NUTRITION REVIEWS

Special Article

Impact of dietary macronutrient distribution on BMI and cardiometabolic outcomes in overweight and obese children and adolescents: a systematic review

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The present systematic review examined the effectiveness of weight management interventions comparing diets with varying macronutrient distributions on BMI and cardiometabolic risk factors in overweight or obese children and adolescents. A systematic search of seven databases for the period 1975–2013 identified 14 eligible randomized or quasi-randomized controlled trials conducted with 6–18-year-old subjects. Seven trials compared a low-fat (≤33% energy or <40 g/day) to an isocaloric (n = 2) or ad libitum (n = 5) low-carbohydrate diet (<20% energy or <60 g/day). Meta-analysis indicated a greater reduction in BMI in the low-carbohydrate group immediately after dietary intervention; however, the quality of the studies was limited and cardiometabolic benefits were inconsistent. Six trials compared increased-protein diets (19–30% energy) to isocaloric standard-protein diets (15–20% energy) and one compared an increased-fat diet (40% energy) to an isocaloric standard-fat diet (27% energy); there were no differences in outcomes in these studies. Current evidence suggests that improved weight status can be achieved in overweight or obese children and adolescents irrespective of the macronutrient distribution of a reduced-energy diet. Tailoring the macronutrient content to target specific cardiometabolic risk factors, such as a low-carbohydrate diet to treat insulin resistance, may be possible, but further research is needed before specific recommendations can be made.

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INTRODUCTION

Childhood and adolescent obesity is a global public health concern and is associated with a range of health problems.[1,2] Published systematic reviews of treatments for childhood obesity conclude that lifestyle interventions, including diet, are effective in the short to medium term.[3–7] The most recent of these also found significant improvements in cardiometabolic outcomes including low-density lipoprotein cholesterol (LDL-C), triglycerides, fasting insulin, and blood pressure up to 1 year from baseline.[7] However, the role of a specific macronutrient distribution in the diet has not been examined.

National dietary guidelines from the United States,[8] the United Kingdom,[9] and Australia[10] currently recommend a high-carbohydrate (45–65% of daily energy), low-fat (less than 35% of daily energy) diet be adopted at the population level. However, the optimal macronutrient distribution of the diet for improving weight status is unclear. In adults, low-carbohydrate and increased-protein diets have been trialled for their effectiveness in achieving weight loss,[11–15] weight loss maintenance,[16–18] and improvements in cardiometabolic risk factors.[19–22] Mechanisms including sustained energy expenditure and satiety have been reported to explain the effectiveness of increased-protein diets.[23]

For adults, a 2009 systematic review[15] of 13 studies demonstrated that low-carbohydrate (<40 g/day) ad libitum diets were more effective than low-fat energy-restricted diets for both weight loss and reducing triacylglycerol levels at 6 months. A 2012 systematic review[19] of 24 articles demonstrated that, in adults, an increased-protein diet compared to an isocaloric standard-protein diet ($30.5 \pm 2.4\%$ versus $17.5 \pm 1.5\%$ energy from protein and $41.6 \pm 3.5\%$ versus $56.9 \pm 3.3\%$ energy from carbohydrate, respectively) can produce greater reduction in weight, fat mass, and triglycerides, with better preservation of fat-free mass and resting energy expenditure. In contrast, results of recent studies in adults examining long-term (2-year) effects suggest that weight loss can be achieved regardless of the macronutrient distribution of the diet and that individual tailoring of the dietary intervention to achieve optimal compliance and, hence, a sustained decrease in total energy intake may be key.[24–27] Individual tailoring may also be used to treat specific cardiometabolic risk markers, such as low fat to treat high blood lipids or low carbohydrate to improve triglycerides, insulin, and/or glucose levels, as demonstrated in systematic reviews of adult studies.[19,20] Additionally, the inclusion of exercise has been shown to produce greater improvements in high-density lipoprotein cholesterol (HDL-C), fasting glucose, and fasting insulin in overweight and obese children and adolescents compared with diet alone.[28]

While the literature for adult populations is conflicting, little is known about the optimal macronutrient distribution of the diet for improved weight status and cardiometabolic outcomes in overweight or obese children and adolescents. It is also unknown whether results observed in adult studies can be applied to younger age groups. Therefore, the aim of the present systematic review was to examine the effectiveness of diets varying in macronutrient distribution as part of a weight management intervention in overweight or obese children and adolescents; the primary measure of interest was BMI and secondary measures included body composition and cardiometabolic outcomes.

METHODS

Search strategy for study identification

This systematic review utilized a peer-reviewed protocol that is registered with the Joanna Briggs Institute.[6] The initial search focused on the English-language literature published between 2003 and June 2013; articles that had been identified using the same search strategy for a prior systematic review of studies from 1975 to 2003 were then added[5] to deliver a complete review of literature published between 1975 and 2013. The searches were conducted by a medical librarian using the following databases: Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Reviews, Current Concepts, Database of Abstracts of Reviews of Effects (DARE), Excerpta Medica Database (EMBASE), PreMedline, Medline, Dissertations and Theses, and Informit. The medical subject headings (MeSH) of the National Library of Medicine were used to devise the key word search terms. The words and terms used and combinations thereof were as follows: dietetic, paediatric (pediatric), child, adolescent, family, parent, school, overweight, obesity, intervention, weight control, weight management, weight loss, and healthy weight.

In addition to the electronic literature searches, the reference lists of retrieved articles and key systematic reviews of childhood obesity treatments[3,4,29,30] were reviewed to identify relevant publications not captured electronically.

Eligibility criteria

Studies were deemed eligible for inclusion if they met all of the following criteria: 1) were randomized or quasi-randomized controlled trials (RCTs) published between 1975 and June 2013; 2) investigated the effectiveness of dietary interventions of varying macronutrient content to improve weight status in overweight and/or obese

children and/or adolescents aged 18 years or younger; 3) described specific dietary macronutrient goals for the intervention; and 4) measured changes in at least one weight-related outcome (i.e., weight, body mass index [BMI; raw or z-score] or body composition) with or without investigation of cardiometabolic risk factors. Participants could be free living or attending obesity clinical units, community programs, camps, schools or one-day programs.

Studies were excluded for any of the following reasons: 1) the study involved an obesity prevention intervention; 2) the study aimed at weight loss maintenance rather than weight loss; 3) the study involved a drug trial or an intervention that dealt with eating disorders; 4) the study included participants suffering from obesity due to secondary or syndromic causes; 5) the report was not published in English; or 6) the study included children who were within the healthy weight range at baseline.

Study selection

Potentially relevant reports were initially assessed for eligibility based on evaluation of the title and abstract by two independent reviewers. The full text of articles for studies that met, or appeared to meet, the inclusion criteria were retrieved. Retrieved studies were assessed for inclusion by two independent reviewers. In case of disagreement, a third independent reviewer made the final decision.

Quality assessment

Two independent reviewers assessed the methodological quality of the included studies using The Joanna Briggs Institute's critical appraisal of study quality tool (Figure 1). The responses to 10 questions assessing the level of randomization, intervention integrity, baseline comparability, study blinding, allocation concealment, retention rate, and potential bias in outcome measurements or statistical analysis determined whether the quality of each study was rated as positive, negative, or neutral. A third reviewer was consulted when necessary to resolve any disagreement between the two initial reviewers.

Data extraction

A standardized form, developed specifically for this review, was used to extract data in relation to the study population, intervention details, intensity, and outcomes. A second reviewer then verified the extracted data for accuracy and, where disagreement existed, a consensus was reached.

Joanna Briggs Institute critical appraisal of study quality tool

1) Were the participants randomised to study groups?
2) Other than the research intervention, were participants in each group treated the same?
3) Were the outcomes measured in the same manner for all participants?
4) Were groups comparable at entry?
5) Was randomisation of participants blinded?
6) Were those assessing outcome blinded to treatment allocation?
7) Was allocation to treatment groups concealed from the allocator?
8) Was an appropriate statistical analysis used?
9) Were weight-related outcomes measured in a valid and reliable way?
10) Was there adequate follow-up of participants?

Yes, No or Unclear response for each question

Figure 1 **Questions included in the Joanna Briggs Institute's quality assessment tool for eligible trials.**

Data synthesis

Review manager (RevMan5.1, The Cochrane Collaboration, Oxford, United Kingdom) was used to conduct the meta-analyses of the primary outcome, BMI (raw and z score). A random effects model was used for this analysis. Heterogeneity was assessed by I^2 statistics; it is considered to be low if I^2 is ≤40% and high if I^2 is ≥75%.[31] The BMI and BMI z-scores for the diet subgroups were examined immediately after the active intervention and at the latest follow-up for which data were available.

Other weight-related outcomes were also examined when data were available, including body composition using body fat mass, body fat percentage, and lean body mass. The cardiometabolic outcomes examined included total cholesterol, LDL-C, high-density lipoprotein cholesterol (HDL-C), triglycerides, fasting glucose and insulin levels, measures of insulin resistance, and systolic and diastolic blood pressure. These outcomes could not be quantitatively combined in a meta-analysis, due to clinical and statistical heterogeneity; they are, therefore, described in a narrative summary.

RESULTS

Literature search results

The literature search identified a total of 9,719 potentially relevant reports (Figure 2). The full-text articles were retrieved for 780 of them and 11 of those articles met all of the inclusion criteria. Two of those 11 articles[32,33] reported data from the same trial, so the data were extracted together. A further four studies[34–37] were identified from the reference lists of retrieved articles and from other sources. In total, 14 unique trials were identi-

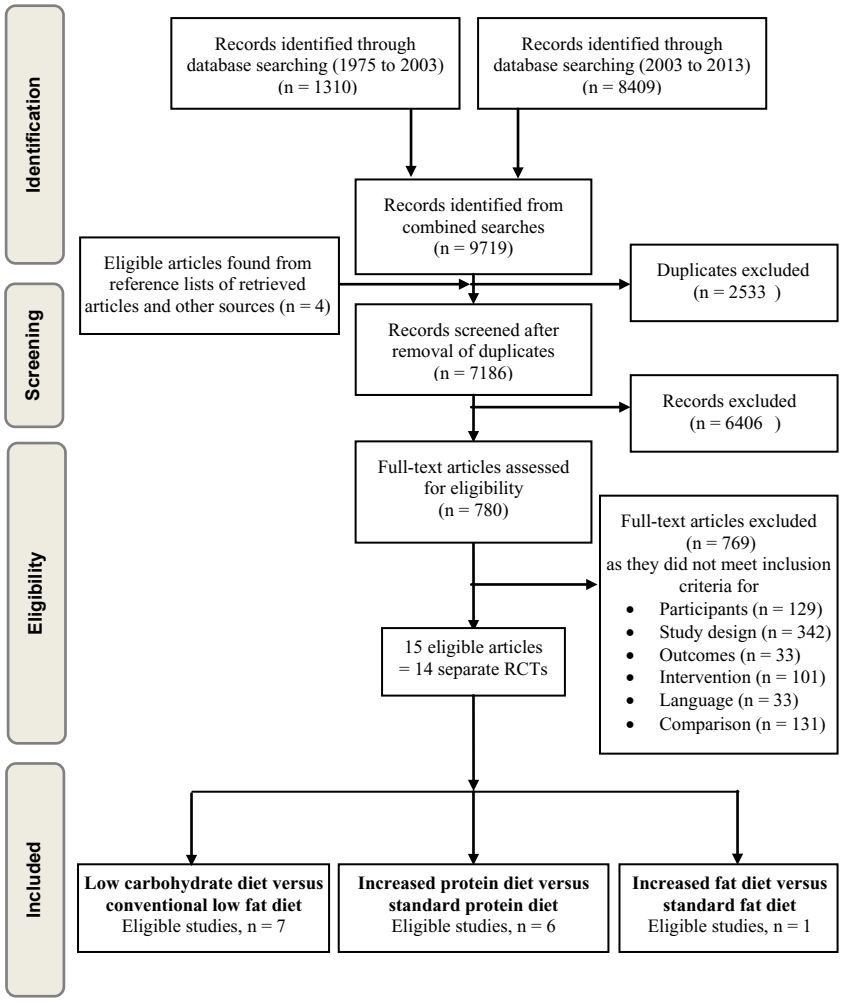


Figure 2 **Flow chart for identification of trials included in the present systematic review.**

fied for inclusion in the review. The main reasons for the exclusion of studies were as follows: 1) inappropriate study design; 2) ineligible study population; 3) inappropriate intervention; 4) inappropriate comparison groups (Figure 2).

Methodological quality

No study fulfilled all of the methodological requirements for quality. The study conducted by Garnett et al.[36] met the most (9 of 10) requirements of all the included studies. Blinding participants to a dietary intervention is clearly difficult; therefore, if reported, it was deemed "unclear" using the study quality tool. Blinding of outcome assessors to participants' treatment allocation and methods of allocation concealment were rarely reported in the included studies. Overall, retention rates for the studies examined were good (66–100% following the active intervention, Table 1). Performance of an intention-to-treat analysis was reported for five studies[32,36,39,42,45] for the primary weight-related or cardiometabolic outcomes following the intervention phase. Although study quality was mixed and often limited, the number of trials identified was small; hence, all were included in the review.

Study description

For ease of description, studies were divided into three groups. One group compared the effectiveness of a low-carbohydrate diet to a conventional low-fat diet and included six RCTs[32,34,39–42] and one quasi-RCT.[38] The low-carbohydrate diets aimed to induce ketosis and either placed a daily limit on carbohydrate intake in grams or used a target maximum percentage of daily energy from carbohydrate. For the purpose of this review, a diet was considered to be low in carbohydrates if it aimed for either less than 60 grams of carbohydrate per day or a maximum of 20% of daily energy from carbohydrate. Hence, these diets were subsequently higher in protein

Table 1 **Description of trials, dietary interventions, and compliance in the included studies examining the optimal macronutrient distribution of the diet for reducing child obesity.**

Reference	Methodological quality (score out of 10)	No. of subjects (M:F)	Age (y); pubertal stage	Intervention duration; follow-up	Subject retention	Dietary intervention	Measure of intervention compliance and outcome
Studies comparing low-carbohydrate with low-fat diets							
Pena et al. (1979)[34]	2	104 (NS)	6–14; NS	8 wk; none	NR	LC: ad libitum ketogenic diet (C <20 g/day) LF: hypocaloric [4.6 MJ] diet (50% C, 20% P, 30% F)	Daily urine samples to measure ketonuria; usually detected on day 3 of LC diet in LC group only
Figueroa-Colon et al. (1993)[38]	6	19 (8:11)	7–16; NS	10 wk; 5.5 and 14.5 mo	100% at 10 wk and 3 mo; 58% at 14.5 mo	LC: hypocaloric diet, 1.5–2 g/kg IBW protein, providing 2,520–3,360 kJ (10% C, 50% P, 40% F), prescribed supplements LF: hypocaloric diet, 3,360–4,200 kJ (50% C, 20% P, 30% F), instructed to maintain reasonable milk and vegetable intake Both groups: weekly outpatient group education with concurrent parent education session Post intervention: all participants placed on 4,200 kJ balanced diet, increased to 5,040 kJ after 3 mo (50% C, 20% P, 30% F), participants seen monthly from wk 10 for 1 y	Both groups during intervention: daily dietary and activity diaries, reviewed weekly by a nutritionist; LC group reported 840 J/day lower intake than LF group LC group: weekly urine samples to check for ketones. If little or no ketosis, child was interviewed during an individual family session Both groups during maintenance period: 3-day food diaries kept monthly
Sondike et al. (2003)[39]	5	39 (NS)	12–18; NS	12 wk; none	80% at 12 wk in the LC group; 74% at 12 wk in the LF group	LC: ad libitum protein, fat, and energy, ≤20 g/day C for 2 wks, ≤40 g/day C wk 3–12 LF: ad libitum fat-free dairy, fruits, and vegetables, <40 g/day F and 5 servings of starch Both groups: fluid and multivitamin intake recommended;"stoplight" meal plan design; bi-weekly reviews by dietitian	Both groups: urinary ketones monitored daily; no ketonuria in LF group, ketonuria most days in LC group Both groups: consecutive 3-day food record (1 weekend day and 2 weekdays) completed by participant and parent and reviewed at baseline and bi-weekly by a dietitian; LC group reported consuming more energy (significantly more fat and less C) compared with LF group
Demol et al. (2009)[32]/ Yackobovitch-Gavan (2008)[33]	7	55 (NS)	12–18; Tanner 4–5	12 wk; 1 y	78% at 12 wk; 53% at 1 y	LCLF: hypocaloric diet, max 60 g/day C [20%], 50% P, 30% F LCHF: hypocaloric diet, max 60 g/day C [20%], 20% P, 60% F HCLF: hypocaloric diet, 50–60% C, 20% P, 30% F Intervention: 1,200 kcal/day menus provided; 3 new menus monthly; weekly sessions with dietitian and psychologist Maintenance: hypocaloric diet, high-C, low-F menus, follow-up visits every 3 months for 9 months	All groups: weekly checks for urinary ketones and protein; ketone bodies found in small portion of subjects in low-C groups but no significant difference between groups. Self-reported food diaries filled out at some diet sessions
Krebs et al. (2010)[40]	6	46 (NS)	12–18; NS	12 wk; 24 and 36 wk	72% at 12 wk; 59% at 24 wk; 48% at 36 wk	LC: ad libitum fat and energy, ≤20 g/day C, 2.0–2.5g/kg IBW/day P LF: hypocaloric diet [70% REE], ≤30% energy F Both groups: diet education booklet given and supplements recommended; participants seen every 2 wks during intervention in outpatient setting	Both groups: 3-day food records kept randomly throughout intervention period (3–14 records obtained per participant): compliance with the prescribed C restriction was imperfect, but mean C intake in LC group was <40 g/day. B-hydroxybutyrate measured to indicate ketosis; significantly higher levels found in LC group
Partsalaki et al. (2012)[41]	6	58 (27:31)	8–18; Tanner 1–5	6 mo; none	66%	LC: ad libitum fat and energy, <20 g/day C, with gradual increase to 30–40 g/day LF: hypocaloric diet (500 kcal/day deficit), 50–55% C, 15–20% P, 28–33% F Both groups: provided with sugar-free mulitivitamins; weekly individual sessions with dietitian for first month then biweekly; written and oral instructions provided along with education and counselling at each session	LC group: urinary ketones measured daily; mild ketosis present in all LC subjects for the majority of the trial Both groups: food diaries kept to determine eating behaviour (quality, frequency, and composition)
Kirk et al. (2012)[42]	7	102 (43:59)	7–12; 43% prepubertal	12 wks; 6 mo and 1 y	82% at 1 y	LC: ≤20 g/day, increased by 5–10 g/week up to a maximum of 60 g/day, ad libitum protein, fat, and energy RGL: limit intake of high-GI foods using a "stoplight" approach LF: portion-controlled diet using calorie-defined meal plans (500 kcal/day deficit). 55–60% C, 10–15% P, 30% F All subjects: advised to take a multivitamin and consume 1.42 L of fluid per day; 12 weekly parent-child sessions, alternating between a 30 min dietitian-led individual counselling and 90-min group exercise/education sessions	LC group: ketones measured daily; only 16% of subjects tested positive at any point All groups: 3 consecutive-day food records (2 weekdays and 1 weekend day) during the week before assessment visit at baseline, 3, 6, and 12 months; food records indicated a decrease in calorie intake by 3 mo, remaining below baseline at 12 mo; dietary adherence consistently high in the RGL group (>75%); adherence in the LC group was lower than in the other 2 groups at all time points
Studies comparing increased-protein with standard-protein diets							

Table 1 **Continued**

Reference	Methodological quality (score out of 10)	No. of subjects (M:F)	Age (y); pubertal stage	Intervention duration; follow-up	Subject retention	Dietary intervention	Measure of intervention compliance and outcome
Rolland-Cachera et al. (2004)[35]	6	121 (32:89)	11–16; NS	Until body weight goal reached, mean stay 9.3 ± 2 mo; 1 and 2 y after end treatment	82% at 9 mo; 69% at 1 y; 59% at 2 y	IP: 50% C, 19% P, 31% F SP: 54% C, 15% P, 31% F Hypocaloric diets providing 1,750 kcal/day until goal body weight reached. Daily intake progressed weekly to 2,200 kcal/day, followed for 4 wks, child then left the center with instructions to maintain the same energy level and intakes at home for 2 years	Both groups: compliance during treatment not measured as participant intake was controlled by center staff; nutritional intakes assessed at inclusion and 1 and 2 y after end of treatment using "dietary history" method; average intake 3,269 kcal/day (14% P, 37% F, 49% C) at baseline, 1,970 kcal/day at 1-y follow up, 2,141 kcal/day at 2-y follow up; no differences between groups except that IP group ate more protein
Gately et al. (2007)[43]	7	98 (38:60)	11–17; NS	Mean stay 29 days; none	90%	IP: 47.5% C, 22.5% P, 30% F SP: 55% C, 15% P, 30% F Children assigned to one of four food hypocaloric diets (1,300, 1,800, 2,300, 2,800 kcal/day) depending on BMR. Mean caloric deficit of 9.8%.	Both groups: compliance controlled by camp staff who served all meals as guided by the dietitian who also designed the composition of the diets
Duckworth et al. (2009)[44]	7	100 (NS)	9–18; NS	Mean stay 31 days; none	95%	IP: 40–45% C, 25% P, 30–35% F SP: 50–55% C, 15% P, 30–35% F Children assigned to one of four hypocaloric diets (1,300, 1,800, 2,300, 2,800 kcal/day) depending on BMR. Mean caloric deficit of 9.8%.	Both groups: compliance controlled by camp staff who served all meals as guided by the dietitian who also designed the composition of the diets; analysis of food consumption revealed very little waste and no differences between diets
Baxter et al. (2013)[37]	7	116 (NS)	10–17; Tanner stage 1–5	12 wk; none	76% (88% in completers analysis)	IP: 35% C, 30% P, 35% F SP: 55% C, 20% P, 25% F Hypocaloric isocaloric diets; structured meal plans given; 5 dietary advice sessions during the 12 wks	Both groups: 4-day food diaries at baseline and 12 wks ; serum urea, urate and B_{12} levels measured; compliance not reported
Mirza et al. (2013)[45]	8	113 (58:55)	7–15; Tanner stage 1–5	12 wk; 1 y and 2 y	79% at 3 mo; 61% at 1 y; 55% at 2 y	IP/LGD: 45–50% LGI C, 20–25% P, 30–35% F SP: 55–60% C, 15–20% P, 25–30% F Instruction manuals specific for each isocaloric diet were developed and structured meal plans were given to each family 12 weekly group sessions, separate for parent and child, and weekly family sessions during the intervention followed by monthly follow-ups for 9 mo and every 3 months thereafter for another year	Both groups: compliance measured by 24-h dietary recall and a 2-wk FFQ; IP/LGD reported decreased GL/kcal compared to SP at 3 mo; no differences detected at 1 y and 2 y follow-up; no significant differences in macronutrient consumption between groups at any time point
Garnett et al. (2013)[36]	9	111 (45:66)	10–18; Tanner stage 1–5	6 mo; 1 y and 2 y	88% at 6 mo	IP: 40–45% C, 25–30% P, 30% F (≤10% saturated fat) SP: 55–60% C, 15% P, 30% F (≤10% saturated fat) Prescriptive isocaloric diets, 2 energy levels depending on age, aiming for approx. 2,000 kJ less than recommended intake Education sessions with dietitian at baseline, 2, 6, 12, and 26 wks with additional support (phone, email, text message) every 4 weeks	Both groups: 24-h recalls conducted at 6, 9,12, and 26 wks to assess dietary compliance; IP reported eating more %E protein; no differences in %E carbohydrate, %E fat, and energy intake; overall, %E protein decreased and %E carbohydrate increased over 6 mo intervention
Study comparing increased-fat with standard-fat diets							
Casazza et al. (2012)[46]	6	26 (0:26)	9–14; Tanner stage 2–5	16 wk; none	100%	IF: 42% C, 18% P, 40% F SF: 55% C, 18% P, 27% F 2-phase isocaloric diets: 5-wk eucaloric diet (weight stable), followed by 11-wk hypocaloric diet (weight loss, approx. 1,000 kcal/day deficit)	Both groups: all food provided for the 2 phases ensuring dietary compliance; participants weighed twice weekly to ensure weight stability or weight loss

Abbreviations: BMR, basal metabolic rate; C, carbohydrate; F, fat; GL, glycemic load; HCLF, high carbohydrate low fat; IBW, ideal body weight; IF, increased fat; IP, increased protein; LC, low carbohydrate; LCHF, low carbohydrate high fat; LCLF, low carbohydrate low fat; LF, low fat; LGIC: low glycemic index carbohydrate; LGD, low glycemic index diet; NR, not reported; NS, not specified; P, protein; REE, resting energy expenditure; SF, standard fat; SP, standard protein.

(ad libitum, 50% of energy or 2–2.5 g/kg/day) and/or fat (ad libitum or 30–60% of energy) than a standard diet.

The second group compared a standard-protein diet to an increased-protein diet and included five RCTs[35,36,43–45] and one quasi-RCT.[37] The carbohydrate content of the standard-protein and increased-protein diet groups of the six studies would be considered moderate to high (35–50% of energy) across studies, while protein was moderately increased (19–30% of energy) in the increased-protein groups compared to the standard-protein groups (15–20% of energy). The fat content of prescribed diets ranged from 25% to 35% of energy.

The remaining study[46] compared two diets varying in fat and carbohydrate content with protein content constant in each diet arm at 18% of energy.

Low-carbohydrate diet compared to conventional low-fat diet

Description of studies. Seven studies[32,34,38–42] were identified that compared a low-carbohydrate diet to a conventional low-fat, hypocaloric diet, as described in Table 1. Four studies were conducted in the United States,[38–40,42] and one each was performed in Cuba,[34] Greece,[41] and Israel[32]; all seven were conducted in a hospital setting. The age range was 6–18 years, with a mean sample size of 71 participants (range, 19–104). The study by Demol et al.[32] had three study arms eligible for review. The study by Kirk et al.[42] also had three study arms, although the reduced glycemic load diet arm was not eligible for inclusion in this review as it did not have specific macronutrient goals. All other studies had two study arms. Five studies specifically reported recruiting obese participants only[32,39–42] (BMI range, 28.1–40.1 kg/m^2 at baseline). Despite the varying descriptions of weight status, the other two studies[34,38] were also considered to have recruited obese participants only: Pena et al.[34] recruited patients with a weight greater than 120% of the ideal weight for actual height; Figueroa-Colon et al.[38] recruited children with a weight that was more than 40% higher than the mean weight for age, sex, and height. Although recruitment of insulin-resistant participants was not specified, four studies reported that participants had high fasting insulin levels and/or high homeostatic model assessment of insulin resistance at baseline.[32,40–42]

Dietary intervention. The carbohydrate content of the low-carbohydrate diet arm at commencement of the intervention in each study was either <20 g/day,[34,39–42] 10% of energy intake (15–20 g/day in a diet with recommended energy intake of 600–800 kcal/day [2,520–3,360 kJ/day]),[38] or 20% of energy intake (approximately 60 g/day of carbohydrate for an energy restriction of 1,200 kcal/day [5,040 kJ/day])[32] (Table 1). In all seven studies, the low-carbohydrate diet was compared to a diet low in fat (≤33% of energy[32,34,38,40–42] or less than 40 g/day[39]) and high in carbohydrate (50–60% of energy).

Three studies[32,38,42] reported dietary reviews every week, and two every 2 weeks,[39,40] during the intervention phase, while the study by Partsalaki et al.[41] had reviews weekly for the first month then every 2 weeks for the following 5 months. The study by Pena et al.[34] did not report the intensity of the dietary intervention. One study[38] delivered the dietary intervention via weekly outpatient group education sessions, another administered the intervention during one-on-one interviews,[41] and another delivered half the sessions individually and the other half during group sessions.[42] The remaining four studies did not state the method of intervention delivery. A dietitian,[32,39,41,42] nutritionist,[38] or bionutritionist[40] was reported to be involved in the delivery of the dietary intervention in all studies, except for the study by Pena et al.[34] for which it was not stated who delivered the intervention.

Dietary compliance. Compliance with the dietary intervention was measured by the presence of urinary ketone bodies in the low-carbohydrate arm of all seven studies daily,[34,39,41,42] weekly,[32,38] or at the end of the intervention.[40] All reported consistent observation of urinary ketones in the low-carbohydrate group, except for the study by Kirk et al.,[42] which reported that only 16% of participants tested positive for urinary ketones during the study. Other compliance measurements, which included daily dietary and activity diaries,[38] 3-day food records,[39,40,42] or self-reported food diaries[32,41] were reported in all studies, except for the study by Pena et al.[34] (Table 1).

Impact of treatment on obesity. Five studies reported BMI[32,38–41] as a weight-related outcome, three reported the subject's BMI z-scores,[32,40,42] and five reported body composition[32,38,40–42] (Table 2). In addition, Figueroa-Colon et al.[38] reported changes in the percentage by which participants were overweight following the active intervention and during the follow-up period. The only study not to report BMI or BMI z-scores was that by Pena et al.,[34] which reported changes in the ratio of ideal weight for actual height.

All seven studies reported improvements in weight-related outcomes after the intervention phase (BMI decreases ranging from 1.2 to 5.2 kg/m^2 across studies), with four studies reporting no difference between the dietary intervention groups[32,34,41,42] and three studies reporting an advantage of a low-carbohydrate diet for at least one weight-related outcome following the active

Table 2 **Results of the main weight outcomes in the included studies examining the optimal macronutrient distribution of the diet for reducing child obesity.**

Reference	Weight-related outcomes	Results at measured time points (no. of subjects): mean (SD[a] or SEM[b] or 95% CIs[c])	Significant changes and differences between groups
Studies comparing low-carbohydrate to conventional low-fat diets			
Pena et al. (1979)[34]	Percentage of usual values of IW/AH at B and 8 wk ($n = 104$)	LC: B, 147.5%, 8 wk, 132% LF: (approximated from graph), B, 142%, 8 wk, 133%	↓ in LC ($P < 0.001$) and LF ($P < 0.05$) No difference between groups
Figueroa-Colon et al. (1993)[38]	BMI (kg/m^2) change from B to 10 wk, 5.5 mo, and 14.5 mo	LC ($n = 10$): 10 wk, −5.2 (1.3)[a]; 5.5 mo −5.6 (2.5)[a]; 14.5 mo, −2.5 (2.8)[a] LF ($n = 9$): 10 wk, −2.4 (1.4)[a]; 5.5 mo, −3.0 (2.6)[a]; 14.5 mo −2.7 (2.8)[a]	↓ at 10 wk in LC ($P \leq 0.001$) and LF ($P \leq 0.001$) Greater ↓ in LC at 10 wk ($P < 0.001$) and 6 mo ($P < 0.05$)
	% overweight change from B to 10 wk, 5.5 mo and 14.5 mo	LC ($n = 10$): 10 wk, −29.5 (7.4)[a]; 5.5 mo, −32.2 (13.4)[a]; 14.5 mo, −23.3 (19.2)[a] LF ($n = 9$): 10 wk, −13.8 (7.7)[a]; 5.5 mo, −17.5 (15.2)[a]; 14.5 mo, −20.3 (16.5)[a]	↓ at 10 wk in each group ($P \leq 0.001$) ↓ persisted at 14.5 mo in LC ($P < 0.02$) only Greater ↓ in LC at 10 wk ($P < 0.001$) and 6 mo ($P < 0.05$)
	Body fat (kg) change in skinfold measurements from B to 10 wk,	LF ($n = 9$): 10 wk, −0.3 (0.5)[a] LC ($n = 10$): 10 wk, −1.1 (1.0)[a]	↓ body fat in LC compared to LF at 10 wk ($P < 0.05$)
Sondike et al. (2003)[39]	BMI (kg/m^2) at B and 12 wk for all participants ($n = 39$) and for completers only ($n = 30$)	LC: B, 35.4 (5.0)[a]; 12 wk, 33.0 (2.7)[a] LF: B, 35.6 (5.8)[a]; 12 wk, 34.4 (1.6)[a] Completers: LC: B, 35.4 (5.0)[a]; 12 wk, 32.1 (3.0)[a] LF: B, 35.6 (5.8)[a]; 12 wk, 34.1 (1.7)[a]	↓ both groups (*P*-values NS); no difference between groups ↓ LC compared to LF ($P < 0.05$)
Demol et al. (2009)[32]/ Yackobovitch-Gavan (2008)[33]	BMI (kg/m^2) at B, 12 wk, and 1 y	LCLF ($n = 18$): B, 35.2 (1.6)[b]; 12 wk, 32.5 (1.6)[b]; 1 y, 32.4 (1.6)[b] LCHF ($n = 17$): B, 33.7 (1.6)[b]; 12 wk, 31.7 (1.6)[b]; 1 y, 32.6 (1.7)[b] HCLF ($n = 20$): B, 33.8 (1.5)[b]; 12 wk, 32.0 (1.5)[b]; 1 y, 31.1 (1.6)[b]	↓ BMI at 12 wk in groups combined, maintained at 1 y ($P < 0.001$); no differences between groups
	BMI z-score (CDC) at B, 12 wk, and 1 y	LCLF ($n = 18$): B, 3.4 (0.3)[b]; 12 wk, 2.8 (0.3)[b]; 1 y, 2.7 (0.3)[b] LCHF ($n = 17$): B, 3.1 (0.3)[b]; 12 wk, 2.7 (0.3)[b]; 1 y, 2.7 (0.4)[b] HCLF ($n = 20$): B, 3.3 (0.3)[b]; 12 wk, 2.9 (0.3)[b]; 1 y, 2.5 (0.3)[b]	↓ BMI z-score at 12 wk in groups combined and maintained at 1 y ($P < 0.001$); no differences between groups
	Body fat (%) determined by BIA at B, 12 wk, and 1 y	LCLF ($n = 18$): B, 43.2 (1.9)[b]; 12 wk, 37.5 (2.0)[b]; 1 y, 38.9 (2.2)[b] LCHF ($n = 17$): B, 42.0 (2.0)[b]; 12 wk, 39.6 (2.1)[b]; 1 y, 42.3 (2.3)[b] HCLF ($n = 20$): B, 39.2 (1.8)[b]; 12 wk, 34.9 (2.0)[b]; 1 y, 37.6 (2.2)[b]	↓ body fat % at 12 wk in groups combined ($P \leq 0.05$); ↑ body fat % from 12 wk to 1 y in groups combined ($P \leq 0.05$); no differences between groups
Krebs et al. (2010)[40]	BMI (kg/m^2) at B and 13 wk	LC: B ($n = 24$), 38.0 (1.2)[b]; 13 wk ($n = 18$), 33.9 (1.4)[b] LF: B ($n = 22$), 40.1 (1.8)[b]; 13 wk ($n = 15$), 36.9 (2.4)[b]	Results NS
	BMI z-score at B and 13 wk	LC ($n = 24$): B, 2.48 (0.06)[b]; 13 wk, 2.1 (0.1)[b] LF ($n = 22$): B, 2.51 (0.05)[b]; 13 wk, 2.4 (0.1)[b]	↓ in each group at 13 wk (*P*-value, NS); ↓ maintained at 24 wk (LC, $P = 0.01$; LF, $P = 0.01$) and 36 wk (LC, $P = 0.04$, LF, $P = 0.002$) follow up; greater ↓ in LC at 13 wk ($P = 0.03$)
	Lean body mass (kg) at B and 13 wk, determined by DEXA	LC ($n = 24$): B, 47.08 (1.69)[b]; 13 wk, 45.84 (2.1)[b] LF: ($n = 22$): B, 44.09 (1.9)[b], 13 wk, 45.34 (2.1)[b]	↓ fat mass in each group (*P*-values, NS); ↓ lean mass in LC at 13 wk($P = 0.05$)
Partsalaki et al. (2012)[41]	BMI (kg/m2) at B and 6 mo (completer analysis)	LC ($n = 21$): B, 30.0 (4.3)[a]; 6 mo, 26.3 (3.9)[a] LF ($n = 17$): B, 28.1 (3.1)[a]; 6 mo, 24.8 (3.0)[a]	Improvements in all weight-related outcomes; no differences between groups
	Body fat (kg) at B and 6 mo, BIA	LC ($n = 21$): B, 26.0 (8.1)[a]; 6 mo, 19.0 (8.0)[a] LF ($n = 17$): B, 21.8 (8.2)[a]; 6 mo, 16.7 (7.4)[a]	
Kirk et al. (2012)[42]	BMI (kg/m2) at B, 6 mo, and 12 mo	LC ($n = 35$): B, 29.9 (4.4)[a]; 6 mo, NS; 12 mo, NS RGL ($n = 36$): B, 29.2 (3.8)[a]; 6 mo, NS; 12 mo, NS LF ($n = 31$): B, 29.1 (3.8)[a]; 6 mo, NS; 12 mo, NS	NS
	BMI z-score at B, 6 mo, and 12 mo	LC ($n = 35$): B, 2.3 (0.2)[a]; 6 mo, NS; 12 mo, NS RGL ($n = 36$): B, 2.3 (0.3)[a]; 6 mo, NS; 12 mo, NS LF ($n = 31$): B, 2.3 (0.3)[a]; 6 mo, NS; 12 mo, NS	↓ in all 3 diet groups at 3 mo ($P \leq 0.0001$); ↓ maintained at 6 ($P \leq 0.0001$) and 12 mo ($P \leq 0.0001$)
	Body fat (%) at B, 6 mo, and 12 mo, determined by DEXA	LC ($n = 35$): B, 41.3 (3.3)[a]; 6 mo, NS; 12 mo, NS RGL ($n = 36$): B, 41.1 (3.4)[a]; 6 mo, NS; 12 mo, NS LF ($n = 31$): B, 39.6 (4.4)[a]; 6 mo, NS; 12 mo, NS	↓ in all 3 diet groups at 3 mo ($P \leq 0.0002$); ↓ maintained at 6 ($P \leq 0.0001$) and 12 mo ($P < 0.002$); no differences in weight-outcomes between groups at any time point
Studies comparing increased-protein with standard-protein diets			
Rolland-Cachera et al. (2004)[35]	BMI (kg/m^2) at B and 9 mo (end of treatment)	IP ($n = 46$): B, 36.4 (5.4)[a]; 9 mo, 24.0 (2.5)[a] SP ($n = 53$): B, 36.1 (4.6)[a]; 9 mo, 24.2 (2.6)[a]	Improvements in all weight-related outcomes in both groups (*P*-values, NS); ↑ weight during follow-up period; no difference in BMI z-score from inclusion to end of follow up (*P*-values, NS)
	BMI z-score at B and 9 mo (end of treatment)	IP ($n = 46$): B, 4.27 (0.7)[a]; 9 mo, 1.72 (0.6)[a] SP ($n = 53$): B, 4.29 (0.6)[a]; 9 mo, 1.74 (0.6)[a]	No differences between groups
	Body fat (%) at B and 9 mo (end of treatment), determined by BIA	IP ($n = 46$): B, 32.1 (3.9)[a]; 9 mo, 20.1 (5.1)[a] SP ($n = 53$): B, 32.0 (3.2)[a]; 9 mo, 19.6 (5.0)[a]	
Gately et al. (2007)[43]	BMI (kg/m^2) at B and end of camp (mean, 29 days)	IP ($n = 41$): B, 31.3 (3.9)[a]; end camp, 29.3 (3.5)[a] SP ($n = 39$): B, 34.5 (6.0)[a]; end camp, 32.4 (5.8)[a]	Improvements in all weight-related outcomes in groups combined (BMI, $P < 0.001$; BMI z-score, $P < 0.001$; body fat %, $P < 0.01$); no differences between groups
	BMI z-score at B and end of camp	IP ($n = 41$): B, 2.83 (0.42)[a]; end camp, 2.54 (0.44)[a] SP ($n = 39$): B, 3.10 (0.50)[a]; end camp, 2.84 (0.58)[a]	
	Body fat (%) at B and end of camp, determined by air displacement plethysmography	IP ($n = 41$): B, 41.0 (6.3)[a]; end camp, 37.7 (7.3)[a] SP ($n = 39$): B, 43.2 (7.5)[a]; end camp, 42.6 (7.8)[a]	

Table 2 **Continued**

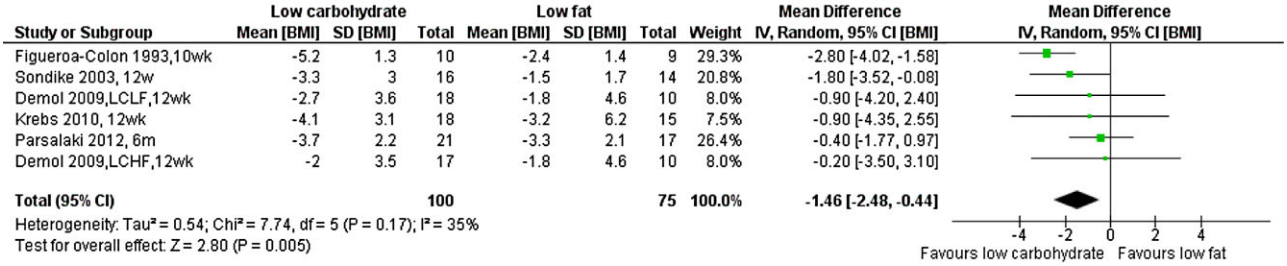
Reference	Weight-related outcomes	Results at measured time points (no. of subjects): mean (SD[a] or SEM[b] or 95% CIs[c])	Significant changes and differences between groups
Duckworth et al. (2009)[44]	BMI (kg/m^2) at B and end of camp (mean 31 days)	IP ($n = 46$): B, 33.7 (4.6)[a]; end camp, 31.9 (4.6)[a] SP ($n = 49$): B, 34.0 (6.8)[a]; end camp, 31.9 (6.3)[a]	Improvements in all weight-related outcomes in groups combined (BMI, $P < 0.001$; BMI z-score, $P < 0.001$; body fat %, $P < 0.001$); no differences between groups
	BMI z-score at B and end of camp	IP ($n = 46$): B, 3.03 (0.51)[a]; end camp, 2.78 (0.61)[a] SP ($n = 49$); B, 3.0 (0.72)[a]; end camp, 2.75 (0.77)[a]	
	Body fat (%) at B and end of camp, air displacement plethysmography	IP ($n = 46$): B, 43.4 (5.6)[a]; end camp, 40.2 (6.2)[a] SP ($n = 49$): B, 44.5 (9.0)[a]; end camp, 41.1 (9.3)[a]	
Baxter et al. (2013)[37]	BMI (kg/m^2) at B and 12 wk	Groups combined ($n = 88$): B, 32.7 (5.7)[a]; 12 wk, 31.5 (5.8)[a]	Improved BMI z-score in groups combined
	BMI z-score at B and 12 wk	Groups combined ($n = 88$): B, 2.20 (0.4)[a]; 12 wk, 2.08 (0.42)[a]	No differences between groups, hence, results are pooled
Mirza et al. (2013)[45]	BMI z-score at B, 3 mo, 1 y, and 2 y	IP/LGD ($n = 57$): B, 2.25 (2.16, 2.34)[c]; 3 mo, 2.12 (2.08, 2.17)[c],; 1 y, 2.10 (2.05, 2.16)[c]; 2 y, 2.10 (2.02, 2.16)[c]	↓ BMI z-score in both groups at 3 mo, 1 y, and 2 y compared with B
		SP ($n = 56$): B, 2.24 (2.17, 2.31)[c]; 3 mo, 2.13 (2.09, 2.18)[c]; 1 y, 2.16 (2.10, 2.11)[c]; 2 y, 2.16 (2.09, 2.22)[c]	No differences in BMI or BMI z-score between groups
Garnett et al. (2013)[36]	BMI (kg/m2) at B, 3 mo, and 6 mo	IP ($n = 56$): B, 34.22 (0.63)[b]; 3 mo, 33.05 (0.63)[b]; 6 mo, 33.16 (0.68)[b] SP ($n = 55$): B, 33.92 (0.80)[b]; 3 mo, 32.82 (0.82)[b]; 33.19 (0.89)[b]	↓ from B to 3 months in both groups; maintained at 6 months in IP group; no differences between groups
	BMI z score at B, 3 mo and 6 mo	IP ($n = 56$): B, 2.39 (0.03)[b]; 3 mo, 2.25 (0.04)[b]; 6 mo, 2.21 (0.05)[b] SP ($n = 55$): B, 2.32 (0.04)[b]; 3 mo, 2.19 (0.06)[b]; 6 mo, 2.16 (0.06)[b]	↓ from B to 3 months in both groups; maintained at 6 months; no differences between groups
	BMI % of 95th percentile at B, 3 mo, and 6 mo	IP ($n = 56$): B, 132.9 (3.1)[b]; 3 mo, 126.8 (2.8)[b]; 6 mo, 124.5 (3.0)[b] SP ($n = 55$): B, 132.5 (3.2)[b]; 3 mo, 126.2 (3.2)[b]; 6 mo, 123.7 (2.9)[b]	↓ from B to 3 months in both groups; maintained at 6 months; no differences between groups
Study comparing increased-fat with standard-fat diets			
Casazza et al. (2012)[46]	Body fat (kg) change from B to 16 wk, determined by DEXA	IF ($n = 12$): −3.4 (1.0)[a] SF ($n = 14$): −2.9 (0.9)[a]	↓ body fat in each group No differences between groups

Abbreviations: B, baseline; %BF, percent body fat; BIA, bioelectrical impedance analysis; CDC, Centers for Disease Control and Prevention; CIs, confidence intervals; DEXA, dual energy X-ray absorptiometry; HCLF, high carbohydrate low fat; IF, increased fat; IP, increased protein; IW/AH, ideal weight for actual height; LC, low carbohydrate; LCHF, low carbohydrate high fat; LCLF, low carbohydrate low fat; LF, low fat; n, number; NS, not specified; RGL, reduced glycemic load; SD, standard deviation; SEM, standard error of the mean; SF, standard fat; SP, standard protein.
[a]Number represents standard deviation.
[b]Number represents standard error of the mean.
[c]Number represents 95% confidence interval.

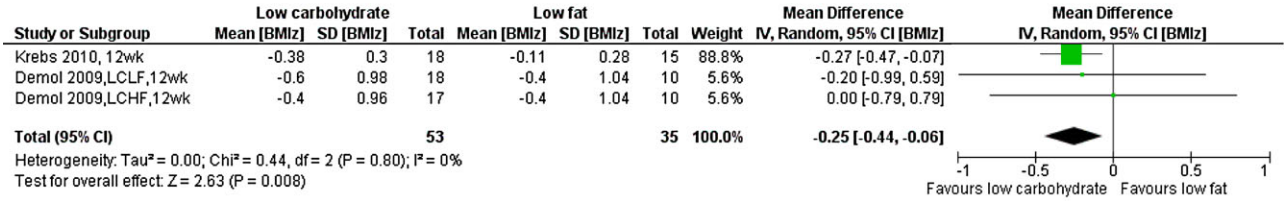
intervention[38–40] (Table 2). Five studies were included in the meta-analyses, which indicated there was a significant decrease in BMI (pooled mean difference, −1.46; 95% confidence interval (CI), −2.48 to −0.44) and BMI z-score (pooled mean difference, −0.25; 95% CI, −0.44 to −0.06) for the low-carbohydrate diet group compared with the low-fat diet group (Figure 3A,B). Meta-analysis at latest follow up included two of seven studies and indicated there was no advantage of either diet with regard to the BMI z-score (pooled mean difference, 0.57; 95% CI, −1.44 to 2.58) (Figure 3C).

Impact of treatment on metabolic parameters. All seven studies examined the impact of dietary interventions on various blood lipid levels, fasting glucose, and/or insulin levels and three studies reported blood pressure outcomes[38,41,42] (Table 3). Three of the seven studies examining blood lipids demonstrated significant reductions in total cholesterol[32,38,40] and/or LDL-C[32,40] post intervention. However, there were no differences between groups. Sondike et al.[39] reported a significant decrease in LDL-C in the low-fat group compared to the low-carbohydrate group (−25.1 ± 25.3 mg/dL [0.6 ± 0.7 mmol/L] versus 3.8 ± 13.0 mg/dL [0.1 ± 0.3 mmol/L], $P = 0.006$). Two studies demonstrated a significant decrease in triglycerides in the low-carbohydrate group only[39,40]; three other studies reported decreased triglyceride levels following the intervention compared with baseline but no differences between the diet groups.[32,34,42]

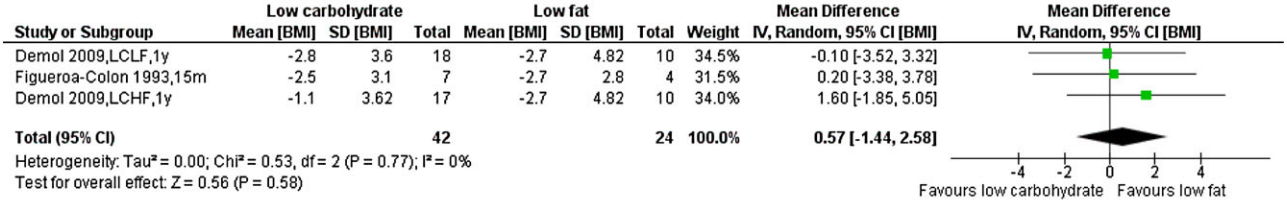
Only one study[32] reported a decrease in fasting glucose levels following the intervention phase, which was observed only when results of groups were combined. One other study[42] reported a significant decrease in the low-fat group at 12 months (9 months following the active intervention) but found no differences between the diet groups. Five studies[32,34,40–42] measured insulin levels and/or reported an index of insulin resistance and all reported improvements following the active intervention. Three of them reported benefits irrespective of diet group,[32,34,41] while the other two studies reported fasting insulin levels[42] or 2–h post glucose load insulin levels during an oral glucose tolerance test[40] to be significantly reduced in the low-carbohydrate diet group compared to the low-fat group. Additionally, the study by Demol et al.[32] found that reduced fasting insulin and improved homeostatic model assessment of insulin resistance were maintained in the low-carbohydrate diet groups only at the 1-year follow up from baseline.



A. Outcome: Change in BMI (kg/m^2) at the end of active intervention



B. Outcome: Change in BMI z-score at the end of active intervention



C. Outcome: Change in BMI (kg/m^2) at the latest follow-up

Figure 3 **Meta-analysis of studies comparing a low-carbohydrate diet to a standard low-fat diet. A**. Outcome: Change in BMI (kg/m^2) at the end of active intervention. **B**. Outcome: Change in BMI z-score at the end of active intervention. **C**. Outcome: Change in BMI z-score at the 2-year follow up.

Three studies examined blood pressure.[38,41,42] One found no intervention effect and no differences between diet groups at any time point.[41] Another study[38] found a decrease in mean systolic blood pressure and diastolic blood pressure when results from the diet groups were pooled at 10 weeks and at the 6- and 14.5-month follow-ups. There were no differences between diet groups in this study at any time point. In the study by Kirk et al.[42] diastolic blood pressure was significantly increased in the low-fat diet group only at 6 months and both systolic and diastolic blood pressure were significantly higher in the low-fat group compared with the low-carbohydrate diet group.

Adverse events. No studies reported adverse events that prevented participants from completing their respective trials. Non-specific side effects were described for four studies and included hunger,[38] fatigue,[38,39] muscle cramps,[38,40] gastrointestinal discomfort,[32,39,40] headaches,[32,39] and nausea.[40] These side effects were not different between diet groups.

Increased-protein diet compared to standard-protein diet

Description of studies. Six studies[35–37,43–45] were identified that investigated the effect of varying the protein content of the diet on weight loss in overweight and obese children and adolescents, as described in Table 1. Two studies were conducted in the United Kingdom,[43,44] two in Australia,[36,37] one in the United States,[45] and one in France.[35] The two UK studies were conducted at a camp and involved both overweight and obese participants.[43,44] The other studies were conducted in a boarding school with obese participants only[35] or in a hospital outpatient clinic setting with obese only[45] or overweight and obese participants.[37] One study specifically targeted recruitment of participants with insulin resistance and/or pre-diabetes,[36] while another two studies indicated from baseline testing that some insulin-resistant participants had been incidentally recruited.[37,45] Studies recruited boys and girls aged 7–18 years, with sample sizes ranging between 98 and 121 participants (mean sample size, 110 participants).

Table 3 **Results of the main metabolic outcomes in the included studies examining the optimal macronutrient distribution of the diet for reducing child obesity.**

Reference	Metabolic outcomes	Results at measured time points (no. of subjects): mean (SD[a] or SEM[b] or 95% CI[c])	Changes and differences between groups
Studies comparing low-carbohydrate to conventional low-fat diets			
Pena et al. (1979)[34]	TC at B and 8 wk	NS	No significant changes in TC
	TG (mg/dL) at B and 8 wk (approximated from graph)	LC: B (n = NS), 148 (14)[a]; 8 wk (n = NS), 132 (14)[a] LF: B (n = NS), 141 (13)[a]; 8 wk (n = NS), 133 (14)[a]	↓ TGs in each group (LC: $P < 0.001$, LF: $P < 0.05$); no differences between groups
	Fasting insulin (μU/mL) at B and 8 wk	LC: B (n = 10), 28.73 (3.55)[a]; 8 wk (n = 10), 7.14 (2.91)[a] LF: B (n = 11), 29.47 (1.78)[a]; 8 wk (n = 11), 22.6 (1.66)[a]	↓ fasting insulin in LC only ($P < 0.001$); no differences between groups
	Insulinogenic index at B and 8 wk	LC: B (n = 10), 0.799 (0.188)[a]; 8 wk (n = 10), 0.289 (0.06)[a] LF: B (n = 11), 0.581 (0.191)[a]; 8 wk (n = 11), 0.391 (0.106)[a]	↓ insulinogenic index in LC only($P < 0.01$); no differences between groups
	Fasting glucose (mg/dL) at B and 8 wk	NS	No change in either group; no differences between groups
Figueroa-Colon et al. (1993)[38]	SBP (mm Hg) at B, 10 wk, 5.5 mo, and 14.5 mo	LC: B (n = 10), 131 (16)[a]; 10 wk (n = 10), 118 (14)[a]; 5.5 mo (n = 10), 121 (18)[a]; 14.5 mo (n = 7), 113 (21)[a] LF: B (n = 9), 124 (11)[a]; 10 wk (n = 9), 115 (14)[a]; 5.5 mo (n = 9), 115 (12)[a]; 14.5 mo (n = 4), 111(8)[a] Groups combined: B (n = 19), 128 (14)[a]; 10 wk (n = 19), 117 (14)[a]; 5.5 mo (n = 19), 118 (15)[a]; 14.5 mo (n = 11), 112 (17)[a]	↓ SBP in groups combined at 10 wk ($P \leq 0.05$), 6 mo ($P \leq 0.05$), and 14.5 mo ($P \leq 0.01$) compared with B; no differences between groups
	DBP (mm Hg) at B, 10 wk, 5.5 mo and 14.5 mo	LC: B (n = 10), 86 (8)[a]; 10 wk (n = 10), 78 (8)[a]; 5.5 mo (n = 10), 78 (6)[a]; 14.5 mo (n = 7), 73 (11)[a] LF: B (n = 9), 82 (6)[a]; 10 wk (n = 9), 78 (8)[a]; 5.5 mo (n = 9), 76 (8)[a]; 14.5 mo (n = 4), 67 (6)[a] Groups combined: B (n = 19), 85 (7)[a]; 10 wk (n = 19), 78 (8)[a]; 5.5 mo (n = 19), 77 (7)[a]; 14.5 mo (n = 11), 71 (9)[a]	↓ DBP in groups combined at 10 wk ($P \leq 0.01$), 6 mo ($P \leq 0.01$), and 14.5 mo ($P \leq 0.0001$) compared with B; no differences between groups
	TC (mmol/L) at B and 10 wk	Groups combined: B (n = 19), 4.47 (0.79)[a]; 10 wk (n = 19), 3.74 (0.84)[a]	↓ TC in groups combined ($P < 0.02$); no differences between groups
	TG (mmol/L) at B and 10 wk	Groups combined: B (n = 19), 1.25 (0.57)[a]; 10 wk (n = 19), 0.98 (0.47)[a]	No change in TG
	Fasting glucose at B and wk 10	Data not presented	Change not reported (all in normal range)
Sondike et al. (2003)[39]	TC (mg/dL) change from B to 12 wk	LC: −3.7 (18)[a] LF: −17.3 (15.8)[a]	↓ TC in LF group only ($P < 0.05$)
	TG (mg/dL) change from B to 12 wk	LC: −48.3 (29)[a] LF: −5.9 (70)[a]	↓ TG in LC group only ($P < 0.05$)
	HDL-C (mg/dL) change from B to 12 wk	LC: 3.8 (7.2)[a] LF: 1.8 (7.7)[a]	No changes in either diet group
	LDL-C (mg/dL) change from B to 12 wk	LC: 3.8 (13)[a] LF: −25.1 (25.3)[a]	↓ LDL-C in LF group ($P < 0.05$); greater LDL-C reduction in LF group compared with LC ($P = 0.006$)
	non-HDL-C (mg/dL) change from B to 12 wk	LC: −26 (22.3)[a] LF: −13.6 (13.4)[a]	↓ non-HDL-C in LF and LC groups ($P < 0.05$)
	Fasting glucose at B and 12 wk	Data not presented	No changes
Demol et al. (2009)[32]/ Yackobovitch-Gavan (2008)[33]		For all tests: LCLF (n = 18); LCHF (n = 17); HCLF (n = 20); total (n = 35)	
	TC (mg/dL) at B, 12 wk, and 1 y	LCLF: B, 171.9 (6.7)[b]; 12 wk, 148.7(7.1)[b]; 1 y, 166.4 (7.7)[b] LCHF: B, 170.5 (6.9)[b]; 12 wk, 152.8 (7.6)[b]; 1 y, 140.7 (8.9)[b] HCLF: B, 163.5 (6.4)[b]; 12 wk, 147.8 (6.9)[b]; 1 y, 150.4 (8.0)[b] Combined: B, 168.6 (3.8)[b]; 12 wk, 149.7 (4.1)[b]; 1 y, 152.3 (4.7)[b]	↓ TC in groups combined at 12 wk; ↓ maintained at 1 y ($P < 0.001$); no differences between groups
	LDL-C (mg/dL) at B, 12 wk, and 1 y	LCLF: B, 103.1(5.5)[b]; 12 wk, 88.4 (5.8)[b]; 1 y, 96.8(6.2)[b] LCHF: B, 98.9 (5.7)[b]; 12 wk, 89.0 (6.2)[b]; 1 y, 82.1 (7.2)[b] HCLF: B, 94.4 (5.3)[b]; 12 wk, 83.9 (5.6)[b]; 1 y, 89.8 (6.5)[b] Combined: B, 98.8 (3.2)[b]; 12 wk, 87.1 (3.4)[b]; 1 y, 89.6 (3.4)[b]	↓ LDL-C in groups combined at 12 wk; ↓ maintained at 1 y ($P < 0.001$); no differences between groups
	HDL-C (mg/dL) at B, 12 wk, and 1 y	LCLF: B, 45.0 (2.0)[b]; 12 wk, 44.4 (2.2)[b]; 1 y, 44.8 (2.4)[b] LCHF: B, 46.3 (2.1)[b]; 12 wk, 43.0 (2.4)[b]; 1 y, 38.3 (2.8)[b] HCLF: B, 48.3 (2.0)[b]; 12 wk, 46.0 (2.1)[b]; 1 y, 44.7 (2.5)[b] Combined: B, 46.5 (1.2)[b]; 12 wk, 44.5 (1.3)[b]; 1 y, 42.6 (1.5)[b]	↓ HDL-C in groups combined at 1 y compared to B ($P \leq 0.05$); no differences between groups
	TG (mg/dL) at B, 12 wk, and 1 y	LCLF: B, 119.3(12.2)[b]; 12 wk, 78.8 (12.8)[b]; 1 y, 121.1(13.9)[b] LCHF: B, 126.3 (12.6)[b]; 12 wk, 105.0 (13.9)[b]; 1 y, 102.7 (16.3)[b] HCLF: B, 106.4 (11.6)[b]; 12 wk, 89.6 (12.5)[b]; 1 y, 78.7 (14.6)[b] Combined: B, 117.3 (6.9)[b]; 12 wk, 91.1 (7.6)[b]; 1 y, 101.0 (8.6)[b]	↓ TG in groups combined at 12 wk; ↓ maintained at 1 y ($P < 0.001$); no differences between groups
	Fasting glucose (mg/dL) at B, 12 wk, and 1 y	LCLF: B, 85.4 (1.8)[b]; 12 wk, 81.3 (2.0)[b]; 1 y, 80.1 (2.3)[b] LCHF: B, 85.0 (1.9)[b]; 12 wk, 81.0 (2.2)[b]; 1 y, 76.4 (2.9)[b] HCLF: B, 87.4 (1.7)[b]; 12 wk, 81.1 (2.2)[b]; 1 y, 81.9 (2.5)[b] Combined: B, 85.9 (1.0)[b]; 12 wk, 81.1 (1.2)[b]; 1 y, 79.5 (1.5)[b]	↓ fasting glucose in groups combined at 12 wk; ↓ maintained at 1 y ($P < 0.001$); no differences between groups
	Fasting insulin (μU/mL) at B, 12 wk, and 1 y	LCLF: B, 20.3(2.3)[b]; 12 wk, 15.0(2.5)[b]; 1 y, 13.1(2.7)[b] LCHF: B, 19.5 (2.4)[b]; 12 wk, 12.9 (2.8)[b]; 1 y, 12.0 (3.3)[b] HCLF: B, 20.0 (2.1)[b]; 12 wk, 18.7 (2.4)[b]; 1 y, 15.1 (2.9)[b] Combined: B, 19.9 (1.3)[b]; 12 wk, 15.5 (1.5)[b]; 1 y, 13.4 (1.7)[b]	↓ fasting insulin in groups combined at 12 wk; ↓ maintained at 1 y ($P < 0.001$) and stand-alone ↓ at 12 wk maintained at 1 y in LCLF (12 wk, $P = 0.026$; 1 y, $P = 0.008$) and LCHF (12 wk, $P = 0.002$; 1 y, $P < 0.001$)
	HOMA-IR at B, 12 wk, and 1 y	LCLF: B, 4.3 (0.5)[b]; 12 wk, 3.1 (0.5)[b]; 1 y, 2.7 (0.6)[b] LCHF: B, 4.1 (0.5)[b]; 12 wk, 2.6 (0.6)[b]; 1 y, 2.3 (0.7)[b] HCLF: B, 4.2 (0.5)[b]; 12 wk, 3.8 (0.5)[b]; 1 y, 3.1 (0.6)[b] Combined: B, 4.2 (0.3)[b]; 12 wk, 3.1 (0.3)[b]; 1 y, 2.7 (0.3)[b]	↓ HOMA-IR in groups combined at 12 wk; ↓ maintained at 1 y ($P < 0.001$) and stand-alone ↓ at 12 wk maintained at 1 y in LCLF (12 wk, $P = 0.014$; 1 y, $P = 0.003$) and LCHF (12 wk, $P < 0.001$; 1 y, $P < 0.001$)

Table 3 **Continued**

Reference	Metabolic outcomes	Results at measured time points (no. of subjects): mean (SD[a] or SEM[b] or 95% CI[c])	Changes and differences between groups
Krebs et al. (2010)[40]		For all tests: LC ($n = 24$) at B and ($n = 18$) at 13 wk; LF ($n = 22$) at B and ($n = 15$) at 13 wk	
	TC (mg/dL) at B and 13 wk	LC: B, 166.8 (7.7)[b]; 13 wk, 154.1 (8.6)[b] LF: B, 161.3 (6.9)[b]; 13 wk, 144.7 (7.0)[b]	↓ TC in each group (*P*-values, NS); no differences between groups
	LDL-C (mg/dL) at B and 13 wk	LC: B, 103.5 (6.8)[b]; 13 wk, 96.8 (7.6)[b] LF: B, 97.4 (5.6)[b]; 13 wk, 85.5 (5.6)[b]	↓ LDL-C in each group (*P*-values, NS); no differences between groups
	HDL-C (mg/dL) at B and 13 wk	LC: B, 39.2 (1.3)[b]; 13 wk, 38.4 (2.2)[b] LF: B, 42.6 (2.3)[b]; 13 wk, 39.1 (2.5)[b]	↓ HDL-C in LF only, but not different between groups (*P*-values, NS)
	TG (mg/dL) at B and 13 wk	LC: B, 125.8 (9.7)[b]; 13 wk, 80.3 (6.5)[b] LF: B, 107 (12.7)[b]; 13 wk, 96.5 (13.8)[b]	↓ TG in LC ($P = 0.0003$); greater ↓ in LC compared to LF group ($P = 0.03$)
	2-h OGTT measuring HOMA-IR at B and 13 wk	LC: B, 4.3 (0.6)[b]; 13 wk, 2.8 (0.4)[b] LF: B, 4.9 (0.7)[b]; 13 wk, 3.3 (0.4)[b]	↓ HOMA-IR in both groups (*P*-values, NS) with no differences between groups; ↓ 2-hr insulin in LC only ($P = 0.03$) with no significant differences between groups; no change in fasting glucose or glucose tolerance
Partsalaki et al. (2012)[41]	TC (mmol/L) at B and 6 mo	LC ($n = 21$): B, 4.40 (0.85)[a]; 6 mo, 4.63 (0.75)[a] LF ($n = 17$): B, 4.05 (0.94)[a]; 6 mo, 4.03 (0.89)[a]	No differences between or within groups and no intervention effect
	LDL-C (mmol/L) at B and 6 mo	LC ($n = 21$); B, 2.72 (0.69)[a]; 6 mo, 2.86 (0.65)[a] LF ($n = 17$): B, 2.6 (0.83)[a]; 6 mo, 2.55 (0.77)[a]	No differences between or within groups and no intervention effect
	HDL-C (mmol/L) at B and 6 mo	LC ($n = 21$): B, 1.27 (0.26)[a]; 6 mo, 1.38 (0.25)[a] LF ($n = 17$): B, 1.13 (0.20)[a]; 6 mo, 1.23 (0.23)[a]	No differences between or within groups and no intervention effect
	TG (mmol/L) at B and 6 mo	LC ($n = 21$): B, 0.83 (0.35)[a]; 6 mo, 0.81 (0.39)[a] LF ($n = 17$): B, 0.89 (0.57)[a]; 6 mo, 0.80 (0.40)[a]	No differences between or within groups and no intervention effect
	SBP (mm Hg) at B and 6 mo	LC ($n = 21$): B, 108 (13)[a]; 6 mo, 103 (10)[a] LF ($n = 17$): B, 106 (11)[a]; 6 mo, 102 (10)[a]	No differences between or within groups and no intervention effect
	DBP (mm Hg) at B and 6 mo	LC ($n = 21$): B, 68 (8)[a]; 6 mo, 67 (8)[a] LF ($n = 17$); B, 62 (11)[a]; 6 mo, 66 (7)[a]	No differences between or within groups and no intervention effect
	Fasting glucose (mmol/L) at B and 6 mo	LC ($n = 21$): B, 4.52 (0.61)[a]; 6 mo, 4.51 (0.29)[a] LF ($n = 17$): B, 4.25 (0.55)[a]; 6 mo, 4.5 (0.5)[a]	No differences between or within groups and no intervention effect
	Fasting insulin (pmol/L) at B and 6 mo	LC ($n = 21$); B, 125 (64)[a]; 6 mo, 65.97 (45.83)[a] LF ($n = 17$); B, 77 (60)[a]; 6 mo, 39.58 (22.91)[a]	↓ in each diet group at 6 mo
	HOMA-IR at B and 6 mo	LC ($n = 21$): B, 3.6 (2.0)[a]; 6 mo, 1.8 (1.4)[a] LF ($n = 17$): B, 2.2 (1.9)[a]; 6 mo, 1.2 (0.6)[a]	↓ in each diet group at 6 mo
Kirk et al. (2012)[42]	TC (mg/dL) at B, 3 mo, 6 mo, and 12 mo	LC: B, 162 (4)[b]; 3 mo, 157 (5)[b]; 6 mo, 160 (5)[b]; 12 mo, 161 (5)[b] RGL: B, 158 (5)[b]; 3 mo, 153 (4)[b]; 6 mo, 157 (4)[b]; 12 mo, 153 (4)[b] LF: B, 159 (5)[b]; 3 mo, 155 (5)[b]; 6 mo, 155 (5)[b]; 12 mo, 160 (6)[b]	No differences between or within groups and no intervention effect
	LDL-C (mg/dL) at B, 3 mo, 6 mo, and 12 mo	LC: B, 95.0 (3.9)[b]; 3 mo, 92.7 (4.4)[b]; 6 mo, 93.4 (4.3)[b]; 12 mo, 91.7 (4.6)[b] RGL: B, 91.1 (4.0)[b]; 3 mo, 87.5 (3.4)[b]; 6 mo, 92.8 (4.0)[b]; 12 mo, 86.1 (3.5)[b] LF: B, 90.8 (4.5)[b]; 3 mo, 89.3 (4.5)[b]; 6 mo, 90.0 (4.2)[b]; 12 mo, 89.9 (4.7)[b]	↓ in the RGL group only at 12 mo; no other changes and no differences between groups
	HDL-C (mg/dL) at B, 3 mo, 6 mo, and 12 mo	LC: B, 47.6 (1.4)[b]; 3 mo, 50.9 (1.5)[b]; 6 mo, 51.6 (1.7)[b]; 12 mo, 52.7 (1.8)[b] RGL: B, 49.8 (1.4)[b]; 3 mo, 49.2 (1.5)[b]; 6 mo, 48.3 (1.4)[b]; 12 mo, 50.3 (1.5)[b] LF: B, 48.2 (2.1)[b]; 3 mo, 48.2 (2.1)[b]; 6 mo, 49.0 (1.7)[b]; 12 mo, 51.7 (2.1)[b]	↑ in LC group at 3 mo, 6 mo, and 12 mo; ↑ in LF group at 12 mo only; no other changes and no differences between groups
	TG (mg/dL) at B, 3 mo, 6 mo, and 12 mo	LC: B, 100 (7)[b]; 3 mo, 69 (6)[b]; 6 mo, 76 (7)[b]; 12 mo, 82 (6)[b] RGL: B, 87 (6)[b]; 3 mo, 81 (7)[b]; 6 mo, 77 (6)[b]; 12 mo, 82 (6)[b] LF: B, 102 (7)[b]; 3 mo, 88 (8)[b]; 6 mo, 82 (6)[b]; 12 mo, 89 (7)[b]	↓ in RGL and LF at 6 mo only; ↓ in LC at 3 mo, 6 mo, and 12 mo; no differences between groups
	SBP (mm Hg) at B, 3 mo, 6 mo, and 12 mo	LC: B, 99.9 (1.3)[b]; 3 mo, 98.6 (1.6)[b]; 6 mo, 98.2 (1.6)[b]; 12 mo, 101.0 (1.8)[b] RGL: B, 98.3 (1.7)[b]; 3 mo, 100.0 (1.7)[b]; 6 mo, 99.0 (1.5)[b]; 12 mo, 100.0 (1.7)[b] LF: B, 102.0 (2.3)[b]; 3 mo, 99.7 (1.7)[b]; 6 mo, 104.0 (1.7)[b]; 12 mo, 99.8 (1.7)[b]	No changes in any diet group, but at 6 mo, SBP was higher in LF group than LC and RGL groups
	DBP (mm Hg) at B, 3 mo, 6 mo, and 12 mo	LC: B, 60.8 (1.4)[b]; 3 mo, 59.3 (1.6)[b]; 6 mo, 59.2 (1.5)[b]; 12 mo, 62.5 (2.2)[b] RGL: B, 57.9 (1.1)[b]; 3 mo, 61.6 (1.9)[b]; 6 mo, 62.4 (1.8)[b]; 12 mo, 60.3 (1.5)[b] LF: B, 59.3 (1.8)[b]; 3 mo, 60.7 (1.8)[b]; 6 mo, 64.8 (1.6)[b]; 12 mo, 59.4 (1.7)[b]	↑ in RGL and LF groups at 6 mo only; no other changes; at 6 mo, DBP was lower in LC group than LF group
	Fasting glucose (mg/L) at B, 3 mo, 6 mo, and 12 mo	LC: B, 93.9 (1.1)[b]; 3 mo, 92.1 (1.0)[b]; 6 mo, 93.5 (1.2)[b]; 12 mo, 94.2 (1.2)[b] RGL: B, 94.5 (1.1)[b]; 3 mo, 93.9 (1.2)[b]; 6 mo, 93.4 (1.0)[b]; 12 mo, 92.5 (1.0)[b] LF: B, 95.5 (1.2)[b]; 3 mo, 93.6 (1.0)[b]; 6 mo, 94.9 (1.0)[b]; 12 mo, 93.1 (1.1)[b]	↓ in LF group at 12 mo only; no other changes and no differences between groups
	Fasting insulin (μU/L) at B, 3 mo, 6 mo, and 12 mo	LC: B, 22.9 (2.4)[b]; 3 mo, 16.9 (1.5)[b]; 6 mo, 19.8 (1.5)[b]; 12 mo, 22.7 (2.3)[b] RGL: B, 23.7 (2.5)[b]; 3 mo, 22.0 (1.8)[b]; 6 mo, 21.1 (1.6)[b]; 12 mo, 20.7 (1.7)[b] LF: B, 30.2 (3.6)[b]; 3 mo, 22.8 (2.5)[b]; 6 mo, 23.9 (2.2)[b]; 12 mo, 22.8 (2.2)[b]	↓ in LC group at 3 mo, RGL group at 6 mo and 12 mo, and LF group at 3 mo, 6 mo, and 12 mo; at 3 mo, LC group was lower than both the RGL and LF groups

Table 3 **Continued**

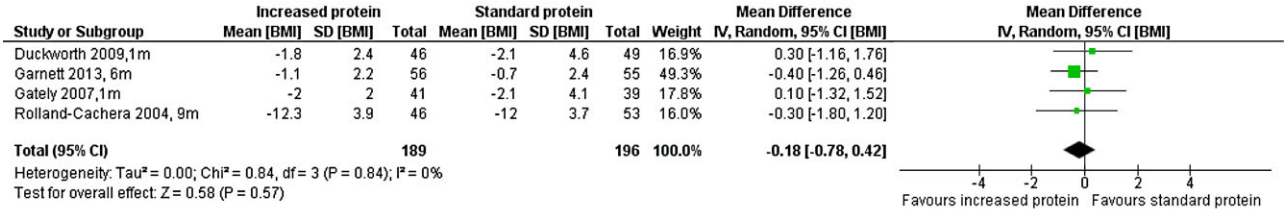
Reference	Metabolic outcomes	Results at measured time points (no. of subjects): mean (SD[a] or SEM[b] or 95% CI[c])	Changes and differences between groups
Studies comparing increased-protein with standard-protein diets			
Rolland-Cachera et al. (2004)[35]	None	Not applicable	Not applicable
Gately et al. (2007)[43]	SBP (mm Hg) at B and end of camp (mean, 29 days)	IP ($n = 41$): B, 113 (9)[a]; end camp, 108 (8)[a] SP ($n = 39$): B, 114 (9)[a]; end camp, 111 (10)[a]	↓ in groups combined ($P < 0.001$); no differences between groups
	DBP (mm Hg) at B and end of camp (mean: 29 days)	IP ($n = 41$): B, 64 (8)[a]; end camp, 59 (6)[a] SP ($n = 39$): B, 67 (10)[a]; end camp, 62 (7)[a]	↓ in groups combined ($P < 0.001$); no differences between groups
	TC (mM) at B and end of camp (mean: 29 days)	IP ($n = 16$): B, 4.26 (0.79)[a]; end camp, 3.40 (1.01)[a] SP ($n = 17$): B, 3.99 (0.73)[a]; end camp, 3.25 (0.50)[a]	↓ in groups combined ($P < 0.001$); no differences between groups
	HDL-C (mM) at B and end of camp (mean: 29 days)	IP ($n = 16$): B, 1.14 (0.28)[a]; end camp, 1.03 (0.23)[a] SP ($n = 17$): B, 1.15 (0.19)[a]; end camp, 0.99 (0.17)[a]	↓ in groups combined ($P < 0.01$); no differences between groups
	LDL-C (mM) at B and end of camp (mean: 29 days)	IP ($n = 16$): B, 2.66 (0.68)[a]; end camp, 2.03 (0.91)[a] SP ($n = 17$): B, 2.48 (0.59)[a]; end camp, 1.94 (0.50)[a]	↓ in groups combined ($P < 0.001$); no differences between groups
	TG (mM) at B and end of camp (mean: 29 days)	IP ($n = 16$): B, 1.05 (0.52)[a]; end camp, 0.83 (0.31)[a] SP ($n = 17$): B, 0.82 (0.40)[a]; end camp, 0.78 (0.28)[a]	↓ in groups combined ($P < 0.01$); no differences between groups
Duckworth et al. (2009)[44]	SBP (mm Hg) at B and end of camp (mean: 31 days)	IP ($n = 46$); B, 120 (15)[a]; end camp, 119 (15)[a] SP ($n = 49$): B, 119 (18)[a]; end camp, 118 (17)[a]	No changes and no differences between groups
	DBP (mm Hg) at B and end of camp (mean: 31 days)	IP ($n = 46$); B, 76 (14)[a]; end camp, 72 (13)[a] SP ($n = 49$); B, 76 (15)[a]; end camp, 71 (11)[a]	↓ in groups combined ($P = 0.009$); no differences between groups
Baxter et al. (2013)[37]	Fasting glucose and insulin to determine HOMA-IR at B and 12 wk	Results not described	
Mirza et al. (2013)[45]	HOMA-IR at B, 3 mo, 1 y, and 2 y (ITT analysis)	IP/LGD ($n = 57$); B, 2.59 (2.11, 3.19)[c]; 3 mo, 2.78 (2.33, 3.31)[c]; 1 y, 2.42 (2.00, 2.94)[c]; 2 y, 2.44 (2.04, 2.92)[c] SP ($n = 56$); B, 2.77 (2.24, 3.41)[c]; 3 mo, 3.03 (2.54, 3.62)[c]; 1 y, 3.01 (2.48, 3.66)[c]; 2 y, 3.12 (2.60, 3.75)[c]	No changes and no differences between groups at any time point
	SBP z-score change from B at 3 mo, 1 y, and 2 y (ITT analysis)	Groups combined ($n = 113$); 3 mo, −0.23 (−0.36, −0.94)[c]; 1 y, −0.18 (−0.30, −0.06)[c]; 2 y, −0.27 (−0.39, −0.15)[c]	↓ SBP at all time points compared with B; no differences between groups, hence pooling of results
	DBP z-score change from B at 3 mo, 1 y, and 2 y (ITT analysis)	Groups combined ($n = 113$): 3 mo, −0.21 (−0.32, −0.09)[c]; 1 y, −0.10 (−0.20, −0.006)[c]; 2 y, −0.05 (−0.15, 0.05)[c]	↓ DBP at 3 mo and 1 y compared with B; no differences at 2 y, no differences between groups, hence, pooling of results
Garnett et al. (2013)[36]	LDL-C (mmol/L) at B, 3 mo, and 6 mo	IP: B, 2.81 (0.09)[b]; 3 mo, 2.75 (0.09)[b]; 6 mo, 2.83 (0.10)[b]	No changes over time
		SP: B, 2.62 (0.09)[b]; 3 mo, 2.55 (0.10)[b]; 6 mo, 2.67 (0.10)[b]	No differences between groups at any time point
	HDL-C (mmol/L) at B, 3 mo, and 6 mo	IP: B, 1.05 (0.03)[b]; 3 mo, 1.07 (0.03)[b]; 6 mo, 1.09 (0.03)[b]	No changes over time
		SP: B, 1.05 (0.03)[b]; 3 mo, 1.06 (0.03)[b]; 6 mo, 1.08 (0.03)[b]	No differences between groups at any time point
	TG (mmol/L) at B, 3 mo, and 6 mo	IP: B, 1.13 (1.02, 1.26)[c]; 3 mo, 1.06 (0.95, 1.18)[c]; 6 mo, 1.10 (0.99, 1.23)[c]	No changes over time
		SP: B, 1.03 (0.92, 1.15)[c]; 3 mo, 1.13 (1.01, 1.27)[c]; 6 mo, 1.06 (0.94, 1.18)[c]	No differences between groups at any time point
	SBP z-score at B, 3 mo, and 6 mo	IP: B, 0.71 (0.16)[b]; 3 mo, 0.40 (0.16)[b]; 6 mo, 0.14 (0.17)[b]	↓ SBP at 3 mo and 6 mo compared with B
		SP: B, 0.75 (0.16)[b]; 3 mo, 0.43 (0.17)[b]; 6 mo, 0.17 (0.17)[b]	No differences between groups at any time point
	DBP z-score at B, 3 mo, and 6 mo	IP: B, 0.90 (0.10)[b]; 3 mo, 0.64 (0.10)[b]; 6 mo, 0.54 (0.10)[b]	↓ DBP at 3 mo and 6 mo compared with B
		SP: B, 0.91 (0.10)[b]; 3 mo, 0.65 (0.10)[b]; 6 mo, 0.55 (0.10)[b]	No differences between groups at any time point
	Fasting glucose (mmol/L) at B, 3 mo, and 6 mo	IP: B, 4.8 (0.06)[b]; 3 mo, 4.7 (0.06)[b]; 6 mo, 4.9 (0.06)[b]	↓ in both groups at 3 mo; at 6 mo, levels had returned to B
		SP: B, 4.7 (0.06)[b]; 3 mo, 4.6 (0.06)[b]; 6 mo, 4.8 (0.06)[b]	No differences between groups at any time point
	Fasting insulin (pmol/L) at B, 3 mo, and 6 mo	IP: B, 243 (217, 273)[c]; 3 mo, 215 (191, 240)[c]; 6 mo, 214 (191, 241)[c]	↓ in both groups at 3 mo compared to B; levels were maintained at 6 mo
		SP: B, 236 (210, 265)[c]; 3 mo, 208 (185, 234)[c]; 6 mo, 208 (185, 234)[c]	No differences between diet groups at any time point
	ISI (from OGTT) at B and 3 mo	Mean increase of 0.3 at 3 mo in groups combined	↑ at 3 mo compared with B; no differences between diet groups at 3 mo
	Insulin:glucose	Mean decrease of 7.2 at 6 mo in groups combined	↓ at 3 mo and 6 mo compared with B; no differences between diet groups at any time point
Study comparing increased-fat with standard-fat diets			
Casazza et al. (2012)[46]	TC (mg/dL) at B and 5 wk	IF ($n = 12$): B, 151.7 (9.5)[a]; 5 wk, 144.2 (7.5)[a] SF ($n = 14$): B, 165.1 (7.7)[a]; 5 wk 157.5 (6.1)[a]	No significant changes or differences between groups
	LDL-C (mg/dL) at B and 5 wk	IF ($n = 12$): B, 98.4 (8.0)[a]; 5 wk, 93.6 (6.8)[a] SF ($n = 14$): B, 109.8 (6.6)[a]; 5 wk, 100.1 (5.6)[a]	No significant changes or differences between groups
	HDL-C (mg/dL) at B and 5 wk	IF ($n = 12$): B, 40.5 (2.8)[a]; 5 wk, 40.8 (2.3)[a] SF ($n = 14$): B, 42.6 (2.3)[a]; 5 wk, 42.1 (1.9)[a]	No significant changes or differences between groups
	TG (mg/dL) at B and 5 wk	IF ($n = 12$): B, 64.3 (8.0)[a]; 5 wk, 49.4 (8.7)[a] SF ($n = 14$): B, 63.6 (6.6)[a]; 5 wk, 76.5 (7.1)[a]	TGs changed significantly over time, significantly higher TGs in SF group than IF group at 5 wks
	Fasting glucose (mg/dL) at B and 5 wk	IF ($n = 12$): B, 95.6 (2.5)[a];5 wk, 99.7 (2.4)[a] SF ($n = 14$): B, 96.0 (2.2)[a]; 5 wk, 98.1 (2.2)[a]	No significant changes or differences between groups
	Fasting insulin (μU/mL) at B and 5 wk	IF ($n = 12$): B, 14.3 (3.3)[a]; 5 wk, 21.0 (2.9)[a] SF ($n = 14$): B, 17.3 (3.0)[a]; 5 wk, 18.9 (2.6)[a]	↑ from B to 5 wk No differences between groups
	SI, $\times 10^4$ μU/mL at B and 5 wk	IF ($n = 12$): B, 3.9 (0.8)[a]; 5 wk, 3.7 (0.8)[a] SF ($n = 14$): B, 3.0 (0.7)[a]; 5 wk, 2.8 (0.7)[a]	No significant changes or differences between groups

Abbreviations: B, baseline; CIs, confidence intervals; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; HCLF, high carbohydrate low fat; IF, increased fat; IP, increased protein; ISI, insulin sensitivity index;LC, low carbohydrate; LCHF, low carbohydrate high fat; LCLF, low carbohydrate low fat; LDL-C, low-density lipoprotein cholesterol; LF, low fat; NS, not specified; OGTT, oral glucose tolerance test; RGL, reduced glycemic load; SBP, systolic blood pressure; SD, standard deviation; SEM, standard error of the mean; SF, standard fat; SP, standard protein; TC, total cholesterol; TG, triglyceride.

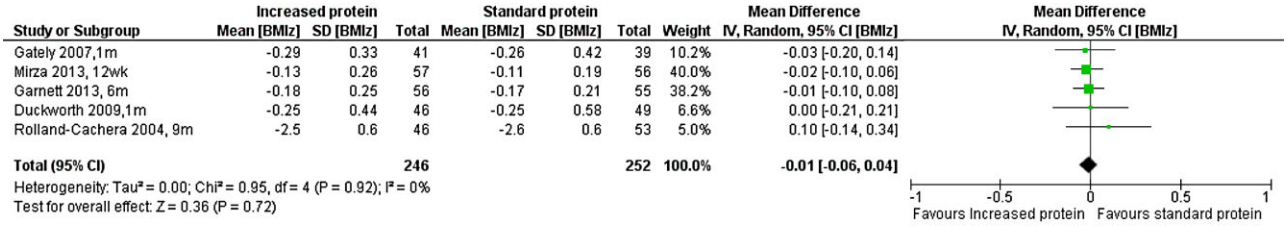
[a]Number represents standard deviation.

[b]Number represents standard error of the mean.

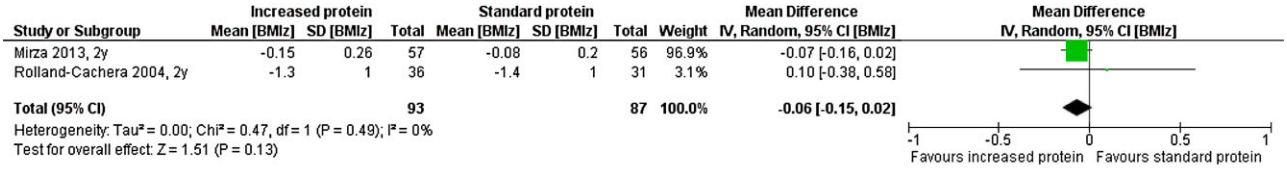
[c]Number represents 95% confidence interval.



A. Outcome: Change in BMI (kg/m^2) at the end of active intervention



B. Outcome: Change in BMI z-score at the end of active intervention



C. Outcome: Change in BMI z-score at the 2-year follow-up

Figure 4 **Meta-analysis of studies comparing an increased-protein diet to a standard-protein diet. A**. Outcome: Change in BMI (kg/m^2) at the end of active intervention. **B**. Outcome: Change in BMI z-score at the end of active intervention. **C**. Outcome: Change in BMI z-score at the 2-year follow-up.

Dietary interventions. Facilitators provided meals for participants in the studies conducted in a boarding school or camp,[35,43,44] resulting in a high level of control over intake (Table 1). In the other three studies, participants were free-living and were given prescriptive and structured meal plans that instructed participants on what to eat.[36,37,45] All six studies compared two isocaloric dietary intervention groups varying primarily in the energy contributions of protein and carbohydrate, as described in Table 1.

In five of the studies, a dietitian was reported to be involved with either menu preparation[43,44] or the support and review of participants.[35–37] Measures of compliance were not considered in two studies due to the high level of control facilitators had over intake during the intervention. Plate wastage was measured for all meals once per week in the study by Duckworth et al.,[44] which found very little wastage and no difference between diet groups. Measures of compliance in other studies included multiple 24-h recalls,[36,45] a 2-week food frequency questionnaire,[45] and a 4-day food diary.[37]

Impact of treatment on obesity. All studies reported on BMI, BMI z-score, and/or body composition (Table 3). Only one study reported waist:height ratio as an outcome measure.[36] There were improvements in weight-related outcomes in all studies, with no differences between diet groups at any time point (Figure 4A–C). The study by Rolland-Cachera et al.[35] achieved massive weight loss, with an average of 30.3 kg per participant during the 9-month intervention phase. However, there was significant weight regain during the maintenance period, with no significant difference in BMI z-score from baseline by the 2-year follow-up. Other studies achieved more modest weight-related improvements (range, 1.2–2.1 kg/m^2 decrease in BMI across studies). In one study, all participants achieved weight loss maintenance at the 2-year follow-up.[45]

Impact of treatment on metabolic parameters. Overall, there were no differences in any cardiometabolic risk factor between the diet groups at any time point in the included studies, Table 3. Studies by Rolland-Cachera et al.[35] and Baxter et al.[37] were the only studies not to report any cardiometabolic outcome measures. Blood lipids were measured in two studies: one reported reduced HDL-C, LDL-C, total cholesterol, and triglycerides after the active

intervention in a subsample of study participants when diet groups were combined[43]; another reported no intervention effect on blood lipids and no differences between diet groups. [36]

Two studies measured glucose, insulin, and/or insulin resistance.[36,45] One found no intervention effect on homeostatic model assessment of insulin resistance levels,[45] while the other found improved fasting glucose, fasting insulin, insulin sensitivity index, and insulin:glucose ratio in both diet groups.[36]

Four studies measured blood pressure.[36,43–45] All reported decreased systolic and/or diastolic blood pressure compared with baseline at all measured time points with no differences between diet groups.

Adverse events. No serious adverse events were reported. Some participants in the study by Garnett et al.[36] experienced expected side effects to the prescribed medication (metformin) including gastrointestinal side effects and migraines. Two participants also reported hair loss, possibly due to metformin use.[47] Of note, no side effects prevented further participation in the study.

Increased-fat compared to standard-fat diet

The literature search identified one US study of 26 African American girls aged 9–14 years, which examined the effect of two diets varying in fat and carbohydrate content (42% energy as carbohydrate, 40% fat, and 18% protein versus 55% carbohydrate, 27% fat, and 18% protein).[46] Participants were overweight or obese and baseline fasting glucose and insulin levels indicated that many were also insulin resistant. The 16-week study incorporated a 5-week eucaloric phase followed by an 11-week weight-loss phase. During both phases, participants were provided with all their food and were weighed twice per week to monitor compliance with the diet and to ensure weight maintenance/loss.

The study examined changes in total body fat and found significant improvements in each group but no between-group differences. Cardiometabolic outcomes were examined only at baseline and at completion of the eucaloric phase. The only significant difference was an increase in triglyceride levels in the standard-fat/high-carbohydrate group compared with the increased-fat/moderate-carbohydrate group at 5 weeks (end of eucaloric phase).

DISCUSSION

This systematic review is believed to be the first to evaluate the effect of varying dietary macronutrient content on BMI and cardiometabolic outcomes in overweight or obese children and adolescents. The literature search identified 14 studies that met all of the inclusion criteria. Seven studies compared a low-carbohydrate diet to a conventional low-fat approach (five incorporated ad libitum diets and two isocaloric diets), six compared an increased-protein diet to an isocaloric standard-protein diet and one compared an increased-fat to an isocaloric standard-fat diet. All studies reported improvements in weight-related outcomes irrespective of the macronutrient distribution. In studies measuring cardiometabolic outcomes, improvements in blood lipids, glucose and insulin homeostasis, and blood pressure were reported. The methodological quality of studies finding differences between diet groups was often limited; hence, these results should be interpreted with caution.

Unlike with adults, the appropriateness of weight loss in children is contentious due to possible physiological and psychological changes. The mean baseline BMI of participants in the studies included this review ranged from 28.1kg/m^2 to 40.1 kg/m^2, indicating that many subjects had a greater BMI than would be considered healthy for an adult (normal BMI range for adults, 18.5–24.9 kg/m^2). Considering the severity of comorbidities associated with this level of obesity in childhood, weight loss is indicated, as supported by a 2007 US Expert Committee, which recommends weight loss for obese children and adolescents over the age of 6 years.[48]

Low-carbohydrate compared to conventional low-fat diet

Overall, a significant beneficial effect of a low-carbohydrate diet on both the BMI and BMI z-score compared with a low-fat diet was observed immediately following the active intervention, Figure 3. However, the high degree of statistical and clinical heterogeneity ($I^2 = 0–35\%$), including pubertal and glycemic status, which may affect weight loss, indicates that these results should be interpreted with caution.

Four of seven included studies reported no differences between diet groups regarding the change in weight status.[32,34,41,42] Two of these studies[41,42] were more recent RCTs with larger sample sizes and better methodological quality than previous studies. Three studies reported a greater improvement in weight status in the low-carbohydrate group. One[38] instructed the low-carbohydrate group to consume a third less energy than the low-fat group, which explains the increased weight loss. Sondike et al.[39] found no difference between groups using intention-to-treat analysis but reported a greater reduction in BMI in the low-carbohydrate group when examining only those with good compliance. Despite the limitations of the included studies, a low-carbohydrate

diet may lead to greater short-term weight loss if indicated, for example, in severe obesity prior to surgery.

A low-carbohydrate diet may assist in facilitating improved body composition,[38] triglycerides,[39,40] and/or insulin levels[32,34]; however, results were reported inconsistently in the evaluated studies. The two studies reporting greater improvements in triglyceride and insulin levels[39,40] in the low-carbohydrate group also reported greater improvement in weight status. This suggests that improvement in weight status, in conjunction with factors such as behavior, exercise, and diet, including carbohydrate quality, play an important role in the reduction of cardiometabolic risk in the short term. No study included in this review reported follow-up past 2 years; therefore, it is not possible to assess the long-term impact that varying the macronutrient content of the diet has on cardiometabolic risk.

Adult systematic reviews report an association between high-protein diets (>1.05 g/kg/day) and preservation of lean body mass during weight loss.[19,49] This is in contrast to the included study by Krebs et al.,[40] which reported a greater reduction in BMI z-score and a greater loss of lean mass, determined by DEXA, in the low-carbohydrate diet group despite a prescribed protein intake of 2–2.5 g/kg/day. Only one study found a beneficial effect of a low-carbohydrate diet for body fat loss (measured by skinfolds),[38] while other studies found no difference in body fat loss or lean mass retention between diet groups.

The carbohydrate quality of the diet, including the glycemic index and glycemic load, is related to the risk of developing type 2 diabetes, cardiovascular disease, and some cancers[50] and is generally poor in children and adolescents.[51,52] Several reports included in this review describe the type of carbohydrate consumed by study subjects.[36,37,39,42,45] Two studies specifically examined diets varying in carbohydrate quality,[42,45] finding no effect on weight-related outcomes and no consistent effect on cardiometabolic outcomes. This is similar to a study examining obese young adults, which found no difference in weight loss among participants following either a low-glycemic-index diet or a low-fat diet.[53] That study reported increased weight loss when individuals with poorer insulin control followed a low-glycemic-index diet, proposing a diet-phenotype interaction. This needs to be examined further, especially in children and adolescents.

In line with other systematic reviews in children[54] and adults,[55] no diet adversely affected the cardiometabolic profile, suggesting the short-term safety of a low-carbohydrate intake. The long-term safety, however, is controversial, as reduced intake of certain foods, such as fiber-containing foods and fruits, may result in some nutritional requirements not being met.[56] Additionally, long-term compliance with a low-carbohydrate diet is difficult,[57] potentially impacting on quality of life due to limited food choices. However, it is important to note that no study included in this review suggested that the low-carbohydrate diet be followed long term.

Increased-protein compared to standard-protein diet

All six studies comparing isocaloric increased-protein and standard-protein diets[35–37,43–45] reported improved weight and cardiometabolic outcomes irrespective of diet group and irrespective of whether participants were free-living or in highly controlled environments. The protein content of the diet appears to have little effect when given isocalorically, supporting the importance of total energy intake for improved weight status in obese children and adolescents.

The isocaloric nature of study diets may have blunted the satiating effect of protein that is thought to contribute to a lower ad libitum total energy intake and consequent increase in weight loss, as reported in adult studies.[11,16,58,59] In contrast, the three studies in this review reporting subjective feelings of hunger and/or fullness (one examining ad libitum low-carbohydrate/low-fat intake and two examining increased-protein/standard-protein intake) showed no differences between the diet groups for changes in BMI or body composition.[40,43,44] Additionally, achieving dietary protein targets in studies of free-living children and adolescents is difficult[60] and may explain the lack of protein effect observed in studies examining a free-living cohort.

The standard-protein diets of the studies reviewed prescribed protein contents in the range of 15–20%, which can be considered low in protein within an energy restriction and may not meet the recommended dietary intake for protein of approximately 1 g/kg/day for children and adolescents aged 4–18 years.[61] Therefore, the increased-protein diets in the included studies might actually be considered to contain normal protein levels rather than increased levels. A recent systematic review[19] of 19 adult studies reported beneficial effects of an increased-protein diet (mean, 30.5 ± 2.4% of energy) compared to an isocaloric standard-protein diet (mean, 17.5 ± 1.5% of energy), including a 0.79 kg greater reduction in weight. Although the difference in weight loss was statistically significant, whether the result is clinically relevant is debatable.

Manipulating the fat content of the diet, as in the study by Casazza et al.,[46] also had no effect on weight-related outcomes, with both groups achieving a similar reduction in body fat. It is unlikely that one approach to macronutrient distribution of dietary intake is suitable for improving weight status in all individuals. Instead. it may be suitable to match patients to macronutrient

distributions depending on their specific needs, preferences, and cardiometabolic and genetic profile.[26,42,53,62] If individuals can be matched to a suitable diet it may increase their potential to achieve success; however, this requires further research.

CONCLUSION

The current evidence indicates that an improvement in weight status can be achieved in overweight or obese children and adolescents, irrespective of the macronutrient distribution of a reduced-energy diet. This suggests that the primary objective of dietary interventions should be to reduce total energy intake. Studies reporting a benefit of a low-carbohydrate diet for short-term weight loss had methodological limitations that restrict their generalizability. It may be appropriate to individually tailor the macronutrient distribution of the diet to target specific cardiometabolic risk factors, such as a low-carbohydrate diet for the treatment of insulin resistance; however, further research is required before recommendations can be made.

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REFERENCES

1. de Onis M, Blossner M, Borghi E. Global prevalence and trends of overweight and obesity among preschool children. Am J Clin Nutr. 2010;92:1257–1264.
2. Andersen LB, Harro M, Sardinha LB, et al. Physical activity and clustered cardiovascular risk in children: a cross-sectional study (The European Youth Heart Study). Lancet. 2006;368:299–304.
3. Whitlock EP, O'Connor EA, Williams SB, et al. Effectiveness of weight management interventions in children: a targeted systematic review for the USPSTF. Pediatrics. 2010;125:e396–e418.
4. Oude Luttikhuis H, Baur L, Jansen H, et al. Interventions for treating obesity in children. Cochrane Database Syst Rev. 2009;(1):CD001872.
5. Collins CE, Warren J, Neve M, et al. Measuring effectiveness of dietetic interventions in child obesity: a systematic review of randomized trials. Arch Pediatr Adolesc Med. 2006;160:906–922.
6. Collins CE, Warren JM, Neve M, et al. Systematic review of interventions in the management of overweight and obese children which include a dietary component. Int J Evid Based Healthc. 2007;5:2–53.
7. Ho M, Garnett SP, Baur L, et al. Effectiveness of lifestyle interventions in child obesity: systematic review with meta-analysis. Pediatric. 2012;130:e1647–e1671.
8. US Department of Agriculture and US Department of Health and Human Services. *Dietary Guidelines for Americans*, 7th ed. Washington, DC: Government Printing Office; 2010:8–19.
9. Food Standards Agency. *FSA Nutrient and Food Based Guidelines for UK Institutions*. London: Food Standards Agency; 2006.
10. National Health and Medical Research Council. *Australian Dietary Guidelines*. Canberra: National Health and Medical Research Council; 2013.
11. Westerterp-Plantenga MS, Nieuwenhuizen A, Tome D, et al. Dietary protein, weight loss, and weight maintenance. Annu Rev Nutr. 2009;29:21–41.
12. Layman DK. Protein quantity and quality at levels above the RDA improves adult weight loss. J Am Coll Nutr. 2004;23(6 Suppl):631S–636S.
13. Skov AR, Toubro S, Ronn B, et al. Randomized trial on protein vs carbohydrate in ad libitum fat reduced diet for the treatment of obesity. Int J Obes Relat Metab Disord. 1999;23:528–536.
14. Due A, Toubro S, Skov AR, et al. Effect of normal-fat diets, either medium or high in protein, on body weight in overweight subjects: a randomised 1-year trial. Int J Obes Relat Metab Disord. 2004;28:1283–1290.
15. Hession M, Rolland C, Kulkarni U, et al. Systematic review of randomized controlled trials of low-carbohydrate vs. low-fat/low-calorie diets in the management of obesity and its comorbidities. Obes Rev. 2009;10:36–50.
16. Westerterp-Plantenga MS, Lejeune MP, Nijs I, et al. High protein intake sustains weight maintenance after body weight loss in humans. Int J Obes Relat Metab Disord. 2004;28:57–64.
17. Lejeune MP, Kovacs EM, Westerterp-Plantenga MS. Additional protein intake limits weight regain after weight loss in humans. Br J Nutr. 2005;93:281–289.
18. Larsen TM, Dalskov SM, van Baak M, et al. Diets with high or low protein content and glycemic index for weight-loss maintenance. N Engl J Med. 2010;363:2102–2113.
19. Wycherley TP, Moran LJ, Clifton PM, et al. Effects of energy-restricted high-protein, low-fat compared with standard-protein, low-fat diets: a meta-analysis of randomized controlled trials. Am J Clin Nutr. 2012;96:1281–1298.
20. Nordmann AJ, Nordmann A, Briel M, et al. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: a meta-analysis of randomized controlled trials. Arch Intern Med. 2006;166:285–293.
21. Nordmann AJ, Suter-Zimmermann K, Bucher HC, et al. Meta-analysis comparing Mediterranean to low-fat diets for modification of cardiovascular risk factors. Am J Med. 2011;124:841–851 e2.
22. Gogebakan O, Kohl A, Osterhoff MA, et al. Effects of weight loss and long-term weight maintenance with diets varying in protein and glycemic index on cardiovascular risk factors: the diet, obesity, and genes (DiOGenes) study: a randomized, controlled trial. Circulation. 2011;124:2829–2838.
23. Westerterp-Plantenga MS, Lemmens SG, Westerterp KR. Dietary protein – its role in satiety, energetics, weight loss and health. Br J Nutr. 2012;108(Suppl 2):S105–S112.
24. Dietitians Association of Australia. *DAA Best Practice Guidelines for the Treatment of Overweight and Obesity in Adults: Report to Inform the 2011 Revision of the 2005 Guidelines*. Dietitians Association of Australia. 25 January 2012; Available at: http://daa.asn.au/wp-content/uploads/2011/03/FINAL-DAA-obesity-guidelines-report-25th-January-2011-2.pdf. Accessed June 26, 2013.
25. Sacks FM, Bray GA, Carey VJ, et al. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. N Engl J Med. 2009;360:859–873.
26. Shai I, Schwarzfuchs D, Henkin Y, et al. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. N Engl J Med. 2008;359:229–241.
27. Foster GD, Wyatt HR, Hill JO, et al. Weight and metabolic outcomes after 2 years on a low-carbohydrate versus low-fat diet: a randomized trial. Ann Intern Med. 2010;153:147–157.
28. Ho M, Garnett SP, Baur LA, et al. Impact of dietary and exercise interventions on weight change and metabolic outcomes in obese children and adolescents: a systematic review and meta-analysis of randomized trials. JAMA Pediatr. 2013;167:759–768.
29. Wilfley DE, Tibbs TL, Van Buren DJ, et al. Lifestyle interventions in the treatment of childhood overweight: a meta-analytic review of randomized controlled trials. Health Psychol. 2007;26:521–532.
30. McGovern L, Johnson JN, Paulo R, et al. Treatment of pediatric obesity: a systematic review and meta-analysis of randomized trials. J Clin Endocrinol Metab. 2008;93:4600–4605.
31. Higgins JPT, Green D. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.1.0 (updated March 2011) ed: The Cochrane Collaboration, 2011. Available at: www.cochrane-handbook.org. Accessed August 18, 2013.
32. Demol S, Yackobovitch-Gavan M, Shalitin S, et al. Low-carbohydrate (low & high-fat) versus high-carbohydrate low-fat diets in the treatment of obesity in adolescents. Acta Paediatr. 2009;98:346–351.

33. Yackobovitch-Gavan M, Nagelberg N, Demol S, et al. Influence of weight-loss diets with different macronutrient compositions on health-related quality of life in obese youth. Appetite. 2008;51:697–703.
34. Pena L, Pena M, Gonzalez J, et al. A comparative study of two diets in the treatment of primary exogenous obesity in children. Acta Paediatr Acad Sci Hung. 1979;20:99–103.
35. Rolland-Cachera MF, Thibault H, Souberbielle JC, et al. Massive obesity in adolescents: dietary interventions and behaviours associated with weight regain at 2 y follow-up. Int J Obes Relat Metab Disord. 2004;28:514–519.
36. Garnett SP, Gow M, Ho M, et al. Optimal macronutrient content of the diet for adolescents with prediabetes; RESIST a randomised control trial. J Clin Endocrinol Metab. 2013;98:2116–2125.
37. Baxter KA, Ware RS, Batch JA, et al. Predicting success: factors associated with weight change in obese youth undertaking a weight management program. Obes Res Clin Pract. 2013;7:e147–e154.
38. Figueroa-Colon R, von Almen TK, Franklin FA, et al. Comparison of two hypocaloric diets in obese children. Am J Dis Child. 1993;147:160–166.
39. Sondike SB, Copperman N, Jacobson MS. Effects of a low-carbohydrate diet on weight loss and cardiovascular risk factor in overweight adolescents. J Pediatr. 2003;142:253–258.
40. Krebs NF, Gao D, Gralla J, et al. Efficacy and safety of a high protein, low carbohydrate diet for weight loss in severely obese adolescents. J Pediatr. 2010;157:252–258.
41. Partsalaki I, Karvela A, Spiliotis BE. Metabolic impact of a ketogenic diet compared to a hypocaloric diet in obese children and adolescents. J Pediatr Endocrinol. 2012;25:697–704.
42. Kirk S, Brehm B, Saelens BE, et al. Role of carbohydrate modification in weight management among obese children: a randomized clinical trial. J Pediatr. 2012;161:320–327.
43. Gately PJ, King NA, Greatwood HC, et al. Does a high-protein diet improve weight loss in overweight and obese children? Obesity. 2007;15:1527–1534.
44. Duckworth LC, Gately PJ, Radley D, et al. RCT of a high-protein diet on hunger motivation and weight-loss in obese children: an extension and replication. Obesity. 2009;17:1808–1810.
45. Mirza NM, Palmer MG, Sinclair KB, et al. Effects of a low glycemic load or a low-fat dietary intervention on body weight in obese Hispanic American children and adolescents: a randomized controlled trial. Am J Clin Nutr. 2013;97:276–285.
46. Casazza K, Cardel M, Dulin-Keita A, et al. Reduced carbohydrate diet to improve metabolic outcomes and decrease adiposity in obese peripubertal African American girls. J Pediatr Gastroenterol Nutr. 2012;54:336–342.
47. Palomba S, Falbo A, Zullo F, et al. Evidence-based and potential benefits of metformin in the polycystic ovary syndrome: a comprehensive review. Endocr Rev. 2009;30:1–50.
48. Barlow SE. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. Pediatrics. 2007;120(Suppl 4):S164–S192.
49. Krieger JW, Sitren HS, Daniels MJ, et al. Effects of variation in protein and carbohydrate intake on body mass and composition during energy restriction: a meta-regression. Am J Clin Nutr. 2006;83:260–274.
50. Brand-Miller J, Hayne S, Petocz P, et al. Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials. Diabetes Care. 2003;26:2261–2267.
51. Somerset SM. Refined sugar intake in Australian children. Public Health Nutr. 2003;6:809–813.
52. Burgess-Champoux T, Marquart L, Vickers Z, et al. Perceptions of children, parents, and teachers regarding whole-grain foods, and implications for a school-based intervention. J Nutr Educ Behav. 2006;38:230–237.
53. Ebbeling CB, Leidig MM, Feldman HA, et al. Effects of a low-glycemic load vs low-fat diet in obese young adults: a randomized trial. JAMA. 2007;297:2092–2102.
54. Kirk JK, Graves DE, Craven TE, et al. Restricted-carbohydrate diets in patients with type 2 diabetes: a meta-analysis. J Am Diet Assoc. 2008;108:91–100.
55. Gibson LJ, Peto J, Warren JM, et al. Lack of evidence on diets for obesity for children: a systematic review. Int J Epidemiol. 2006;35:1544–1552.
56. Meckling KA, O'Sullivan C, Saari D. Comparison of a low-fat diet to a low-carbohydrate diet on weight loss, body composition, and risk factors for diabetes and cardiovascular disease in free-living, overweight men and women. J Clin Endocrinol Metab. 2004;89:2717–2723.
57. Brinkworth GD, Noakes M, Keogh JB, et al. Long-term effects of a high-protein, low-carbohydrate diet on weight control and cardiovascular risk markers in obese hyperinsulinemic subjects. Int J Obes Relat Metab Disord. 2004;28:661–670.
58. Paddon-Jones D, Westman E, Mattes RD, et al. Protein, weight management, and satiety. Am J Clin Nutr. 2008;87(Suppl):1558S–1561S.
59. Westerterp-Plantenga MS, Lejeune MP. Protein intake and body-weight regulation. Appetite. 2005;45:187–190.
60. Papadaki A, Linardakis M, Larsen TM, et al. The effect of protein and glycemic index on children's body composition: the DiOGenes randomized study. Pediatrics. 2010;126:E1143–E1152.
61. Australian National Health and Medical Research Council and New Zealand Ministry of Health. *Nutrient Reference Values for Australia and New Zealand Including Recommended Dietary Intakes*. 2006. Available at: https://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/n35.pdf. Accessed July 10, 2013.
62. Klein S. Clinical trial experience with fat-restricted vs. carbohydrate-restricted weight-loss diets. Obes Res. 2004;12(Suppl 2):141S–144S.