) -20.1 [-25.4, -14.4] | 4.75 (1.71) 4.08 (1.57) -14.2 [-20.2, -7.8] | 0.63 >0.001 0.164 |
| IL-6 (pg/mL)                | 1.35 (2.86)       | 1.12 (1.99) -16.9 [-28.9, -3.0] | 1.17 (1.95) 0.97 (1.27) -17.6 [-30.0, -3.0] | 0.291 <0.001 0.946 |

**Vascular Adhesion and Coagulation Markers**
|                  | SC  | SC+EP |
|------------------|-----|-------|
| **E-selectin (pg/mL)** | 4.12 (4.18) | 4.31 (3.92) |
| **P-selectin (pg/mL)**  | 37.4 (24.9) | 45.9 (28.4) |
| **sICAM-3 (ng/mL)**      | 0.51 (0.38) | 0.57 (0.29) |
| **Thrombomodulin (ng/mL)** | 1.76 (0.87) | 1.83 (0.72) |

**Adipokines**

|                  | SC  | SC+EP |
|------------------|-----|-------|
| **Adiponectin (mg/mL)** | 87.3 (48.4) | 84.1 (48.5) |
| **Leptin (ng/mL)**      | 25.6 (33.0) | 24.7 (34.1) |

1Number of parents with both baseline and 1-y values: BMI (99 in SC and 94 in SC+EP); blood pressure (100 in SC and 94 in SC+EP); glucose metabolism, lipid profile, and hsCRP (103-106 in SC and 97-99 in SC+EP); other inflammatory, vascular adhesion, and coagulation markers and adipokines (98-99 in SC and 92-93 in SC+EP).

2F-tests on fixed effects of study group, time, and group by time interaction from a mixed-effects random intercept linear model.

3Values are geometric means (STD); STD was estimated from log-transformed values.

4Values are mean percent difference [95% CI], calculated from model-based least square means.

hsCRP, high-sensitive C-reactive protein; TNFα, tumor necrosis factor alpha; IL, interleukin; sICAM-1, soluble intercellular adhesion molecule-1.