Over the span of the last decades there has been an alarming worldwide increase in childhood obesity [1], which tends to track into adulthood [2]. Childhood obesity is associated with a significant risk for the development of type 2 diabetes, hypertension, dyslipidemia, metabolic syndrome, and is also a risk factor for early cardiovascular events. The timing of the obesity epidemic is parallel to the increased availability of calorie-dense foods and a more sedentary lifestyle – the ‘obesogenic environment’ [3]. However, not all individuals become obese while living in the same environment. Therefore, variability among individuals is suspected to result from heritability of obesity susceptibility genes that interact with components in the ‘obesogenic environment’ to promote positive energy balance responsible for weight gain [4].

Recent evidence, primarily from animal studies and observational data in humans, suggests that the epigenome can be altered by maternal diet during the periconceptual period and that these programming events may underlie later disease risk. In one of the works cited below it was demonstrated that the periconceptual micronutrients altered methylation at the differentially methylated regions of imprinted genes associated with obesity. These results may support the concept that nutrition in critical periods of life can permanently influence the development of chronic diseases. The ‘obesogenic environment’ is a complex of contributing factors that influence the dietary choice, physical activity, or metabolism responsible for maintaining energy balance. Both sedentary behavior and reduced physical activity promote the overconsumption of dietary macronutrients, particularly fats and refined carbohydrates [5]. It is widely accepted that high-fat diets, characterized by enhanced palatability and high-energy density, may be primarily responsible for the current obesity epidemic. Also, increased consumption of carbohydrates, particularly refined carbohydrates and sugar-sweetened beverages, can contribute to the increased prevalence of obesity [6]. The dietary pattern, food frequency, and breakfast consumption may also have an im-
impact on body weight and on markers of the metabolic syndrome. Finally, the connection between gut microbiota, energy homeostasis, and inflammation and its role in the pathogenesis of obesity-related disorders are emerging as a new break for intervention. Although current childhood obesity intervention programs have traditionally focused only on generalized population guidelines, further investigation and insight into gene-diet interactions may serve an important role in both the prevention and treatment of childhood obesity by using targeted nutritional and drug therapies. This chapter reviews a selection of important articles published between July 2012 and June 2013 focusing on the relation between nutrition, obesity and metabolic syndrome in the pediatric age group.

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**DNA methylation profiling at imprinted loci after periconceptional micronutrient supplementation in humans: results of a pilot randomized controlled trials**

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FASEB J 2012; 26: 1782–1790

**Background:** Nutrition around conception and during pregnancy was associated with earlier onset of diseases of affluence, particularly coronary heart disease (CHD), obesity and type 2 diabetes (T2D). Several animal trials support these observations, however no randomized controlled trial existed to test this in humans. The influence of nutrition on epigenome (DNA methylation and histone modification) could at least in part cause the observed association. Imprinted genes confer monoallelic (from 1 parent) expression of one or more transcripts likely to be caused by different methylation of differentially methylated regions (DMRs). The methylation imprints at maternally methylated gametic DMRs are thought to be set up postnatally during the final stages of oocyte maturation and may be particularly susceptible to nutritional insufficiencies in the pre- and periconceptional period. After fertilization, methylation at gametic DMRs resists genome-wide demethylation events that occur in early embryo until implantation.

**Aims:** The randomized controlled trial of United Nations International Multiple Micronutrient Preparation (UNIMMAP) periconceptional supplementation in rural Gambia was utilized to investigate if periconceptional nutritional exposures affect DNA methylation at imprinted loci.

**Methods:** Non-pregnant women aged 17–45 were randomized to receive daily supplementation with either UNIMMAP or placebo. Once pregnancy was confirmed in a woman who ceased supplementation. DNA was extracted from cord blood of 22 newborns of compliant mothers in the intervention group and 36 newborns from the control group. The loci chosen for quantification of methylation using mass spectrometry included paternally or maternally methylated germline and so-
matic DMRs, previously associated with known human disorders (Prader-Willi syndrome, Angelman syndrome, Beckwith-Wiedemann syndrome, Silver-Russell syndrome, pseudohypoparathyroidism, and transient neonatal diabetes mellitus syndrome).

**Results:** The difference in methylation was statistically significant for 2 of the 13 regions, IGF2R-DMR and GTL2-DMR, when analyzed separately by gender. UNIMMAP intervention significantly reduced methylation levels at IGF2R-DMR in girls and GTL2-DMR in boys.

**Conclusions:** Despite several limitations of this trial the present observations indicate that from a randomized controlled trial independent of seasonal effects, periconceptional nutrition could influence gender-specific methylation of critical fetal imprints.

**Comments**

This study provides preliminary pilot results obtained in nucleated cells from cord blood. The statistical analysis did not include Bonferroni correction for multiple comparisons and thus the results may not be statistically significant using a more rigorous analysis. Additionally, findings from the cord blood were not confirmed in samples taken at the age of 9 months. Despite several important limitations, this is the first randomized controlled trial demonstrating that periconceptual micronutrients may alter methylation at the DMRs in imprinted genes. If confirmed in a larger trial, these results may support an important concept that nutrition in critical periods of life can permanently influence the development of chronic diseases.

**Sexual dimorphism in the early life programming of serum leptin levels in European adolescents: the HELENA study**


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*J Clin Endocrinol Metab 2011; 96: E1330–E1334*

**Background:** Adverse intrauterine circumstances reflected in lower birth weight are associated with earlier onset of chronic diseases such as obesity and type 2 diabetes.
**Aims:** This study tested the relationship between birth weight and serum leptin concentration in adolescents, and its possible gender dimorphism.

**Methods:** Healthy Lifestyle in Europe by Nutrition in Adolescence (HELENA) cross-sectional study involved 3,546 adolescents. The present study selected 757 adolescents born at >37 weeks after amenorrhea with complete and valid data on birth weight, serum leptin concentration, body mass index (BMI), and pubertal status (Tanner). Physical activity was assessed with accelerometry over 7 days. Fasting serum leptin concentrations were measured with ELISA.

**Results:** There was a significant interaction between birth weight and gender on serum leptin levels (p < 0.04). Body weight at birth was significantly negatively associated with serum leptin levels in female adolescents controlled for center, duration of gestation and breastfeeding, pubertal status, and BMI. Results remained significant when controlled for physical activity (β = –0.115; p = 0.016). Likewise, the results did not substantially change when the analysis was controlled for z-score BMI (β = –0.119; p = 0.003), body fat percentage (β = –0.100; p < 0.015), or waist circumference (β = –0.117; p = 0.006) instead of BMI. Similarly, results remain significant when overweight and obese were excluded from the analysis.

**Conclusions:** Further evidence for a possible gender-specific programming effect of birth weight on the energy homeostasis in adolescence is provided. The association between lower birth weight and the increased long-term risk of developing obesity and type 2 diabetes may be in part mediated by different programming of energy metabolism.

**Comments**

This study has several limitations due to its retrospective (questionnaire-based) and cross-sectional design. Additionally, estrogen concentrations, known to influence leptin concentration in females, were not measured. However, reported results are in line with more than a few similar reports from animal models and are of obvious clinical relevance. Further prospective studies are warranted to investigate the relationship between intrauterine nutritional environment and later abundance-associated morbidity.

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**A trial of sugar-free or sugar-sweetened beverages and body weight in children**

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**Background:** Beverages containing sugar are assumed to cause a more significant increase in body weight than solid foods because they do not lead to a sense of satiety. Consumption of sugar-sweetened beverages may be associated with undiminished intake of calories from other foods and beverages, resulting in weight gain.

**Aims:** As the existing results were not conclusive, a Double-blind, Randomized Intervention Study in Kids (DRINK) was commenced to examine the effect of masked replacement of sugar-sweetened beverages with non-caloric, artificially sweetened beverages on weight gain.

**Methods:** In this 18-month, double-blind, randomized, controlled trial, 641 schoolchildren living in the community who were 4 years 10 months to 11 years 11 months of age were enrolled, stratified according to school, sex, age, and initial body mass index (BMI), and individually randomly assigned to 1 can daily of a non-caloric, artificially sweetened, non-carbonated beverage or a sugar-containing non-carbonated beverage. Children in the same household received
the same type of blinded beverage. Body weight, height, skinfold thickness, waist circumference, and arm-to-leg electrical impedance were measured and urine samples at 0, 6, 12, and 18 months were collected. Adherence to the protocol was monitored.

**Results:** The adherence beverage consumption was 88% at 6 months, 81% at 12 months, and 74% at 18 months. Children who dropped out had a slightly higher BMI at baseline, and their parents had completed fewer years of school. The 477 children who completed the study consumed 5.8 out of 7 (83%) cans per week, with no difference between the groups or over time. The level of urinary sucralose confirmed the adherence in the control group. In the full cohort of 641 children with missing values imputed, the mean BMI z-score increased by 0.02 ± 0.41 SD units in the sugar-free group and by 0.15 ± 0.42 SD units in the sugar group; the mean difference of 0.13 SD units was significant, also when adjusted for age. The sugar-free group gained significantly less body fat, as evidenced by skinfold thickness, waist-to-height ratio, and electrical impedance. The mean weight increased by 6.35 ± 3.07 kg in the sugar-free group and by 7.37 ± 3.35 kg in the sugar group, with the mean difference of 1.01 kg being significant, also when adjusted for height change. Children in the sugar-free group who completed the study gained 35% less fat according to impedance measurements and 19% less fat according to four skinfolds measurements (a gain of 1.47 vs. 1.82 kg of body fat).

**Conclusions:** Weight gain and body fat gain in healthy children were significantly reduced by masked replacement of a sugar-containing beverage with a sugar-free beverage.

**Comments**

This study provides extremely important and strong evidence that sugar-sweetened beverages increase body weight and body fat in children. Similar results were obtained in adolescents, which considerably adds to the weight of evidence. Interestingly, further evidence suggests that sugar-sweetened beverages can have a particularly strong negative effect on persons genetically susceptible for obesity [7]. Taking this together, all professionals involved in the care of children and adolescents as well as parents and society as such should act upon this evidence and reduce the risks these young people are exposed to through sugar-sweetened beverages.

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**A randomized trial of sugar-sweetened beverages and adolescent body weight**

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**Background:** The consumption of sugar-sweetened beverages among adolescents has increased in tandem with the prevalence of pediatric obesity, suggesting a causal relationship. At present, a substantial proportion of high-school students habitually consume sugar-sweetened beverages, including carbonated soda, energy drinks, and highly sweetened coffees and teas. Short-term feeding studies show greater energy intake and weight gain with the consumption of sugar-sweetened beverages than with beverages containing artificial sweeteners.
**Objective:** This study was designed to test the hypothesis that overweight and obese adolescents who received an intervention to reduce the consumption of sugar-sweetened beverages would gain weight at a slower rate than those who did not receive the intervention.

**Methods:** Overweight and obese adolescents who regularly consumed sugar-sweetened beverages (n = 224) were randomly assigned to intervention and control groups. The intervention group received a 1-year intervention designed to decrease consumption of sugar-sweetened beverages, with follow-up for an additional year without intervention.

**Results:** The retention rate for study participants was 97% at 1 year and 93% at 2 years, with no significant difference between groups in the percentage of participants available at 2 years for assessment of the primary outcome. Reported consumption of sugar-sweetened beverages was similar at baseline in the intervention and control groups (1.7 servings/day), declined to nearly zero in the intervention group at 1 year, and remained lower than in the control group at 2 years. The change in mean BMI at 2 years did not differ significantly between the groups. At 1 year, there were significant between-group differences for changes in BMI and weight. Only among Hispanic participants (27 in the intervention group, 19 in the control group) there was a significant between-group difference in the change in BMI at 1 and 2 years. The change in the percentage of body fat did not differ significantly between groups at 2 years.

**Conclusions:** The provision of non-caloric beverages virtually eliminated reported consumption of sugar-sweetened beverages and reduced total reported energy intake among overweight and obese adolescents after a 1-year intervention, with persistent effects on diet through follow-up at 2 years. Replacement of sugar-sweetened beverages with non-caloric beverages did not improve body weight over a 2-year period, but group differences in dietary quality and body weight were observed at the end of the 1-year intervention period.

**Comments**

Over the past years, the notion of the coincident increase in sugar-sweetened beverages consumption with increased prevalence of obesity raised the possibility to limit the consumption of caloric soft drinks, especially in children and adolescents, in order to fight the epidemic of obesity. Caloric drinks are marketed for young people by intensive advertising strategies. These drinks may drive greater energy intake and weight gain through satiety signaling and compensatory dietary responses. A recent published paper [7] provides evidence that individuals with a more pronounced genetic predisposition to obesity may be more susceptible to the adverse effects of sugar-sweetened beverages on BMI. In the present study, education and behavioral counseling focused specifically on decreasing consumption of sugar-sweetened beverages, a single dietary behavior that may be particularly important for controlling body weight. The significant intervention effect for the change in BMI observed at 1 year, together with the findings of de Ruyter et al. (in the previous abstract), provides support for public health guidelines that recommend limiting consumption of sugar-sweetened beverages. The lack of effect at 2 years could reflect increasing energy intake from sugar-sweetened beverages or fruit juices in the intervention group on discontinuation of the intervention or decreasing intake of sugar-sweetened beverages or fruit juices in the control group, possibly due to the efforts to eliminate these beverages from schools.
Prospective associations between sugar-sweetened beverage intakes and cardiometabolic risk factors in adolescents

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**Background:** Sugar-sweetened beverages have been linked with weight gain, type 2 diabetes, and increased cardiovascular disease risk in adults. However, a better understanding of the relations between sugar-sweetened beverages and cardiometabolic health in children and adolescents is required. It was hypothesized that increases in sugar-sweetened beverages consumption between 14 and 17 years of age would be positively associated with a greater odds of overweight or obesity and unfavorable changes in cardiovascular disease risk factors, independent of body weight.

**Objective:** This study investigated prospective associations between sugar-sweetened beverages consumption and cardiometabolic risk factors in a cohort of adolescents for whom diet has been well characterized.

**Methods:** Data were provided by adolescents (n = 1,433) offspring from the Western Australian Pregnancy Cohort (Raine) Study, in which 2,900 pregnant women at 16–20 weeks' gestation were recruited through public and private antenatal clinics in Western Australia between 1989 and 1991. Of these subjects, 2,804 women (97%) had 2,868 live births. These children and their families have been followed up at regular intervals since. The data were derived from follow-ups at 14 and 17 years of age about sugar-sweetened beverages intakes estimated by a food-frequency questionnaire, and measurements of BMI, waist circumference (WC), blood pressure (BP), fasting serum lipids, glucose, and insulin. The overall cardiometabolic risk was estimated. Associations between sugar-sweetened beverages intake and cardiovascular disease risk factors were done adjusted for age, pubertal stage, physical fitness, socioeconomic status, and major dietary patterns.

**Results:** Sugar-sweetened beverages were the most consumed beverage type in both genders, and 89% of respondents were sugar-sweetened beverages consumers at each follow-up. Sugar-sweetened beverages provided 4–5% of total energy intakes of which ~50% came from carbonated or soft drinks. At baseline (14 years of age), the average BMI, WC, total energy intake, systolic BP, fasting triglycerides, and z-score for the Western dietary pattern increased, whereas the average HDL cholesterol, glucose, and z-score for the healthy dietary pattern decreased, with increasing intakes of sugar-sweetened beverages (p trend <0.05). The prevalence of obesity, low maternal education, and low family income increased with higher sugar-sweetened beverages intakes (p < 0.05). Girls who moved into the highest tertile of sugar-sweetened beverages consumption (>1.3 servings/day) between the ages 14 and 17 years had a 4.8 times greater odds of overweight or obesity (p trend <0.0001) and a 3 times greater odds (p trend = 0.001) of being classified at a greater metabolic risk at 17 years than did girls who remained in the lowest sugar-sweetened beverages tertile. These associations were not observed in boys. Compared with staying in the lowest sugar-sweetened beverages tertile, moving into the highest tertile of sugar-sweetened beverages intake between the ages 14 and 17 years was associated with an average increases in BMI of 3.8% (p trend <0.001) in girls, and with increases in WC in both genders. With higher sugar-sweetened beverages intake, there was an increasing trend in fasting triglycerides in both genders (p trend ≤0.003), and decreasing in HDL cholesterol concentrations in boys (p trend ≤0.02), even after adjustment for total energy intake.
Conclusion: Greater sugar-sweetened beverages intakes during adolescence were prospectively associated with greater overweight and obesity risk and higher overall cardiometabolic risk in girls and unfavorable changes in WC and triglycerides (for both genders), and HDL cholesterol (for boys), independent of BMI.

Comments
Sugar-sweetened beverages which include carbonated (soft) drinks and fruit drinks with added sugar are supposed to increase obesity risk primarily because they provide a liquid form of energy that has less impact on satiety than isoenergetic food. Sugar-sweetened beverages may also have direct effects on cardiometabolic health, independent of weight gain. Experimental and observational studies have shown that high sugar-sweetened beverages consumption increases the dietary glycemic load, which can lead to insulin resistance, impaired β-cell function, and inflammation. In addition, high intakes of fructose sweeteners in sugar-sweetened beverages have been linked to visceral adiposity, hepatic lipogenesis, and hypertension [8]. The follow-up period in this cohort of adolescents was relatively short (2 years), and these changes may accumulate over time. Thus, the results of this study suggest that sugar-sweetened beverages consumption should be limited in young people not only for obesity prevention, but also in order to reduce future cardiometabolic risk.

Dietary salt intake, sugar-sweetened beverage consumption, and obesity risk
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Pediatrics 2013; 131: 14–21

Background: Greater consumption of sugar-sweetened beverages over the previous two decades may be associated with the rise in childhood obesity rates. Emerging evidence suggests that a reduction in dietary salt intake may reduce sugar-sweetened beverages consumption. The mechanism behind this relationship lies in the homeostatic trigger of thirst in response to the ingestion of dietary salt. It is suggested that in an environment where soft drinks are readily available, a high-salt diet may encourage greater consumption of soft drinks in children.

Objective: The aim was to examine the association between dietary salt intake, overall fluid consumption, as well as sugar-sweetened beverages consumption, and to examine the association between sugar-sweetened beverages consumption and weight status.

Methods: The study was based on cross-sectional data from the 2007 Australian National Children’s Nutrition and Physical Activity Survey of children aged 2–16 years. Consumption of dietary salt, fluid, and sugar-sweetened beverages was determined via two 24-hour dietary recalls. Height and weight were recorded and served for BMI calculation. The association between salt, fluid, sugar-sweetened beverages consumption, and weight status was assessed using regression analysis.

Results: 62% of all the 4,283 participants reported consuming sugar-sweetened beverages, without a difference between genders. Salt intake and fluid consumption increased with age, with a positive correlation between salt intake and total fluid consumption (r = 0.42, p < 0.001), even after adjustment for age, gender, socioeconomic status (SES), and BMI (p < 0.001). Older age and lower SES were both significantly associated with higher sugar-sweetened beverages consumption (both p < 0.001). Consumers of sugar-sweetened beverages were more likely to be overweight and obese than non-consumers (p < 0.05). In sugar-sweetened beverages consumers (n = 2,571), salt intake was
positively associated with sugar-sweetened beverages consumption ($r = 0.35, p < 0.001$), adjusted for age, gender, SES, and energy ($p < 0.001$). Children who consumed >1 serving of sugar-sweetened beverages were 26% more likely to be overweight/obese ($p < 0.01$).

**Conclusions:** The consumption of sugar-sweetened beverages is relatively common in Australian children aged 2–16 years and dietary salt intake was positively associated with overall fluid consumption. Furthermore, within consumers of sugar-sweetened beverages, dietary salt intake predicted sugar-sweetened beverages consumption, which was associated with an increased risk of obesity.

**Comments**
The major strengths of this study include the use of a large, nationally representative sample of Australian children, with a comprehensive and standardized collection of dietary intake, anthropometric, and demographic data. Over the life course, minor changes in energy balance can increase the risk of obesity. In children on relatively high salt intakes, experiencing a drive for fluid, with easy access to sugar-sweetened beverages, a greater consumption of sugar-sweetened beverages may occur. The consumption of sugar-sweetened soft drinks is associated with reduced vegetable and milk consumption (typically low-salt foods) and higher consumption of fast food (e.g. hamburgers and french fries, typically high-salt foods). Thus, it is possible that some of the association reported in the current study is a result of the overall clustering of ‘unhealthy’ dietary behaviors. Thus, in addition to the known benefits of salt reduction on reducing blood pressure, a reduction in salt intake in children may assist in reducing the amount of sugar-sweetened beverages consumed, which in turn may help to reduce energy intake and could be useful in obesity prevention efforts.

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**Longitudinal evaluation of milk type consumed and weight status in preschoolers**

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**Background:** The American Academy of Pediatrics recommends that children ≥2 years old consume low-fat milk. Data have been mixed regarding the associations between consumption of low-fat milk, weight status and weight gain over time in preschoolers.

**Objective:** It was hypothesized that low-fat milk would be associated with lower BMI z-score and less weight gain over time. Thus the aim of the study was to evaluate the relationship between milk fat consumption and BMI among a large cohort of preschool children.

**Methods:** In this longitudinal cohort study, a representative sample of US children, 10,700 children were examined at age 2 and 4 years. The BMI z-score and overweight/obese status as a function of milk type intake were assessed.

**Results:** The majority of children drank whole or 2% milk (87% at 2 years, 79.3% at 4 years). Drinkers of 1%/skim milk had higher BMI z-scores than 2%/whole-milk drinkers. In multivariable analyses, increasing fat content in the type of milk consumed was inversely associated with BMI z-score ($p < 0.0001$). Children 2 and 4 years old drinking 1%/skim milk compared to those drinking 2%/whole milk had an increased adjusted odds of being overweight (age 2, OR 1.64, $p < 0.0001$; age 4, OR 1.63, $p < 0.0001$) or obese (age 2, OR 1.57, $p < 0.01$; age 4, OR 1.64, $p < 0.0001$). In longitudinal
analysis, children drinking 1%/skim milk at both 2 and 4 years were more likely to become overweight/obese in this time period (adjusted OR 1.57, p < 0.05).

**Conclusions:** Consumption of low-fat milk did not prevent weight gain in preschoolers over time and was associated with an increased risk of overweight/obesity between 2 and 4 years of age.

**Comments**

In both children and adults, key contributors to the current obesity epidemic are the high-fat diets increasingly consumed worldwide. The AAP first started recommending low-fat milk for all children >2 years old in 2005 [9] after the onset of the current epidemic of obesity. Encouraging consumption of low-fat/skim milk instead of high-fat milk promotes a reduction of daily consumed fat and calories among children drinking milk. Using a large, nationally representative database, the researchers of this study found multiple associations between intake of 1%/skim milk and higher BMI z-scores in preschoolers, even across racial/ethnic and SES categories. These data may reflect the fact that parents of children with higher BMIs are more likely to adhere to recommendations of healthcare providers in selecting low-fat milk. Nevertheless, the prevalence of consumption of 1%/skim milk in preschool children remains low, as less than 20% of overweight or obese children consumed 1% or skim milk. Thus, healthcare practitioners following preschool children will have to focus on weight-control practices with a stronger evidence base than available for consumption of low-fat milk in order to reduce the risk of obesity.

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**Meal frequencies modify the effect of common genetic variants on body mass index in adolescents of the northern Finland birth cohort 1986**


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PLoS One 2013; 8: e73802

**Background:** Several obesity-related genetic loci have been identified through genome-wide association studies (GWAS) in adult populations, with common single nucleotide polymorphisms (SNPs) in the FTO and MC4R genes also associated with weight gain in children and adolescents. Interestingly, behavioral modification can influence genetic risk: dietary fat composition was found to modify the association between the FTO gene variant rs9939609 and obesity risk in pediatric population, and in highly physically active adolescents the risk of higher BMI was significantly attenuated even among those carrying two risk alleles in the FTO gene.
**Aims:** The aim of the present study was to investigate the impact of two meal frequencies, 5 meals a day and <4 meals a day, on the association between obesity-related genotypes and BMI among adolescents.

**Methods:** From the prospective Finish neonatal cohort, 80% (n = 7,344) of the adolescents responded to a postal questionnaire concerning their health behavior and wellbeing and 74% (n = 6,798) participated in a clinical examination at the 16-year follow-up. Eight SNPs were genotyped at or near the **FTO** (fat mass- and obesity-associated), **MC4R** (melanocortin-4 receptor), **BDNF** (brain-derived neurotrophic factor), **GNPDA2** (glucosamine-6-phosphate deaminase-2), **MAF** (v-maf musculoaponeurotic fibrosarcoma oncogene homolog), **TMEM18** (transmembrane protein-18), **KCTD15** (potassium channel tetramerization domain containing-15), and **NEGR1** (neuronal growth regulator-1) genes, respectively.

**Results:** Carriers of two risk alleles in FTO rs1421085 had an increased BMI (21.7 [95% CI 21.5, 22.0] kg/m$^2$) compared with individuals with 0 or 1 risk allele (20.9 [95% CI 20.8, 21.1] kg/m$^2$ and 21.2 [95% CI 21.0, 21.3] kg/m$^2$, respectively). Similarly, carrying both of the risk-conferring alleles of rs17782313 at the MC4R locus was associated with a greater BMI (22.2 [95% CI 21.6, 22.9] kg/m$^2$) compared with the other two genotypes (TT 21.1 [95% CI 21.0, 21.2] kg/m$^2$ and CT 21.3 [95% CI 21.1, 21.5] kg/m$^2$). Regular meals were associated with lower BMI (20.7 [95% CI 20.6, 20.8] kg/m$^2$) as compared to skipping meals (21.6 [95% CI 21.5, 21.7] kg/m$^2$). The difference in BMI between the individuals with a high GRS (>8 BMI-increasing alleles) and those with a low GRS (<8 BMI increasing alleles) was 0.90 (95% CI 0.63, 1.17) kg/m$^2$ with irregular meals, whereas with the regular meals, this difference was only 0.32 (95% CI 0.06, 0.57) kg/m$^2$ (p interaction = 0.003). Moreover, gender-stratified analysis demonstrated significant interaction between the FTO rs1421085 and meal frequencies on BMI in boys (p interaction = 0.015) but not in girls (p interaction = 0.617). The difference in BMI between the carriers of the two MC4R rs17782313 risk alleles and non-carriers was elevated to 1.92 kg/m$^2$ with irregular meals, and reduced to 0.34 kg/m$^2$ (p interaction = 0.016) with irregular meals.

**Conclusions:** Each additional BMI-increasing allele was associated with an increase in BMI of 0.21 kg/m$^2$ which corresponds to a 0.61-kg increase in body weight for a person of 170 cm height. This was attenuated to 0.15 kg/m$^2$ (0.43 kg) with regular eating and increased to 0.27 kg/m$^2$ (0.78 kg) with irregular eating.

**Comments** This interesting study indicates that a regular five-meal-a-day habit tempers the effects of genetic susceptibility to increased BMI. Promoting a regular eating habit consisting of five meals including breakfast seems to be a powerful obesity prevention approach conveying additional important health benefits. We all are expecting confirmatory results, ideally from national large-scale randomized controlled intervention trials.

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**Eating frequency and overweight and obesity in children and adolescents: a meta-analysis**

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*Pediatrics* 2013; 131: 958–967

**Background:** The existing dietary etiological models cannot fully explain the development and maintenance of childhood obesity. Dietary patterns and eating behaviors may contribute to this epidemic more than consumption of specific nutrients and foods.
**Objectives:** The research question addressed here was to evaluate to what extent eating frequency is associated with body weight status (overweight/obesity), in children and adolescents. Total eating frequency was evaluated since there is no scientific consensus on the most appropriate definition to categorize the different eating occasions (i.e. meals vs. snacks).

**Methods:** Original research, observational studies published until October 2011, examining the association between eating frequency and overweight/obesity status in children and adolescents, were selected through a literature search in the PubMed database for this meta-analysis. Specific key words were used for this search: 'eating frequency', 'meal frequency', 'meals' and 'eating episodes,' in combination with the term 'overweight' or 'obesity' in children and adolescents. Pooled effect sizes were calculated using a random effects model.

**Results:** The presented meta-analysis of 21 substudies, with an overall incorporated population of 18,849 participants (aged 2–19 years), revealed an inverse association between eating frequency (i.e. the total number of meals/eating episodes consumed on a daily basis) and overweight/obesity status in children and adolescents. Specifically, children and adolescents who had a higher number of eating episodes per day had 22% lower probabilities of being overweight or obese compared with those who had fewer episodes. Interestingly, the inverse association was evident only in boys, suggesting that there are gender-related differences in dietary patterns and behaviors with their effect on overweight/obesity.

**Conclusions:** An inverse association was found between eating frequency and overweight/obesity status in children and adolescents. Gender-related differences emerged when this association was assessed separately in boys and girls, as the effect of eating frequency was only evident in boys.

**Comments**

Several pathways have been proposed to explain the association between higher eating frequency and lower body weight in children. In adults, it was found that increased eating frequency attenuates a series of postprandial metabolic and endocrine responses to dietary intake. The presented results are in accordance with a previous cross-sectional study in Greek adolescents, showing that the daily frequency of eating episodes was associated with obesity indices in boys, but not in girls [10]. However, it has to be emphasized that the subanalysis in girls was underpowered, and there was heterogeneity of the effect sizes of the selected studies leading to the inconsistencies between studies. Other limitations of this meta-analysis include: a significant heterogeneity in the pooled analysis, which caveats the generalization of the results, the methodological differences between studies, and the difference in the definition used for overweight/obesity in children and adolescents and the way that eating frequency was assessed, and finally confounding factors that were included in the analysis that varied between studies. Therefore, additional clinical trials are warranted to clarify potential mechanisms that may be responsible for a gender-dependent effect, to evaluate the clinical practice applicability, and support a public health recommendation. Future studies should also evaluate the size and types of meals and snacks in terms of volume, energy content, macronutrient composition, or glycemic index and take this evaluation into account when investigating the associations between eating/meal patterns and obesity.
Identification of a dietary pattern prospectively associated with increased adiposity during childhood and adolescence

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Background: Dietary intake is an important determinant of energy balance, but it is difficult to accurately measure energy intake (EI) in large population studies. Estimated EI is prone to dietary underreporting regardless of the dietary assessment method. The resulting imprecision in EI measurement makes it difficult to identify associations between EI and weight gain. Dietary pattern (DP) analyses have been increasingly used to consider total food intake and the potentially synergistic effects of foods and nutrients. Studies in adults suggest that dietary energy density, fat and fiber are critical dietary factors.

Objective: It was hypothesized that the same energy-dense, high-fat, low-fiber DP would be observed at 7, 10 and 13 years of age, and that this pattern would be prospectively associated with greater body fatness at 11, 13 and 15 years of age. As innate appetite control is stronger at younger ages, a second hypothesis was that the relationship between this DP and body fatness would strengthen with age. The longitudinal relationships between a DP characterized by dietary energy density, % total energy from fat and fiber density and fat mass (FM) was examined in children.

Methods: Children aged 7–15 years of age from the UK Avon Longitudinal Study of Parents and Children (n = 6,772) participated in the study. Their dietary intake was assessed using a 3-day food diary at 7, 10 and 13 years of age. An energy-dense, high-fat, low-fiber DP was identified using reduced rank regression and subjects scored for the DP at each age. Fat mass (FM) was measured at 11, 13 and 15 years and fat mass index (FMI) calculated as FM/height (χ).

Results: Girls had a higher prevalence of overweight or obesity based on BMI, at all ages. An increasing score for the energy-dense, high-fat, low-fiber DP at 7 years of age was associated with greater intakes of dietary energy density, % energy from fat and saturated fat, and lower fiber density, % energy from protein and carbohydrate, vitamin C and folate. Associations were similar at 10 and 13 years of age. DP z-scores at all ages were positively associated with later FMI. For each 1 SD unit increase in DP z-score, the odds of being in the highest quintile for FMI (as a marker of excess adiposity) increased by 13% (95% CI 1–27).

Conclusions: This analysis indicates that a DP that is high in energy density, high in fat and low in fiber is prospectively associated with greater adiposity in childhood and adolescence.

Comments: This study has several major strengths. Data were collected approximately every 2 years, enabling a longitudinal analysis spanning 7–15 years of age. The use of 3-day food diaries provides detailed characterization of dietary intake and avoids reliance on dietary recall. The observed associations between the DP and adiposity in this study were independent of physical activity measured objectively with accelerometers, whereas most other studies have relied on physical activity questionnaires. Therefore, this study provides important information for possible interventions and policy in the area of obesity prevention in young people.
Beneficial effects of a higher-protein breakfast on the appetitive, hormonal, and neural signals controlling energy intake regulation in overweight/obese, ‘breakfast-skipping,’ late-adolescent girls

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Background: Recent evidence has isolated several key factors that play a critical role in the etiology of obesity, including the unhealthy dietary habit of breakfast skipping. In addition, breakfast skippers have poor diet quality and make poor food choices (e.g. snacking on nutrient-poor, high-fat, and/or high-sugar foods and beverages) compared with breakfast consumers. A diet rich in high-quality protein is considered a successful strategy to promote weight loss and/or prevent weight gain or regain in adults by improvement in appetite control and satiety. A protein-rich breakfast has been shown to reduce pre-lunch neural activation in brain regions that control food motivation/reward compared with skipping breakfast or consuming a normal-protein breakfast.

Objective: To examine in overweight/obese teenage girls who skip breakfast whether a high-protein (HP) breakfast leads to daily improvements in appetite control, satiety, food motivation/reward, and evening snacking compared with normal protein (NP) breakfast meals.

Methods: 20 overweight or obese teenage girls (mean age 19 ± 1 years, BMI 28.6 ± 0.7) who skip breakfast participated in this randomized crossover study. The participants randomly completed the following breakfast patterns at home for 6 days: (1) breakfast skipping, (2) consumption of 350-kcal NP breakfast meals cereal-based (13 g protein), or (3) consumption of 350-kcal HP breakfast meals egg- and beef-rich (35 g protein). On the 7th day of each pattern, a standardized NP lunch was provided 4 h after breakfast, and a 10-hour testing was completed that included appetite and satiety questionnaires, blood sampling, pre-dinner food cue-stimulated functional MRI brain scans, ad libitum dinner, and evening snacking.

Results: The consumption of breakfast reduced daily hunger compared with breakfast skipping with no differences between meals. Breakfast, especially that containing HP, increased daily fullness, and reduced evening snacking of high-fat foods compared with breakfast skipping. HP breakfast also reduced daily ghrelin and increased daily peptide YY concentrations compared with breakfast skipping. Both meals reduced pre-dinner amygdala, hippocampal, and midfrontal cortico-limbic activation compared with breakfast skipping.

Conclusions: The consumption of 350-kcal breakfast meals led to daily reductions in perceived hunger, desire to eat, and prospective food consumption; daily increases in perceived fullness, and reduced dinner-time neural activation in selected cortico-limbic brain regions that control food motivation/reward in overweight/obese breakfast-skipping teens. Additional benefits were observed with the consumption of the HP breakfast compared with the NP cereal-based version with greater increases in daily perceived fullness and greater reductions in cortico-limbic activation compared with the NP breakfast, daily reductions in the hunger-stimulating hormone ghrelin, increases in the satiety hormone PYY, and reductions in evening snacking, particularly of high-fat foods, compared with skipping breakfast. Thus, the addition of breakfast, particularly one rich in protein, might be an important dietary strategy to improve satiety, reduce food motivation/reward, and improve diet quality in overweight/obese teen girls.
Comments
Young people consume nearly half of their daily calories between 16:00 and 24:00 h; the snack foods often craved and consumed consist of highly palatable, but calorically dense foods with little nutritional value. These habits contribute substantially to the shift away from eating according to physiologic need toward reward-driven eating which leads to positive energy balance and obesity. Skipping breakfast exacerbates the desire to snack. Adolescents who skip breakfast typically snack on more desserts, high-fat salty foods, and sodas compared with breakfast consumers. The consumption of dietary protein appears to modulate key gastrointestinal hormones, which provide signals to the central, homeostatic, neuronal pathways to alter appetite, satiety, and regulate energy intake. The current study design allowed exploring sustained effects over the course of an 8-hour day. Only the HP breakfast led to sustained alterations in perceived desire to eat, prospective food consumption, fullness, and reduced plasma ghrelin into the afternoon periods, with elevated plasma PYY throughout the morning and afternoon periods. These data support the role of increased dietary protein at the morning meal to provide immediate and/or sustained improvements in the appetitive and hormonal signals that control food intake regulation. The HP breakfast also led to reduced amygdala, hippocampus, and midfrontal activation compared with skipping breakfast, and to reduced hippocampus and parahippocampal activation compared with the NP breakfast. These findings suggest that an HP breakfast affects homeostatic and non-homeostatic reward signals that control food intake regulation in teen girls.

Optimal macronutrient content of the diet for adolescents with pre-diabetes: RESIST a randomized control trial
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Background: Insulin resistance and glucose intolerance are considered as continuous parameters that increase the likelihood of developing type 2 diabetes. Current methods of dietary intervention in children and adolescents for weight management include the traffic light diet, a hypocaloric diet or general healthy eating advice. An alternative approach is a moderate-carbohydrate, increased-protein diet.

Objective: The aim of this trial was to determine the effectiveness of two different structured lifestyle interventions differing in diet composition on insulin sensitivity, anthropometry, and cardiometabolic profile in adolescents with pre-diabetes and/or clinical features of insulin resistance treated with metformin.
**Methods:** This was a randomized controlled trial of overweight or obese children and adolescents aged 10 to 17 years with either pre-diabetes and/or clinical features of insulin resistance. Participants were prescribed metformin and randomized to a structured isocaloric diet, which was either high carbohydrate or moderate carbohydrate with increased protein. The program commenced with a 3-month dietary intervention, with the addition of physical activity intervention in the next 3 months.

**Results:** 111 subjects (66 girls) were recruited and 98 subjects (58 girls) completed the 6-month intervention. At baseline significantly more participants had pre-diabetes in the increased-protein diet group compared with those in the high-carbohydrate diet group (11 and 3, p < 0.024, respectively). No other significant differences were observed in other baseline parameters between the intervention groups. After 3 months of dietary intervention and treatment with metformin, there were significant decreases in the BMI 95th percentile and waist-to-height ratio (both p < 0.001) and there was an estimated mean increase in insulin sensitivity index (ISI) of 0.3 (95% CI 0.2–0.4). At 6 months, BMI 95th percentile and waist-to-height ratio remained significantly different from baseline. The insulin-to-glucose ratio decreased over the first 3 months and remained statistically different from the baseline measures at 6 months, with an estimated mean decrease of 7.2 (95% CI 2.3–12.0). No significant differences were observed between the diet groups at any time point, and there was no significant change over time in the lipid profile in either diet group. Systolic BP (SBP) z-scores and diastolic BP (DBP) z-scores decreased over 3 months and remained statistically lower at 6 months compared with baseline, without a difference between diet groups at any time point.

**Conclusions:** In adolescents at high risk of developing type 2 diabetes, a 6-month lifestyle intervention with metformin can achieve modest weight loss and increased insulin sensitivity. Many adolescents had difficulty adhering to their prescribed diets and the diets had no differential effect on change in ISI or the BMI 95th percentile relative to one another. Further strategies are required to better address pre-diabetes and the clinical features of insulin resistance in adolescents.

**Comments** The lack of observed differences in outcomes between dietary groups may be due to poor or variable dietary adherence or limitations of monitoring and reporting in both groups. Many of the adolescents had difficulty adhering to their prescribed diet, and few were able to reach the target protein or carbohydrate intake. The lack of improvement in insulin sensitivity and weight loss observed in this study during the exercise program is consistent with a recent systematic review that concluded that the addition of exercise to a dietary intervention does not result in greater weight loss in overweight and obese adolescents [11]. However, it is possible that the exercise program prevented weight gain. The limitations of the study include: lack of data about dietary intake measurements at baseline, with inability to determine whether the energy intake was altered by either intervention; the measures of dietary compliance that were based on a standardized 24-hour recall and non-blinding of participants and dietitians who implemented the dietary intervention. Further strategies are required to better address pre-diabetes and the clinical features of insulin resistance in adolescents.
Childhood nutrition in predicting metabolic syndrome in adults: the cardiovascular risk in Young Finns Study


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Background: The metabolic syndrome (MetS) is a major medical and public health problem that has increased in prevalence during the past decades. It represents a clustering of interrelated cardiometabolic risk factors, including obesity, hypertension, dyslipidemia, hyperglycemia, and hyperinsulinemia. In adults, the vegetarian dietary pattern has been shown to have a beneficial effect on metabolic risk factors and to lower the risk of MetS.

Objective: The aim of the study was to examine the associations between childhood lifestyle factors (i.e. the frequency of certain food consumption and physical activity) and MetS in adulthood.

Methods: The study cohort included 2,128 individuals from the Cardiovascular Risk in Young Finns Study participating in the baseline study in 1980 (3–18 years of age) and the 27-year follow-up in 2007. The average of lifestyle factor measurements taken in 1980, 1983, and 1986 in the analyses were used. Childhood dietary factors and physical activity were assessed by self-reported questionnaires.

Results: Participants with MetS had lower HDL cholesterol, were more males than females, and had higher age, triglycerides, systolic blood pressure, CRP, insulin, and BMI in childhood than those without MetS. The difference was significant for all risk variables, with the exception of LDL cholesterol. Those who had adult MetS reported having less consumption of fruit and vegetables than those who did not have adult MetS. There were no significant differences in physical activity index, fish consumption, meat consumption, and butter use between these two groups. Childhood vegetable consumption frequency was inversely associated with adult MetS (OR 0.86, p = 0.02) in a multivariable analysis adjusted with age, gender, childhood metabolic risk factors (lipids, systolic blood pressure, insulin, BMI, and C-reactive protein), family history of type 2 diabetes and hypertension, and socioeconomic status. Decreased frequency of childhood vegetable consumption predicted high blood pressure (OR 0.88, p = 0.01) and a high triglyceride value (OR 0.88, p = 0.03) after adjustment for the above-mentioned risk factors.

Conclusions: Childhood vegetable consumption frequency had a significant inverse association with adult MetS after adjustment for several lifestyle and traditional risk factors. Every effort to support a healthy lifestyle in childhood is needed to prevent the increase in the prevalence of MetS.
Previous studies have shown that childhood obesity, high triglycerides, high insulin, high CRP, and family history of type 2 diabetes and hypertension were determinants of adult MetS during the 21-year follow-up. Rizzo et al. [12] reported that a vegetarian dietary pattern had a favorable effect on metabolic risk factors and lowered the risk of MetS. Higher intakes of vegetables and fruit and dietary patterns rich in these foods, as in the Mediterranean diet, have also been associated with a lower risk of MetS in several studies [13]. Food choices and physical activity are established early in childhood and these behaviors may track into adulthood. Multiple risk factors for cardiovascular diseases have also been shown to cluster already in young adults. Therefore, it appears important to focus on dietary education in childhood if the prevention of the development of these adverse risk factors is to be maximized. It seems that a child should eat vegetables every day or almost every day at all ages to get the protective effect of vegetables against the MetS in adulthood. The strength of this study was the large, randomly selected study population of young men and women who were prospectively followed up for 27 years since childhood. Surprisingly, there was a lack of association between adult MetS and the traditional lifestyle factors: total caloric intake, diet composition, and physical activity in childhood.

Correcting vitamin D insufficiency improves insulin sensitivity in obese adolescents: a randomized controlled trial

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Background: Obese adolescents may have vitamin D deficiency due to poor-quality nutrition and vitamin D sequestration in excessive adipose tissue. Low vitamin D concentrations are associated with a higher prevalence of the metabolic syndrome or type 2 diabetes.

Aims: The efficacy and safety of 4,000 IU vitamin D3 daily in obese adolescents was investigated in a randomized controlled trial.

Methods: The efficacy and safety of 4,000 IU vitamin D3 daily in obese adolescents was investigated in a randomized controlled trial. Circulating concentrations of 25-hydroxyvitamin D [25(OH)D] were determined and association with markers of insulin sensitivity, resistance and inflammation were investigated. 35 obese adolescents [mean ± SD age 14.1 ± 2.8 years; BMI 39.8 ± 6.1 kg/m2; 25(OH)D 19.4 ± 7.3 ng/ml] were recruited and randomly assigned to receive either vitamin D3 (4,000 IU/days) or placebo as part of their standard care. Anthropometric measurements, inflammatory markers (IL-6, TNF-α, C-reactive protein), adipokines (leptin, adiponectin), fasting glucose, fasting insulin, and HOMA-IR values were measured at baseline, and after 3 and 6 months of follow-up.

Results: No significant differences between groups in BMI, serum inflammatory markers, or plasma glucose concentrations were appreciated at 6 months. Vitamin D3 supplementation increased serum 25(OH)D concentrations (to 38.9 ng/ml compared to 22.2 ng/ml for placebo; p < 0.001), fasting insulin (−6.5 compared with +1.2 μU/ml for placebo; p = 0.026), HOMA-IR (−1.363 compared with +0.27 for placebo; p = 0.033), QUICKI (−0.016 compared with −0.004 for placebo; p = 0.016) and leptin-to-adiponectin ratio (−1.41 compared with +0.10 for placebo; p = 0.045). There was a significant negative linear correlation between serum 25(OH)D concentrations and leptin-to-adiponectin ratio (p < 0.01).
**Conclusions:** Supplementing vitamin D to obese adolescents may be an effective strategy for reducing insulin resistance in addition to the standard treatment for obesity.

**Comments**
The study was conducted in a very limited population and as such adds to the controversy of the efficacy of vitamin D supplementation in obesity and pre-diabetes. Fifteen vitamin D trials were included in a recent systematic review [14]: no significant improvement was seen in fasting glucose, HbA1c or insulin resistance in those supplemented with vitamin D compared to placebo when all studies were combined. Meta-analysis for patients with impaired glucose tolerance or diabetes indicated a small effect on fasting glucose (−0.32 mmol/l, 95% CI −0.57 to −0.07) and insulin resistance (standard mean difference −0.25, 95% CI −0.48 to −0.03). No effect was seen HbA1c in patients with diabetes and no differences were seen for any outcome in patients with normal fasting glucose. It is therefore difficult to propose a universal supplementation of vitamin D to all people with obesity, however a larger well-designed and controlled trial in pre-diabetes and diabetes is warranted.

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**Probiotics to adolescents with obesity: effects on inflammation and metabolic syndrome**

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**Background:** Evidence from animal studies indicates that the composition of the gut microbiota is involved in extraintestinal disorders such as obesity. The connection between gut microbiota, energy homeostasis, and inflammation, and its role in the pathogenesis of obesity-related disorders are increasingly recognized. Despite this, studies investigating the effect of probiotics on obesity-related inflammation are few and mainly based on animal models.

**Objective:** To investigate the effect of the probiotic strain, *Lactobacillus salivarius* Ls-33, on biomarkers related to inflammation and the metabolic syndrome in adolescents with obesity.

**Methods:** This was a double-blind, randomized, placebo-controlled intervention study including 50 obese 12- to 15-year-old adolescents. Participants were randomized to receive a daily dose of either *L. salivarius* Ls-33 ATCC SD5208 (10^10 CFU) or placebo daily for 12 weeks.

**Results:** 14% of the adolescents fulfilled the criteria for metabolic syndrome. There were no differences between the groups at baseline in BMI z-score, waist/hip ratio, body fat percentage, blood pressure or metabolic and inflammatory biomarkers. Compliance based on calculation of remaining capsules and self-reported diaries was ~91.3%. The BMI z-score did not change significantly in either of the groups from baseline to after intervention. Concentrations of fasting insulin, HOMA-IR, and C-peptide decreased significantly and FFA increased significantly from baseline to after intervention in the placebo group, without a significant difference compared with the Ls-33 intervention group. There were no differences in change for any of the inflammatory markers, adjusted for baseline values, from baseline to after intervention between the groups. *L. salivarius* was detected in 89% of the subjects of the probiotic group after intake of Ls-33 at the mean level of 5.55 (±0.95) log_{10} cells per gram stool.

**Conclusions:** No effects of the intervention with the probiotic strain Ls-33 on either the inflammatory markers or the markers of metabolic syndrome were found.
It is estimated that the gut microbiota contains, at least, 100-fold more genes than the mammalian genome. These bacteria can live in a symbiotic way but, in certain cases, promote disease. In the last decade, a great body of evidence and knowledge about the gut microbiota and its interaction with the host, immunity, energy metabolism and insulin sensitivity has provided new insights regarding the influence of this forgotten ‘organ’ on the most prevalent metabolic disease, obesity. Gut bacteria influence the chronic low-grade inflammation that culminates in insulin resistance and the increase in fat deposition and body weight gain, characteristic of obese individuals. The issue of the ‘healthy’ bacterial group profile is a very important point in gut microbiota research and needs to be further explored. Thus, no proposed treatment attempting to induce the proliferation of certain bacterial phyla has been suggested until now. Probiotics are defined as live microorganisms that confer unspecified health benefits to the host. Evidence from metagenomic profiles indicates that the obese phenotype shows an increased prevalence of Firmicutes in the gut microbiota profile, inferring a negative correlation with metabolism and insulin sensitivity. The most commonly used probiotics are Lactobacillus, which belong to Firmicutes and Bifidobacterium. Although the mechanism by which Lactobacillus control excessive adiposity has not been described, changes in fat storage genes expression have been proposed to mediate this probiotic effect. The recent study failed to demonstrate a beneficial effect of the probiotic intervention on inflammatory markers or parameters related to the metabolic syndrome, which may be explained by the reality that results from in vitro and animal studies could not be translated to humans for this strain. The negative results of the probiotic impact might also be affected by the amount of daily administrated probiotic that was not enough to get a significant impact, or the relatively short period of administration and follow-up. However, we also cannot exclude that other strains of bacteria will have beneficial effects in populations with high levels of risk factors for obesity-related comorbidities. Therefore, more studies, especially randomized controlled trials, within this research area are needed.

Role of carbohydrate modification in weight management among obese children: a randomized clinical trial

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Background: Effective weight management strategies for obese children became an important issue in pediatrics. Guidelines for pediatric weight management include increased physical activity, less sedentary time, and a nutritionally balanced diet, with an emphasis on fat and sugar restriction to
limit caloric intake. However, the standard recommendations for achieving ‘negative energy balance’ are typically associated with only modest and transient improvements in weight status, often because of poor long-term adherence.

**Objective:** To compare the safety and efficacy of low-CHO (LC) and reduced glycemic load (RGL) diets and a standard portion-controlled (PC) dietary intervention for the management of obesity in young children aged 7–12 years.

**Methods:** Obese children (n = 102) were randomly assigned to a 3-month intervention of a LC, RGL, or standard PC diet, along with weekly dietary counseling and biweekly group exercise. Subjects in the LC diet group were instructed to limit CHO intake and to measure ketones daily. The subjects were instructed to follow a 2-week induction phase with ≤20 g CHO/day and unrestricted intake of high-protein foods and added fats. After induction, CHO intake was increased by 5–10 g/week up to a maximum of 60 g/day, with no limit on intake of high-protein foods and fats. Subjects in the RGL diet group were instructed to limit their intake of high-glycemic index (GI) foods. A ‘stoplight approach’ was modified to classify foods according to GI values (‘red’ foods, high GI: ≥70; ‘yellow’ foods, medium GI: 56–69; ‘green’ foods, low GI: ≤55). Green foods were not restricted. Yellow foods were to be consumed less frequently. Red foods were restricted to ≤7 servings/week and ≤2 servings/day. Subjects in the PC diet group were instructed to consume age-appropriate, PC amounts of grains, vegetables, fruits, lean proteins, and skim/low-fat dairy products. Calories were distributed as 55–60% CHO, 10–15% protein, and 30% fat. Anthropometry, dietary adherence, and clinical measures were evaluated at baseline and 3, 6, and 12 months.

**Results:** 85 children (83%) completed the 12-month assessment. Dietary adherence was consistently high in the RGL group (>75%), and adherence was significantly lower in the LC group than in the other two groups at all visits. At 3 months, body mass index z-score was lower in all diet groups (LC –0.27 ± 0.04; RGL –0.20 ± 0.04; PC –0.21 ± 0.04; p < 0.0001) and was maintained at 6 months, with similar results for waist circumference and percent of body fat. At 12 months, participants in all diet groups had lower BMI z-scores than at baseline (LC –0.21 ± 0.04; RGL –0.28 ± 0.04; PC –0.31 ± 0.04; p < 0.0001), and lower percent of body fat, but the reductions in waist circumference was not maintained. Despite similar overall energy intake, subjects in the different diet groups consumed diets with differing macronutrient compositions.

**Conclusions:** The 3 diets, which differed in macronutrient content and GL, resulted in similar and significant improvements in BMI z-score and related health measures in children. Although strict adherence to the LC diet was more difficult to achieve in children, all diets were effective in decreasing adiposity and improving clinical outcomes. These findings suggest that practitioners may offer any of these dietary approaches for achieving a healthier weight in obese children.

**Comments**

The results of the recent study do not support the hypothesis that CHO-modified diets would be more effective in improving weight status than a standard PC diet in obese children. Subjects in all 3 diet groups showed significant improvements in adiposity measures during the initial 3-month intervention with relatively intensive intervention and contact with study dietitians. At 12 months, improvements in BMI z-score and percent of body fat were maintained in all 3 diet groups, however none of the groups sustained improvements in waist circumference. Subjects in all 3 diet groups successfully maintained a reduced caloric intake and altered dietary composition even in the final 9 months without intervention contact. These findings raise the possibility that intensive guidance with the initial clinical application of weight management diets can lead to long-term success in children. Recently it has been suggested that strategies to individualize diet interventions to match patients’ metabolic profiles could have increased efficacy [16]. This trial provides limited support for this hypothesis, with detection of differential effects on specific metabolic profiles (e.g. lipids vs. insulin resistance) by dietary intervention. The sustained high adherence to the RGL diet,
coupled with anthropometric and clinical improvements, may make this diet the most promising intervention for the long-term weight management of children. Alternatively, prescribing one of the 3 diets based on the patient’s preferences for the initial intervention and then transitioning to the RGL diet for longer-term maintenance may also be an effective strategy.

**Summary:** People usually describe food as either good or bad or something in between. The overview of the above recent publications provides evidence that food can be beneficial or dangerous to young people, particularly to those with certain genetic predispositions, and can in specific time-windows even determine several long-term risks. There is considerable confusion both in the professional and lay communities as the facts on nutrition are blurred with a conundrum of poorly controlled, poorly executed, observational or biased studies. Therefore, the aim of this overview was to shed some clear light on this extremely important field by discussing data from recent trials that addressed pertinent questions on nutrition of the young. An important message from the recent research in nutrition related to obesity and diabetes is that behavioral modification can defy our thrifty genes. We should find more successful ways to efficiently convey this scientific discovery to the minds of people.

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