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REVIEW

Carbohydrate intake and obesity

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The prevalence of obesity has increased rapidly worldwide and the importance of considering the role of diet in the prevention and treatment of obesity is widely acknowledged. This paper reviews data on the effects of dietary carbohydrates on body fatness. Does the composition of the diet as related to carbohydrates affect the likelihood of passive over-consumption and long-term weight change? In addition, methodological limitations of both observational and experimental studies of dietary composition and body weight are discussed. Carbohydrates are among the macronutrients that provide energy and can thus contribute to excess energy intake and subsequent weight gain. There is no clear evidence that altering the proportion of total carbohydrate in the diet is an important determinant of energy intake. However, there is evidence that sugar-sweetened beverages do not induce satiety to the same extent as solid forms of carbohydrate, and that increases in sugar-sweetened soft drink consumption are associated with weight gain. Findings from studies on the effect of the dietary glycemic index on body weight have not been consistent. Dietary fiber is associated with a lesser degree of weight gain in observational studies. Although it is difficult to establish with certainty that fiber rather than other dietary attributes are responsible, whole-grain cereals, vegetables, legumes and fruits seem to be the most appropriate sources of dietary carbohydrate.
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Keywords: obesity; diet; carbohydrate; fiber; sugar; glycemic index

General introduction

Background

The prevalence of overweight and obesity has increased rapidly worldwide during recent decades, acquiring epidemic proportions in children and adults and in industrialized as well as transitional and developing countries (Popkin and Gordon-Larsen, 2004; Ogden *et al*., 2006). Excess adiposity increases risk of type 2 diabetes, arthritis, sleep apnea, hypertension, dyslipidemia, cardiovascular diseases, various types of cancer and premature death (Willett *et al*., 1999). Therefore, the importance of prevention and treatment of obesity is widely acknowledged. Changes in energy storage as body fat are affected by the balance of energy intake and energy expenditure, making diet and physical activity obvious targets for interventions. Effects of dietary composition on both energy intake and energy expenditure (dietary induced thermogenesis and resting energy metabolism) are plausible, based on results from animal experiments and metabolic studies in humans (Poppitt and Prentice, 1996; Ludwig, 2002; Bray *et al*., 2004a, b; Halton and Hu, 2004; Slavin, 2005). Although substantial short-term weight loss can be achieved by many people, successful long-term maintenance of weight loss is much more difficult and compensatory physiological processes appear to stimulate weight regain (Hirsch *et al*., 1998). Effects on body weight found in short-term metabolic studies can therefore not be readily extrapolated to long-term effects. This overview will present evidence for the effects of dietary composition related to carbohydrates on body fatness. Dietary factors that will be discussed include the proportion of total carbohydrates in the diet, free-sugars, sugar-sweetened beverages, the dietary glycemic index (GI) and dietary fiber. Studies have been identified through systematic and narrative reviews on these topics supplemented with searches in MEDLINE (PubMed) until July 2007. The emphasis is on longer-term studies, but shorter-term studies are also discussed depending on the availability of data for different exposures.

Methodological considerations for studies relating diet to body weight

Methodological limitations have to be considered in the interpretation of results on macronutrient composition in

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relation to weight change or the incidence of obesity. We will discuss these methodological limitations separately for observational and experimental studies.

Observational studies. In these studies, individuals typically report their food intakes by interviews or questionnaires, and the obtained estimates are related to their body mass index (BMI) or change in body weight. There are several methodological issues that make results from observational studies of diet and body weight difficult to interpret. First, the possibility of an effect of perceived body weight or changes in body weight on dietary habits ('reverse causation') should be considered. In contrast to various other health outcomes, people tend to be highly aware of their body weight and changes therein. In addition, many people hold strong beliefs about the relation between the composition of the diet and body weight and have control over two of the main determinants of body weight: energy intake and energy expenditure through physical activity. Cross-sectional studies where diet and measures of obesity are assessed simultaneously are therefore difficult to interpret: the perception that their body weight is high or increasing may lead persons to change their dietary habits (for example, dieting). For this reason, prospective observational studies relating dietary intakes to changes in body weight would be preferable. However, because changes in energy balance are likely to almost directly translate into changes in body weight, it seems biologically most relevant to study changes in dietary intakes in relation to changes in body weight over the same period. Because the exposure is not assessed before the outcome, such an analysis is not truly prospective and associations may still reflect an effect of perceived changes in body weight on changes in dietary habits over the same period.

Second, selective underreporting of dietary intakes can be correlated with the degree of overweight (Heitmann and Lissner, 1995; Heerstrass *et al*., 1998). There are indications that intakes of carbohydrates and fat are more subject to underreporting than intakes of protein and this can bias results of studies of macronutrient composition and body weight.

Third, dietary intakes and reporting thereof can be correlated to many other characteristics such as age, sex, socioeconomic status and other health-related habits that may affect energy balance (Braam *et al*., 1998). These characteristics can confound the association between dietary intakes and body weight. For example, individuals who are able to adhere to a generally recommended diet for weight management (for example, a low-fat diet) are also more likely to be able to adhere to limited total energy intake. Also, associations between (changes in) dietary intakes and energy balance have to be interpreted in the context of (changes in) energy expenditure. The latter is notoriously difficult to assess and is also subject to reporting bias. These methodological issues complicate the interpretation of data on macronutrient intakes and changes therein in relation to adiposity in observational studies.

Experimental studies. In evidence-based medicine, a stronger weight is generally given to long-term randomized experimental studies than to observational studies. In the last several decades, many disputes have been published on the interpretation of experimental studies that have manipulated macronutrient composition of diets and evaluated changes in body weight. The same data can be interpreted in different ways. Some authors have argued that an increasing proportion of energy coming from fat leads to greater weight gain (Bray *et al*., 2004b), whereas others have concluded that the proportion of energy from fat does not substantially influence body weight (Willett, 2002). An important issue here is that the outcomes of experimental studies seem to be dependent on the choice of subjects (for example, overweight versus normal weight subjects), the duration of the experiment (short-term trials of days or weeks versus trials that last several years) and the choice of foods that have been used to manipulate macronutrient composition. With respect to the latter issue, a low-fat, high-carbohydrate diet can be a diet consisting mainly of highly refined grains and products with added sugar, or a diet that is close to being a traditional vegetarian diet (that is, with plenty of whole grains, legumes, fruits and vegetables). In addition, the effect of macronutrients on satiety and energy expenditure may depend on the way diets are administered. Energy intake is the outcome of the portion size $\times$ energy density $\times$ frequency of consumption, and all the three factors can be altered experimentally in relation to macronutrient composition. Furthermore, experimental studies in humans rely on the degree of successful (preferably double blinded) randomization and on the compliance of subjects with dietary regimens. Because both issues are problematic for long-term trials of macronutrient intakes and weight change, the strength of the evidence provided by randomized controlled trials can be limited. Finally, experimental studies can be performed by changing macronutrient intake with fixed or *ad libitum* energy intakes and only the latter will provide us with insights that are directly relevant for public health.

Effects of dietary intakes in the context of weight management in obese persons may be different from the effects on prevention of weight gain in leaner persons. The transition from normal weight to obesity can result in changes in the levels of hormones such as insulin, leptin and adiponectin, which may alter relative substrate oxidation (fat versus carbohydrates) and appetite control (Blaak, 2004; Schwartz and Porte, 2005). In addition, the obese state alters basal and 24-h energy requirements as well as the sensitivity to various hormones such as insulin and leptin. One should therefore be cautious in the extrapolation of findings from experimental studies on macronutrient composition and weight loss in obese persons, to the role of macronutrients in the prevention of weight gain.

Total carbohydrate intake

Introduction

Weight gain is the result of higher energy intake than energy expenditure. This is also known as a positive energy balance. The total amount of energy (expressed in units of kilocalories or kilojoules per day) ingested by food and drinks come from four major nutrients (macronutrients).

Macronutrient	*kJ/g*	*kcal/g*
Fat	37	9
Alcohol	29	7
Protein	17	4
Carbohydrate	16	4

As shown in the table above, fat contains more energy per gram than carbohydrates. Carbohydrates, however, also provide energy and therefore contribute to the total energy intake per day and thus potentially to a positive energy balance. One of the most controversial questions in human nutrition in recent decades has been whether it matters for energy balance what the relative contribution of macronutrients is to the total energy intake. Potentially, there could be the differences because of variations in effects on appetite and satiety or in effects on oxidation and energy expenditure for different macronutrients. Specifically, it has been suggested that a higher proportion of fat in the diet can lead to weight gain through excess energy intake, because it is less satiating than the same amount of energy from carbohydrates (Bray *et al.*, 2004b). Others have suggested that proteins are particularly satiating (Halton and Hu, 2004). The answer to this question is important because if energy intake in the form of one macronutrient is more likely to lead to a positive energy balance than energy intake from other macronutrients, this would provide the basis to emphasize the reduction of the intake of the former macronutrient in recommendations for prevention of weight gain or for achieving weight loss in overweight persons. Before discussing evidence on the relation between carbohydrate content of the diet and body weight, we will discuss research on energy density, because it is frequently considered to be an important mediator of effects of dietary composition on energy balance.

Energy density

Carbohydrates and energy density. The energy density is the amount of energy per unit of weight of foods, meals or diets (Prentice and Jebb, 2003; Stubbs and Whybrow, 2004). Carbohydrate provides less energy per gram than fat and is thus less energy dense. However, few foods only contain macronutrients, and the fiber and particularly the water content (or conversely, the dryness) has a major effect on the energy density of foods (Drewnowski *et al.*, 2004). As a result, foods with a high energy percentage of carbohydrates can range from a low (for example, raw vegetables and fruits) to a high (for example, sugary candy) energy density (Drewnowski *et al.*, 2004). Figure 1 shows the energy density of commonly used foods, illustrating that a dry high-carbohydrate food such as pretzels can have similar energy density as high-fat foods such as cheese (Klein *et al.*, 2002). The carbohydrate content of diets tend to have a modest inverse association with the energy density of diets, whereas a higher fat content is generally associated with a higher energy density of diets (Stookey, 2001; Drewnowski *et al.*, 2004). However, whether a diet with a moderately high energy percentage of fat has a high or low energy density depends to a large extent on the amount of fruits and vegetables consumed (Ledikwe *et al.*, 2006). Because of their high water content, beverages generally have a lower energy density than solid foods. However, in the interpretation of the energy density of diets and foods it seems appropriate to consider foods and beverages separately given indications that energy intake from beverages is regulated differently (Mattes, 1996; Rolls *et al.*, 1999).

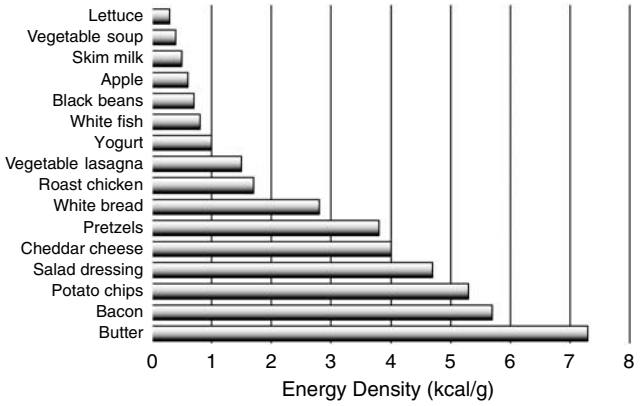

Figure 1 Energy density of selected commonly used foods. Reprinted from Klein *et al.* (2002) copyright 2002, with permission from Elsevier (figure provided courtesy of Liane Roe).

Short-term studies of energy density. Laboratory studies testing covertly manipulated foods for a few days or less found that under these conditions, the weight or volume of foods is the major determinant of satiation and satiety with persons consuming a relatively constant weight of food regardless of energy density (Poppitt and Prentice, 1996; Stubbs and Whybrow, 2004). Results from intervention studies lasting up to 2 weeks suggest that the lower satiety and satiation for fat as compared with carbohydrate intake (per unit of energy) can be explained by the lower energy density of carbohydrate (Poppitt and Prentice, 1996). A randomized cross-over study in six men using covert manipulation of a mixed diet, tested effects of foods of three levels of energy density (low, 373 kJ/100 g; medium, 549 kJ/100 g; high, 737 kJ/100 g), with virtually identical macronutrient composition for 14 days each (Stubbs *et al.*, 1998). Participants

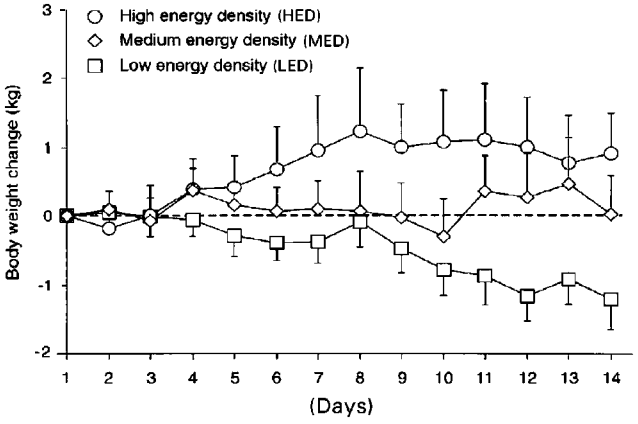

Figure 2 Mean (±standard error) change in body weight during three 14-day periods in which foods of different energy densities were provided. Reprinted by permission from Macmillan Publishers Ltd: International Journal of Obesity, (Stubbs *et al.*, 1998) copyright 1998.

compensated for the energy density of diets (that is, consuming a lower weight of foods with higher energy density), but this compensation was incomplete resulting in statistically significant differences in changes in body weight: −1.20 kg for low, +0.02 kg for medium and +0.95 kg for high energy density (Figure 2). In a cross-over trial in 13 women, a contrast in the energy density of diets was obtained by offering participants foods that contained 35–40 energy percent as fat (intervention diet) or 20–25 energy percent as fat (control diet) (Kendall *et al.*, 1991). A statistically significant 2.5 kg greater weight loss was found for the low-fat diet in the first cross-over period, but in the second cross-over period only a non-significant 0.4 kg difference was found. Furthermore, comparison of energy intakes for the intervention and control diet indicated that over time, participants compensated better for the higher energy density of the intervention diet. These observations suggest that it is uncertain whether the effect on weight change can be extrapolated to long-term effects on weight. Also, compensation would probably have been more complete if participants would have been able to change the type in addition to the amount of food eaten, because there is evidence that people compensate by choosing lower energy density foods after consumption of higher energy density foods (Poppitt and Prentice, 1996). In addition, when foods differ in taste, texture and appearance, instead of being covertly manipulated, as in many of the short-term trials (Stubbs *et al.*, 1998), physiological consequences of foods can be paired to these characteristics, resulting in learning effects and more complete compensation for energy density (Stubbs and Whybrow, 2004; Yeomans *et al.*, 2005). On the longer-term, people appear to acquire a greater degree of sensory-specific satiety for foods of a higher energy density based on their post-ingestive effects (Stubbs and Whybrow, 2004). Compensation for high energy density through learning effects may, however, be less effective in an environment with a wide availability of novel unfamiliar foods (Stubbs and Whybrow, 2004) or in combination with large portion sizes (Ello-Martin *et al.*, 2005). The considerations stated above and the difference in effects on body weight that tend to be found for long-term as compared with short-term interventions in general warrant caution with regard to the extrapolation of short-term effects of energy density in laboratory studies to long-term consequences for body weight.

Longer-term studies of energy density and weight change. Few longer-term studies have directly examined the association between energy density and body weight. Results from cross-sectional studies of energy density of the diet and adiposity have been inconsistent (Drewnowski *et al.*, 2004) and prospective observational data are sparse. The association between energy density and weight change was examined in a cohort of middle-aged Danish men and women (Iqbal *et al.*, 2006). In the overall cohort, energy density at baseline was not substantially associated with 5-year weight gain. In women, energy density was positively associated with 5-year weight gain among the obese and inversely associated with weight gain in normal-weight women, whereas no significant interaction with baseline weight was observed among men. In a 1-year trial, 200 overweight and obese participants were randomized to receive low-energy density soups or high-energy density snacks (Rolls *et al.*, 2005). All participants received instructions from dietitians to follow an exchange-based energy restricted diet. Weight loss was 8.1 kg for the control group without provided foods, 7.2 kg for the two-soup per day group, 6.1 kg for the one-soup per day group and 4.8 kg for the two-snack per day group. Interpretation of these results is not straightforward, because the greatest weight loss was achieved in the control group and because the smaller weight loss for the snack group may have related to characteristics other than energy density such as detrimental effects of snacking in a non-hungry state (Rolls *et al.*, 2005). Further long-term studies of energy density and body weight are needed.

Weight loss trials comparing diets of different carbohydrate contents

Below, studies on the effects of weight-loss diets with variable proportions of carbohydrate on body weight are reviewed. This includes studies comparing energy-restricted diets with low and high carbohydrate contents, very-low-carbohydrate diets with low-fat energy-restricted diets, high-protein and high-carbohydrate diets, low-fat and energy-restricted diets and low-fat and control diets. Although all these diets may affect body weight through reductions of energy intake, 'energy-restricted' refers to explicit instructions to participants about energy restriction.

Energy-restricted diets: high versus low carbohydrate. In trials with strictly controlled energy intakes, macronutrient

composition of the diet did not substantially affect body weight or fat mass. Golay *et al*. (1996) compared the effects of diets containing 4.2 MJ per day that contained 45% (26% fat) or 15% (53% fat) of energy as carbohydrates in 43 obese persons. After a 6-week hospital stay during which all foods were provided, loss of body weight and fat mass did not differ between the two diets. However, the important question remains whether a specific macronutrient composition of the diet can facilitate reduction of energy intake under realistic *ad libitum* conditions. Table 1 shows the characteristics and results of randomized trials that compared diets that had the same explicit energy intake target, but differed in carbohydrate content (Baron *et al*., 1986; Pascale *et al*., 1995; Lean *et al*., 1997; McManus *et al*., 2001). Although dietary advice included a specific target for energy intake, the long duration of these studies and 'free living' conditions precluded strict control of the energy intake of the participants. Therefore, it is of interest what carbohydrate composition of the diet best facilitated participants to adhere to the advice to restrict energy intakes and to lose weight as a result. In the study by Baron *et al*. (1986), no difference in weight loss between the high- and the low-carbohydrate diets was observed. However, the limited 3-month duration of the intervention probably reduced the contrast in dietary composition at 12 months. The authors reported that weight loss differed much more by weight loss club than by macronutrient composition of the diet. Pascale *et al*. (1995) compared an energy-restricted diet with the recording of fat intake with an energy-restricted diet with less emphasis on fat. The low-fat dietary advice resulted in a greater weight loss in persons with type 2 diabetes, but not in persons with only a family history of diabetes. Lean *et al*. (1997) compared two diets with a 23 energy percent difference in targets for the carbohydrate content of the diet. No difference in weight loss between the high- and low-carbohydrate diet was observed after 6 months. In a subgroup of postmenopausal women who were followed for 12 months, the low-carbohydrate diet was associated with greater weight loss than the low-fat diet. The 'moderate-fat' diet in the trial by McManus *et al*. (2001) was not particularly low in carbohydrates, but was more liberal with regard to unsaturated fat intake than conventional low-fat diets, and included nuts, avocados and olive oil. The greater weight loss and substantially lower drop-out for the 'moderate-fat' diet as compared with the low-fat diet suggest that this more liberal approach may be beneficial for long-term adherence to diets aimed at weight loss. In summary, in trials where participants were explicitly instructed to restrict total energy intake, advice to consume a low-fat, high-carbohydrate diet did not consistently lead to more or less weight loss than advice to consume a lower-carbohydrate diet.

Very low-carbohydrate diet versus low-fat, energy-restricted diet. Table 2 shows the characteristics and results of five 12-month weight loss trials that randomized participants to very-low carbohydrate 'Atkins' type diets or low-fat diets (Foster *et al*., 2003; Samaha *et al*., 2003; Stern *et al*., 2004; Dansinger *et al*., 2005; McAuley *et al*., 2005, 2006; Gardner *et al*., 2007). In four of the five studies, a substantially larger weight loss was found after 6 months of the low-carbohydrate diet as compared with the low-fat diet (Foster *et al*., 2003; Samaha *et al*., 2003; McAuley *et al*., 2005; Gardner *et al*., 2007). This agrees with findings from two other (6 month) trials (Brehm *et al*., 2003; Yancy *et al*., 2004), and results from a recent meta-analysis that reported a pooled 3.3 kg (95% confidence intervals 1.4, 5.3) greater weight loss for the low-carbohydrate as compared with the low-fat diet after 6 months (Nordmann *et al*., 2006). However, during an additional 6 months, regain of weight diminished the differences between the diets, resulting in lack of substantial differences in weight after 12 months (Table 2). This was also found in the trial with the most intensive intervention that continued monthly meetings until the 12-month measurements (Stern *et al*., 2004). The ketogenic effect of very-low carbohydrate diets has been suggested to facilitate weight loss though urinary excretion of ketones or suppression of appetite by circulating ketones. However, the amount of energy lost through urinary excretion of ketones is minimal (Astrup *et al*., 2004). Furthermore, Foster *et al*. (2003) did not observe an association between urinary ketones and weight loss. The simplicity of the diet, the restriction of the variety of food choices and possibly a greater satiating effect of protein seem more plausible explanations for the greater initial weight loss on very-low carbohydrate diets (Astrup *et al*., 2004). In summary, in overweight individuals in the US and New Zealand, instructions to consume a very-low carbohydrate diet generally led to greater weight loss during the first 6 months than instructions to consume low-fat diets, but due to subsequent regain of weight this may not result in a greater long-term weight loss.

High carbohydrate versus high protein. Effects of increasing the proportion of carbohydrates in the diet may depend on the macronutrient that is replaced: protein or fat. The very-low-carbohydrate diets discussed in the previous section also had a higher protein content than the low-fat diets: a 3–7 energy percent higher protein intake was reported at 6 months (Brehm *et al*., 2003; Samaha *et al*., 2003; Yancy *et al*., 2004; McAuley *et al*., 2005). Other trials however, have more specifically attempted to replace carbohydrates with protein. A Danish group compared the effects of two *ad libitum* reduced-fat (30 energy percent) diets: a diet high in carbohydrates and a diet high in protein (Skov *et al*., 1999). During the first 6 months, foods were supplied through a laboratory shop system, followed by 6 months of consultation with a dietitian once every 2 weeks. The energy percentage of protein in the high-protein diet (24.3% registered in the shop at 6 months; 21.2% reported at 12 months) was substantially higher (12.5% at 6 months, 7.3% at 12 months) than in the high-carbohydrate diet. Furthermore, regular measurement of 24-h urinary nitrogen excretion agreed with these differences in protein intake. After 6

Table 1 Long-term randomized intervention studies of hypocaloric diets: high carbohydrate (low fat) versus lower carbohydrate

Reference/country	*Participants*[a]	*Duration*	*Intervention*	*'High carbohydrate'*	*'Low carbohydrate'*	*Compliance*	*Results*
(Baron *et al.*, 1986) UK	M/F. High carb: $n=61$, age 40, BMI 28.5; low carb: $n=59$, age 40, BMI 39.5. An additional $n=8$ (high carb) and $n=7$ (low carb) were lost to follow-up and not included in the analysis	12 months	3 months: participation in weekly diet club meetings and written material. Target: 1000–1200 kcal per day	Fat <30 g per day	Carbohydrate <50 g per day	FFQ: higher fiber intake (18.4 vs 15.1 g per day), bread and potato intake for high-carb vs low-carb diet	High carb: -1.6 kg Low carb: -2.3 kg Difference: 0.7 kg (95% CI -1.2, 2.6)
(Pascale *et al.*, 1995) US	M/F Type 2 diabetes, age 57 ± 8, BMI 36.3 ± 4.7. Low fat: $n=15$; higher fat: $n=16$. An additional $n=7$ (low fat) and $n=6$ (higher fat) were lost to follow-up and not included in the analysis	12 months	16 weekly group sessions and meetings at 5, 6, 8 and 10 months. Target: 1000–1500 kcal per day (depending on baseline weight)	Target: 20 en% fat. Recording of both amount of calories and fat of foods used	Emphasis on low energy intake. Recording of calories of foods used. Fat <30 en% encouraged	Diet records (12 months): low-fat 26 en% fat, higher fat 34 en% fat	Low fat: -5.2 kg (s.d. 7.3) Higher fat: -1.0 kg (s.d. 3.9) ($P=0.06$)
	M/F family history of diabetes, age 43 ± 8, BMI 35.9 ± 4.7. Low fat: $n=16$; higher fat: $n=13$. An additional $n=7$ (Low fat) and $n=10$ (higher fat) were lost to follow-up and not included in the analysis					Diet records (12 months): low-fat 26 en% fat, higher fat 34 en% fat	Low fat: -3.1 kg (s.d. 8.9) Higher fat: -3.2 kg (s.d. 7.2)
(Lean *et al.*, 1997) UK	F. High carb: $n=42$, age 51 ± 14, BMI 32.3 ± 5.5. Low carb: $n=40$, age 50.1 ± 14, BMI 32.8 ± 5.1. An additional $n=15$ (high carb) and $n=13$ (low carb) lost to follow-up at 6 months not included in the analysis	6 months; 12 months follow-up for $n=46$	6 months: counseling by dietitian and written material. Target: 1200 kcal per day	Target: 58 en% carb, 21 en% fat, 21 en% protein	Target: 35 en% carb, 35 en% fat, 30 en% protein	Not assessed	6 months: High carb: -4.2 kg. Low carb: -5.4 kg ($P=0.22$). 12 months (subgroup): High carb: -3.0 kg Low carb: -6.5 kg ($P<0.05$)
(McManus *et al.*, 2001) US	M/F. Low fat: $n=30$, age 44 ± 10, BMI 33 ± 3. Moderate fat: $n=31$, age 44 ± 10, BMI 34 ± 5. In addition $n=21$ (high carb) and $n=19$ (low carb) lost to follow-up at 18 months and included in 'last value carried forward' intention to treat analysis	18 months	Weekly group sessions with dietitian for whole period. Target: 1200 (F) or 1500 kcal per day (M)	Target: 60–65 en% carb, 20 en% fat, 15–20 en% protein	Target: 45–50 en% carb, 35 en% fat, 15–20 en% protein. 'Moderate fat'	Attendance of sessions (20% for low-fat vs 54% for moderate fat, $P<0.01$). FFQ at 18 months: low-fat 50 en% carb, 35% fat; moderate-fat 47% carb and 35% fat	Low fat: $+1.1$ kg Moderate-fat: -2.5 kg ($P=0.005$)

Abbreviations: BMI, body mass index (kg/m^2); en%, energy percent; F, female; FFQ, food frequency questionnaire; M, male; s.d., standard deviation.
All trials had a parallel design.
None of the trials reported/conducted blinding of the assessors of outcomes or allocation concealment.
[a]Values are means$\pm$s.d.

Table 2 Randomized intervention studies comparing very low carbohydrate diet and low-fat energy-restricted diets: results after 6 and 12 months

Reference/ country	*Participants*	*Intervention*	*'Low-carb' diet*	*'Low-fat' diet*	*Follow-up*	*Compliance*	*Weight loss (kg)*		
							Low carb[a]	*Low fat*[a]	*Difference*
(Samaha *et al.*, 2003; Stern *et al.*, 2004) US	M/F. BMI $\geqslant 35$, 83% diabetes or metabolic syndrome. Low carb: $n=64$. Low-fat: $n=68$; lost to follow-up: $n=14$ at 6 months, $n=6$ at 12 months	Group counseling: weekly sessions for 4 weeks and 11 monthly session; written materials	Carbohydrate intake <30 g per day	Fat <30 energy% and 500 kcal per day energy deficit	6 months	24-h recall (energy %). Low carb: C 37, F 41, P 22[†]. Low-fat: C 51, F 33, P 16	−5.8 (8.6)	−1.9 (4.2)	$P=0.002$[b]
					12 months	24-h recall (g per day). Carbohydrate: low carb 120; low-fat 230	−5.1 (8.7)	−3.1 (8.4)	$P=0.20$[c]
(Foster *et al.*, 2003) US	M/F. Obese (mean BMI 34). Low carb: $n=33$. Low-fat: $n=30$; lost to follow-up: $n=21$ at 6 months, $n=26$ at 12 months	One consultation with dietitian; a book/manual	Carbohydrate <20 g per day for 2 weeks, followed by a gradual increase	Fat $\sim 25\%$, protein $\sim 15\%$, carbohydrate $\sim 60\%$ of energy. Energy restricted	6 months	Testing of urinary ketone concentrations. Significant difference between groups up to 12 weeks	−6.9 (6.4)	−3.1 (5.5)	$P=0.02$[d]
					12 months		−4.3 (6.6)	−2.5 (6.2)	$P=0.26$[d]
(Dansinger *et al.*, 2005) US	M/F. BMI 27–42 (mean 35) with metabolic risk factors. Low carb: $n=40$. Low-fat: $n=40$; lost to follow-up: $n=19$ for low carb and $n=20$ for low-fat	Advice during four group sessions in first 2 months; written materials and diet book	Carbohydrate <20 g per day with gradual increase to 50 g per day	Vegetarian 'Ornish' diet with 10 energy% fat	6 months	Diet records (g per day): low carb: C 190 g, F 81 g; low-fat: C 237 g, F 55 g	−3.2 (4.9)	−3.6 (6.7)	$P=0.76$[d]
					12 months	Diet records (g/d): low carb: C 190 g, F 81 g; low-fat: C 218 g, F 64 g	−2.1 (4.8)	−3.3 (7.3)	$P=0.40$[d]
(McAuley *et al.*, 2005, 2006) New Zealand	F. Insulin resistant, BMI >27. Low carb: $n=31$. Low-fat: $n=32$; lost to follow-up: $n=6$ at 6 months, $n=7$ at 12 months	Weekly counseling for 16 weeks; written materials	Carbohydrate <20 g per day for 2 weeks with gradual increase	Conventional high-fiber, low-fat, reduced sugar diet. No explicit energy-restriction	6 months	Diet records (energy %): low carb: C 26, F 47, P 24; low fat: C 45, F 28, P 21	−7.1	−4.7	$P<0.05$[c]
					12 months	Diet records (energy %): low carb: C 33, F 41, P 21; Low fat: C 45, F 29, P 22	−5.4	−4.4	$P>0.05$[c]

Table 2 *Continued*

Reference/ country	Participants	Intervention	'Low-carb' diet	'Low-fat' diet	Follow-up	Compliance	Weight loss (kg)		
							Low carb[a]	*Low fat*[a]	*Difference*
(Gardner *et al.*, 2007) US	F. Premenopausal (25–50 years), BMI 27–40. Low carb: $n=77$. Low fat $n=79$; lost to follow-up: $n=21$ at 6 months, $n=27$ at 12 months	Weekly counseling for 2 months; diet books	Carbohydrate $\leqslant$ 20 g per day for $\sim$2–3 months followed by $\leqslant$ 50 g per day	'LEARN' program: 55–60% carbohydrate and $<$10 energy% saturated fat, caloric restriction, exercise	6 months	24-h recalls (energy %): low carb: C 30, F 47, P 22; Low fat: C 48, F 31, P 18	~ -5.8	~ -3.1	$P<0.05$[d]
					12 months	24-h recalls (energy %): low carb: C 35, F 44, P 21; low-fat: C 47, F 33, P 19	-4.7 (-6.3, -3.1)	-2.2 (-3.6, -0.8)	$P>0.05$[d]

Abbreviations: BMI, body mass index (kg m^{-2}); C, carbohydrates; F, fat; F, female; M, male; P, protein.
All trials had a parallel design, allocation concealment was performed for all studies, and blinding of outcome assessors was not reported.
[a]Values are means (s.d. or 95% CI).
[b]Intention to treat: last value carried forward.
[c]Random coefficient analysis.
[d]Intention to treat: baseline value carried forward.

months, weight loss was 9.4 kg in the high-protein group and 5.9 kg in the high-carbohydrate group (difference 3.5 kg, $P=0.008$; Skov *et al.*, 1999). After 12 months, weight loss was 6.2 kg for the high-protein group and 4.3 kg for the high-carbohydrate group (difference 1.9 kg, $P>0.05$; Due *et al.*, 2004). Thus, despite a remaining substantial difference in protein intake, some weight was regained and it was unclear whether a greater long-term weight loss could be maintained for the high-protein protein group. The reduction in waist circumference remained statistically significantly greater after 12 months for the high-protein as compared with the high-carbohydrate group (Due *et al.*, 2004). An Australian intervention study also compared effects of a high-protein with a high-carbohydrate diet (McAuley *et al.*, 2005). At 6 months, the higher protein diet was associated with a 5 energy percent higher protein intake (26 versus 21%) and a statistically significant 2.2 kg greater weight loss (6.9 versus 4.7 kg). Regain of weight in the subsequent 6 months was 0.5 kg for the high-carbohydrate and 0.9 kg for the high-protein group (McAuley *et al.*, 2006). After 12 months, the energy percent of protein was identical for the two groups, whereas a non-statistically significant 2.3 kg lower body weight remained for the high-protein as compared with the high-carbohydrate group. In two intervention studies by Brinkworth and co-workers, a high-protein diet and a high-carbohydrate diet resulted in similar weight loss after 68 weeks, but the intervention only lasted for 16 weeks and the urinary urea/creatinine ratio indicated no difference in protein content after the intervention (Brinkworth *et al.*, 2004a, b). In summary, two trials suggest that exchanging protein for carbohydrates can facilitate weight loss over 6 months, but more research is needed to clarify whether this beneficial effect can be maintained after 12 or more months.

Low-fat (high carbohydrate) versus energy-restricted diet. Several long-term intervention studies compared dietary advice focused on reducing fat intake with dietary advice focused on restriction of total energy intake. These trials reported worse (Harvey-Berino, 1998), similar (Jeffery *et al.*, 1995; Dansinger *et al.*, 2005) and better (Toubro and Astrup, 1997) effects on body weight for the low-fat approach, as compared with the energy-restricted approach. These differences in the results probably reflect differences in the energy-restricted program (for example, a complicated color-coded system (Toubro and Astrup, 1997) versus a simpler method of calorie counting (Dansinger *et al.*, 2005)) rather than effects of differences in macronutrient composition of the diet.

Intervention studies of carbohydrate intake not primarily aimed at weight loss

Effect of dietary advice to consume a low-fat diet on body weight. The Women's Health Initiative Dietary Modification Trial tested the effect of advice to decrease fat intake and increase consumption of fruit, vegetables and grains on body weight for a mean follow-up of 7.5 years in 48 835

postmenopausal US women (Howard *et al.*, 2006). The intervention included 18 group sessions during the first 12 months, followed by four group sessions per year for the duration of the trial supplemented with individual sessions. The control group only received dietary educational materials. According to self-reported data from a food frequency questionnaire, the percentage of energy from fat decreased by 8.8%, the percentage of energy from carbohydrates increased by 8.2%, the number of servings of fruits and vegetables increased by 1.4 servings per day and fiber intake increased by 2.2 g per day in the intervention group, whereas no substantial changes were reported by the control group. Body weight decreased 1.9 kg after 1 year and 0.4 kg after an average of 7.5 years for the intervention as compared with the control group (both *P*-value 0.001). Trends in body weight for the intervention and control group were similar: an increase in women who were not overweight, little change in those who were moderately overweight and a decrease in those who were obese before the study (Figure 3). Weight loss was not an aim of this study and data on dietary change only relied on self-reports. However, the findings do not support a substantial long-term effect of an educational intervention aimed at reducing the proportion of fat (or increasing the proportion of carbohydrates) in the diet on body weight in US women. Even the small effect on body weight may reflect changes other than fat intake as a result of the more intensive dietary advice in the intervention as compared with the control group.

The results of earlier smaller randomized interventions of at least 12 months duration that tested advice to consume low-fat diets and were not aimed at weight loss showed a similar lack of substantial effects on body weight (Willett, 2002). A meta-analysis of intervention studies suggested a more substantial 3.2 kg greater weight loss as a result of an *ad libitum* low-fat diet as compared with the control group. (Astrup *et al.*, 2004) However, interpretation of the results is limited by the inclusion of shorter term (duration was 2–12 months) and non-randomized studies. Moreover, in most studies, only the low-fat intervention group received intensive dietary advice, making it unclear whether effects were due to changes in fat intake *per se* or other behavioral changes related to the greater awareness of diet. In summary, randomized intervention studies do not consistently show that educational efforts aimed at reducing the percentage of energy intake from fat (or increase the percentage of energy from carbohydrates) without additional efforts to reduce energy intakes have important long-term effects on body weight.

Effect of provision of reduced fat foods on body weight. In the double-blinded multicenter 'First Study' of National Diet-Heart Study, foods of variable fat contents were provided to approximately 1000 middle-aged US men (Anonymous, 1968). The participants were provided low-fat foods resulting in 29.7% of energy from fat (based on diet records), high-fat/high-polyunsaturated fat foods resulting in 34.4% of energy

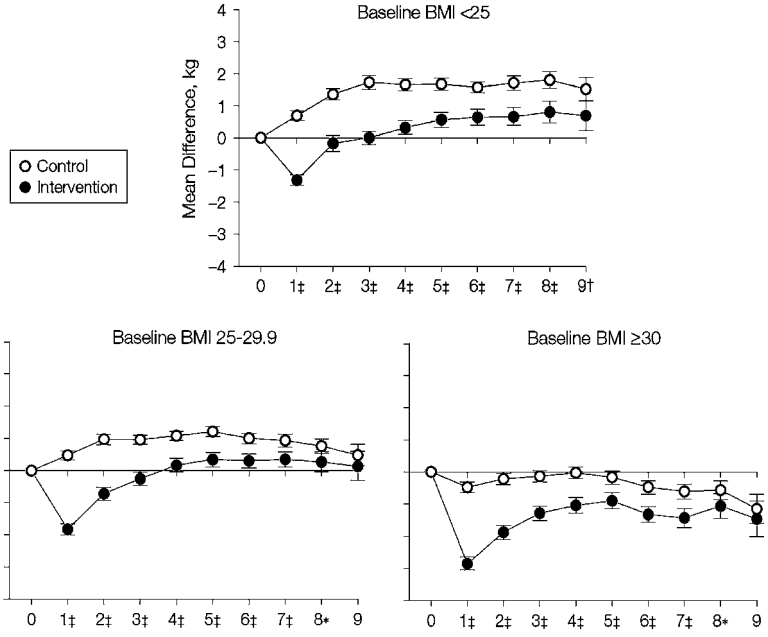

Figure 3 Effects of advice to consume a low-fat diet high in fruits and vegetables on body weight: differences (from baseline) in body weight by intervention group and BMI at screening in the Women's Health Initiative. Error bars indicate 95% confidence intervals. *$P \leqslant 0.05$ and > 0.01 †$P \leqslant 0.01$ and > 0.001 ‡$P \leqslant 0.001$ for the difference between the intervention and control group. Reprinted from Howard *et al.* (2006) copyright (2006), American Medical Association. All rights reserved. BMI, body mass index.

from fat or high-fat/low-polyunsaturated fat foods resulting in 34.9% of energy from fat. Over 44 weeks, men in all groups lost weight (2.3, 1.4 and 1.8 kg respectively), with a 0.5–0.9 kg greater weight loss for the low-fat group. In a randomized trial of 241 Dutch non-obese individuals with no intention to lose weight, free access was provided to ~45 different foods either in reduced fat or full fat version, covering between 30 and 40% of energy intake. The group that consumed the reduced-fat products had on average a 7 energy percent lower fat intake and a 0.7 kg (95% confidence interval 0.1, 1.4) decrease in body fat over 6 months as compared with those that consumed the full-fat products (Westerterp *et al*., 1996; Weststrate *et al*., 1998). In the randomized CARMEN trial (Carbohydrate Ratio Management in European National Diets), diets high in carbohydrates were compared with a control diet that had a macronutrient composition that was typical for each country (Saris *et al*., 2000). The intervention was *ad libitum* and consisted of providing foods through a laboratory shop system in 398 men and women with a BMI between 26 and 35 kg/m^2. Allocation concealment and blinding procedures were not described and no intention-to-treat analysis was conducted. According to diet records intake of fat, protein, and carbohydrates changed significantly by −8.7, +2.7 and +6.3 energy percent for the low-fat high-starch group relative to the control group. Weight loss over 6 months was 2.6 kg for the low-fat high-starch group as compared with the control group. This weight loss was substantially larger than for the National Diet-Heart-Study, possibly due to the greater contrast in fat intake, the higher protein intake for the high-starch diet relative to the control diet or to all the CARMEN participants being overweight. Furthermore, in the CARMEN study participants were not blinded and the high-starch diet required a substantial change and reconsideration of dietary habits, whereas the control diet was similar to the usual dietary intake.

In all trials discussed above, full-fat foods were replaced by reduced-fat versions of the foods. One could argue that the observed small effects of this product change on body weight may be worthwhile on a population level. However, exchange of reduced-fat foods for full-fat versions may reflect the effect of reducing the amount of energy per portion without substantially changing the participants' perception of the satiety value of the food. Thus, findings do not necessarily apply to exchanging carbohydrates for fat and replacement of full-calorie carbohydrate foods with reduced-calorie versions may have similar effects.

Observational studies of carbohydrate intake and body weight

Cohort studies of fat intake and long-term weight change. As reported in section 1.2, observational studies of dietary intakes and body weight are prone to various biases. People tend to hold particularly strong ideas about the effects of the proportion of fat or carbohydrate on body weight favoring for example commonly recommended low-fat diets or popular low-carbohydrate diets. A person's ability to adhere to the macronutrient composition of such a diet is likely to be associated with a person's ability to control total energy intake. Therefore, an association between the proportion of carbohydrates in the diet with lower weight or less weight gain may well be confounded by the ability to control energy intake. Other methodological issues include selective underreporting of fat intake that is related to weight and residual confounding by other dietary factors (Seidell, 1998). Results from prospective cohort studies that study the proportion of energy from fat in the diet (and thus indirectly the proportion of energy from carbohydrate in the content) have been inconsistent (Seidell, 1998). In addition to the aforementioned methodological limitations, differences in results may relate to differences in genetic susceptibility. In two cross-sectional studies, the association between fat intakes and adiposity differed by peroxisome proliferator-activated receptor-α Pro12Ala genotype (Memisoglu *et al*., 2003; Franks *et al*., 2004). This variant also modified the weight loss as result of a lifestyle intervention (Lindi *et al*., 2002), but not the response to an energy restricted high or low-fat diet (Sorensen *et al*., 2006).

Weight control registry. The National Weight Control Registry is a registry of persons in the US that maintained a weight loss of 13.6 kg or more for at least 1 year (Phelan *et al*., 2006). The majority of these successful weight losers consumed a low-fat, high-carbohydrate diet, but the average percentage of energy from carbohydrates had decreased from 56% in 1995 to 49% in 2003, and the proportion of persons on a low-carbohydrate diet (<90 g/d carbohydrate) increased from 5.9 to 17.1% during that period (Phelan *et al*., 2006). These results indicate that the diet associated with weight loss at a certain point in time is to some degree dependent on the types of diet that are generally believed to be beneficial for weight. Still, these registry data support the findings from intervention studies that substantial weight loss is possible over a wide range of macronutrient compositions of the diet.

Conclusions on the carbohydrate content of the diet

Findings from the dietary intervention studies discussed above suggest that similar weight loss can be achieved over the course of a year with diets of substantially different carbohydrate contents. Positive energy balance and weight gain can be achieved with a wide range of energy percentage of carbohydrates in the diet; thus, neither a diet with a high nor a low energy percentage of carbohydrates will necessarily protect a person from weight gain on the long term.

In trials in which dietary advice for weight loss was provided in overweight persons in the US and New Zealand, weight loss was greater after 6 months for low-carbohydrate diets as compared with low-fat diets, although this difference greatly attenuated after longer follow-up (Nordmann *et al*., 2006; Gardner *et al*., 2007). Interestingly, in the European CARMEN trial in which macronutrient intake was manipulated by providing foods through a laboratory shop system,

weight loss was greater after 6 months with a low-fat high-carbohydrate diet as compared with a higher fat control diet (Saris *et al*., 2000). There are several possible explanations for this difference in results. First, in the trials with dietary advice, protein intake was substantially higher for the low-carbohydrate relative to the low-fat diet, whereas the opposite was true for the CARMEN trial. The promising hypothesis that a higher protein content of the diet may contribute to weight management requires further research. Second, the nature of the foods included in the low-fat diet may have differed: in the CARMEN trial the low-fat diet included many reduced-calorie versions of otherwise similar full-fat foods, whereas diverse self-chosen high-carbohydrate foods may have been included in the low-fat diets in the trials with dietary advice. Third, the characteristics of the interventions unrelated to physiological effects of macronutrient composition may have played an important role. In the trials with dietary advice, the low-carbohydrate diet was probably the most novel, simple and restrictive diet, whereas in the CARMEN trial the lower carbohydrate diet was a control diet that required little change in food choice.

Long-term dietary and lifestyle interventions ($\geqslant$2 years) show that consumption of a relatively high-carbohydrate diet ($\sim$55% of energy) that includes high amounts of fiber-rich foods can be compatible with clinically relevant weight loss (Tuomilehto *et al*., 2001; Knowler *et al*., 2002; Esposito *et al*., 2004; Mayer-Davis *et al*., 2004). A Mediterranean-style moderate-fat diet with a lower carbohydrate content ($\sim$50% of energy) was also associated with substantial weight loss after 18 months (McManus *et al*., 2001). Taken together, the available data do not provide strong evidence that either increasing or decreasing the energy percentage of carbohydrate in the diet by itself has an important effect on body weight.

Free sugars

Introduction

Free sugars are defined as added sugars plus concentrated sugars in honey, syrups and fruit juices. Because glucose chains in starches can be rapidly broken down in the gastrointestinal tract, many starchy foods induce a more rapid increase of blood glucose concentrations than many foods high in free sugars (Foster-Powell *et al*., 2002). However, other characteristics of free sugars can be relevant for energy balance. Foods high in free sugars have been proposed to contribute to weight gain as compared with starchy foods because of lack of dietary fiber and high energy density (Poppitt and Prentice, 1996), higher palatability because they are sweeter (Raben *et al*., 1997), unique effects of fructose (Elliott *et al*., 2002) and because these are often consumed in the form of high-caloric liquids instead of solid foods (Mattes, 1996).

Micronutrient dilution

'Micronutrient dilution' refers to a reduction of the micronutrient content of the diet as a result of the displacement of micronutrient-rich foods by foods high in free sugars. Studies in children, adolescents and adults have reported that a high energy percentage of the diet as free sugars is associated with lower intakes of various micronutrients (Alexy *et al*., 2003; Charlton *et al*., 2005; Kranz *et al*., 2005). In addition, a high free-sugar content of the diet has been associated with lower intakes of fiber (Kranz *et al*., 2005) and fruit and vegetables (Charlton *et al*., 2005). Regular consumption of foods high in free sugars does not have to be associated with micronutrient deficiencies (Ruxton, 2003). However, given that the energy intake that is compatible with avoiding weight gain in modern societies with little occupational physical activity is limited, it should be considered that a high intake of energy as free sugars will generally make it more difficult to achieve optimal intakes of micronutrients, phytochemicals, fiber and fruit and vegetables.

Postprandial insulin secretion and body weight

The effect of postprandial insulin secretion on energy balance is controversial. On the one hand, it has been postulated that a high postprandial insulin response may lead to weight gain through various mechanisms. First, a high postprandial insulin response may rapidly lower blood glucose and free fatty acid concentrations, which might in turn induce the secretion of counter-regulatory hormones. These hormones may stimulate hunger and energy intake and may also lower resting energy expenditure through a proteolytic effect that reduces lean body mass over time (Ludwig, 2002; McMillan-Price and Brand-Miller, 2006). Second, it has been suggested that high postprandial insulin responses may reduce fat oxidation and increase fat synthesis and storage (McMillan-Price and Brand-Miller, 2006). However, hyperinsulinemia has been associated with reduced weight gain in several longitudinal studies (Valdez *et al*., 1994; Hoag *et al*., 1995; Schwartz *et al*., 1995), and the quantitative significance of the effect of higher insulin levels on *de novo* fatty acid synthesis in adipose tissue in humans has been questioned (Wolever, 2006).

On the other hand, it has been postulated that low postprandial insulin responses may lead to reduced satiety (Elliott *et al*., 2002). Lack of insulin response can lead to reduced leptin production by adipose tissue and both leptin and insulin can play a role in inducing satiety (de Graaf *et al*., 2004; Schwartz and Porte, 2005); however, in short-term experiments, the effect of insulin infusion on appetite and food intake has not been consistent (Wolever, 2006). Taken together, it has not been established whether variation in postprandial insulin responses has substantial effects on body weight regulation in humans.

Fructose intake, satiety and body weight

In contrast to glucose, fructose ingestion elicits little response in blood glucose and insulin concentrations. It has been suggested that high intake of fructose intake may

lead to excess energy intake because of this lack of insulin response as well as failure to suppress secretion of the 'hunger hormone' ghrelin (Elliott *et al.*, 2002; Teff *et al.*, 2004). The effect of fructose intake on body weight has not been examined in randomized trials. A diet supplemented with 50–60 g fructose resulted in weight gain in 14 persons with type 2 diabetes during 23 weeks, but this study did not include a control group (Anderson *et al.*, 1989).

Studies of mostly solid sugary foods

A cross-over study in 20 non-overweight women (mean BMI 23 kg/m^2) in which all foods were provided compared 14 days of *ad libitum* consumption of a high-starch/high-fiber diet with a high-sucrose diet (Raben *et al.*, 1997). The high-starch/high-fiber diet resulted in a 0.7 kg reduction in body weight, whereas the sucrose diet resulted in a non-significant 0.2 kg increase in weight ($P<0.05$ for difference between diets). Possibly, this difference in weight change is related to the participants' higher palatability ratings for the high-sucrose diet or to the sugar-sweetened beverages in the high-sucrose diet. In the 6-month randomized CARMEN trial, a diet higher in mono-and disaccharides was compared with a diet higher in starch in men and women with BMI 26–35 kg/m^2 (Saris *et al.*, 2000). The intervention was *ad libitum* and consisted of providing foods through a laboratory shop system. The diet high in mono-/disaccharides was associated with a non-significant 0.9 kg smaller weight loss than the high-starch diet. The same intervention in persons with the metabolic syndrome resulted in a 4 kg greater reduction in weight for the high-starch as compared with the high mono- and disaccharide diet (Poppitt *et al.*, 2002). These two diets did not only differ in the solid foods consumed, but also in the types of beverages used: beverages high in free sugars in the high-mono-and disaccharide diet versus artificially sweetened beverages in the high-starch diet (Poppitt *et al.*, 2002). Middle-aged male office workers who were asked to cut out sucrose from their diet and replace it with other foods, reduced their sucrose intake from 85 to 12 g per day according to diet records and were reported to have lost weight after 22 weeks (Mann *et al.*, 1970). Similar interventions showed a non-significant tendency for greater weight loss as compared with the control group in hypertriglyceridemic individuals (Smith *et al.*, 1996), whereas no difference in weight loss was found in non-obese women (Gatenby *et al.*, 1997).

Sugar-sweetened beverages and body weight

Intervention studies of sugar-sweetened beverages. Several trials have specifically examined the effects of sweetened beverages on body weight (Table 3). Energy consumed as liquids may induce less satiety as compared with the same foods in a solid form because of the rapid transit of liquids through the stomach and intestines that may lead to reduced stimulation of satiety signals, differences in the regulation of thirst and hunger, and lower cognitively perceived energy content (Mattes, 1996; DiMeglio and Mattes, 2000). Reported energy intake in intervention studies of sugar-sweetened beverages suggested a lack of compensation for the energy provided through these liquids by reduced subsequent energy intake (Tordoff and Alleva, 1990; DiMeglio and Mattes, 2000). Trials of sugar-sweetened beverage consumption and body weight varied from blinded interventions of several weeks (Tordoff and Alleva, 1990; Raben *et al.*, 2002) to an education program on carbonated beverages of 1 year (James *et al.*, 2004; Table 3). Findings in all trials were consistent with a detrimental effect of consumption of sugar-sweetened beverages on body weight. Both trials in which participants were blinded with regard to both the aim of the study and the sweeteners in the beverages they received found a statistically significant effect the sugar-sweetened intervention on body weight (Tordoff and Alleva, 1990; Raben *et al.*, 2002). Figure 4 shows the results of one of these blinded trials conducted by Raben *et al.* (2002). A 1-year dietary educational program at schools mainly aimed at reducing use of carbonated beverages was associated with a reduced incidence of overweight (James *et al.*, 2004). However, given the very limited effect on sugar-sweetened soft drink consumption, it is uncertain whether the effect of the program on obesity are due to reduced consumption of these beverages, to the apparently greater reduction in consumption of artificially sweetened soft drinks or to other behavioral changes. In a 25-week intervention that mainly consisted of the free delivery of non-caloric beverages, consumption of non-caloric beverages instead of sugar-sweetened beverages was associated with weight loss among participants with a higher baseline BMI (Ebbeling *et al.*, 2006). The result of this trial are also of interest because the changed availability of beverages resulted in a marked decrease in consumption of sugar-sweetened beverages over 25 weeks (reported 82% decrease in the intervention group) (Ebbeling *et al.*, 2006). Drewnowski and Bellisle (2007) have pointed out that liquid meal replacement shakes containing amounts of sugars that are similar to the amount in sugar-sweetened beverages are commonly used for weight loss treatment. However, in contrast to sugar-sweetened soft drinks, liquid meal replacement shakes contain substantial amounts of protein and fiber and are used instead of meals rather than in addition to meals (Drewnowski and Bellisle, 2007).

Cohort studies of sugar-sweetened beverages and long-term weight change. In a real-life setting, as compared with the described trials, additional factors may link the consumption of sugar-sweetened beverages to excess energy intake. These factors include huge serving sizes, free refills, massive advertising campaigns for soft drinks and the ubiquitous availability of soft drinks including vending machines at schools (Bray *et al.*, 2004a). Recently, the literature on intake of sugar-sweetened beverages and weight gain has been systematically reviewed and 10 prospective cohort studies

Table 3 Intervention studies of sugar-sweetened soft drinks and body weight

Reference/country	*Participants*[a]	*Trial design*[b]	*Duration*	*Intervention*	*Control*	*Compliance*	*Results*
(Tordoff and Alleva, 1990) US	$n=30$. 9 F: age 28.7 ± 2.7, BMI 25.4 ± 1.4; 21 M: age 22.9 ± 0.8, BMI 25.1 ± 0.5; 11 others dropped out and were not included in the analysis	Cross-over, participants were blinded	3×3 weeks	1135 g per day of supplied HFCS-sweetened soft drinks	Two control interventions: 1135 g per day aspartame-sweetened drinks or no specific instructions	Diet records	HFCS drinks vs no instructions: F $+0.97$ kg, M $+0.72$ kg. HFCS drinks vs aspartame drinks: F $+0.72$ kg, M $+0.99$ kg (P overall <0.01 for both F and M)
(DiMeglio and Mattes, 2000) US	$n=15$ M/F: age 22.8 ± 2.7, BMI 21.9 ± 2.2. All participants included in the analysis	Cross-over	2×4 week and 4-week washout	1880 kJ per day of sugar-sweetened soft drinks ('liquid')	1880 kJ per day of jelly beans ('solid')	Diet records	$P<0.05$ for weight change during liquid period ($+0.5$ kg), but not significantly different from change in the solid period ($+0.3$ kg)
(Raben *et al.*, 2002) Denmark	$n=41$ overweight M/F. Sucrose group: $n=21$, age 33.3 ± 2.0, BMI 28.0 ± 0.5. Sweetener group: $n=20$, age 37.1 ± 2.2, BMI 27.6. One drop-out was not included in the analysis	Randomized parallel; participants were blinded	10 week	Sucrose supplements ($\sim70\%$ as drinks)	Artificial sweetener supplements	Diet records	2.6 (95% CI 1.3–3.8, $P<0.001$) kg increase in weight and 1.6 (95% CI 0.4–2.8, $P<0.01$) increase in fat mass for the sucrose as compared with the artificial sweetener group
(James *et al.*, 2004) UK	$n=644$ M/F, children age 7–11 year from six schools. 20% were overweight or obese	Cluster randomized (29 clusters = classes)	1 year	Educational nutrition program mainly discouraging carbonated beverage use	None	Drink diaries completed by 36%: 0.7 glass per day reduction of mainly diet carbonated beverages	No substantial decrease in mean BMI (0.1 kg/m^2, 95% CI -0.1–0.3), but a 7.7% (95% CI 2.2–13.1) decrease in prevalence of overweight/obesity as compared with control
(Ebbeling *et al.*, 2006) US	$n=103$ M/F, age 13–18 year. No loss to follow-up	Randomized, parallel, allocation concealment	25 weeks	Home delivery of non-caloric beverages (four servings per day) and instructions	Instruction to continue usual beverage consumption	24-h recalls: 82% reduction of sugar-sweetened beverages in intervention group	BMI: -0.14 (SE 0.21, $P>0.05$) for the total group and -0.75 (SE 0.34, $P=0.03$) for the upper baseline-BMI tertile as compared with the control group

Abbreviations: BMI, body mass index (kg/m^2); F, female; HFCS, high fructose corn syrup; M, male.
[a]Values are means$\pm$s.d.
[b]None of the trials reported on blinding of the assessors of outcomes, except for Ebbeling and co-workers allocation concealment was not reported.

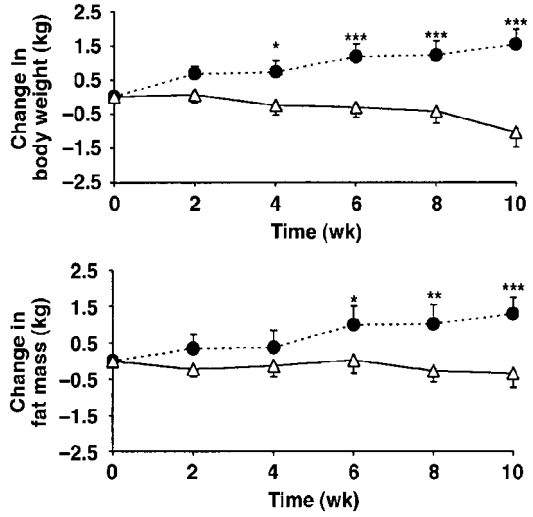

Figure 4 Mean (±standard error) changes in body weight and fat mass during an intervention in which overweight subjects consumed supplements containing either sucrose (●; $n=21$) or artificial sweeteners (△; $n=20$) daily for 10 weeks. In the sucrose group, sucrose was mostly consumed as beverages (~70%). At specific time points for changes in body weight and fat mass, there were significant differences between the sucrose and sweetener groups: *$P<0.05$, **$P<0.001$ and ***$P<0.0001$. Reprinted from Raben *et al.* (2002) copyright 2002, with permission from the American Society for Nutrition.

were identified (Malik *et al.*, 2006). In most of these studies, increases in sugar-sweetened soft drink consumption were associated with weight gain. The lack of significant association in some of the studies may have been due to small sample sizes, short periods of follow-up and limited variation in soft drink consumption. In the largest study in children ($n=11\,654$, age 9–14 years), an increase of two or more servings of sugar-sweetened soft drinks per day over a year was associated with an increase in BMI in both boys (0.14 kg/m^2, $P=0.01$) and girls (0.10 kg/m^2, $P<0.05$; Berkey *et al.*, 2004). In the largest study of adults, 51 603 women were followed for two 4-year periods (Schulze *et al.*, 2004). Women who increased their sugar-sweetened soft drink consumption from less than weekly to daily had the largest weight gain (4.7 kg for the first and 4.2 kg for the second period), whereas women who reduced their consumption from daily to less than weekly had the smallest weight gain (1.3 kg for the first and 0.2 kg for the second period; *P*-value differences between groups 0.001). The finding of an association between sugar-sweetened beverage consumption and weight gain has not been limited to US populations (Bes-Rastrollo *et al.*, 2006b). Although these prospective studies considered confounding in detail, remaining confounding by other dietary and lifestyle factors cannot be excluded. However, the results of cohort studies are consistent with the findings from intervention studies and suggest that consumption of sugar-sweetened soft drinks is relevant for long-term weight management. It is plausible that findings for sugar-sweetened soft drinks also apply to juices high in free sugars such as apple juice, but effects of juices on body weight have not been tested experimentally and results from observational studies have been mixed (Malik *et al.*, 2006).

High-fructose corn syrup versus sucrose-sweetened beverages. It has been suggested that the use of high-fructose corn syrup to sweeten soft drinks has contributed to the increased prevalence of obesity in the US (Bray *et al.*, 2004a). The most commonly used type of high-fructose corn syrup contains 55% fructose and 45% glucose, which is similar to sucrose. Theoretically, the separated glucose and fructose (as in high-fructose corn syrup) may have different effects than conjoined molecule (as in sucrose before it is broken down in the intestine) related to slightly higher sweetness and higher osmolarity (Bray *et al.*, 2004a). It should be noted, however, that the Danish trial found effects of sucrose-sweetened foods on weight gain (Raben *et al.*, 2002). Therefore, reduction of the consumption of both sucrose-sweetened and high-fructose corn syrup sweetened soft drinks is warranted.

Conclusion on free sugars and sugar-sweetened beverages

Short-term experiments suggest that satiety and satiation may be lower for carbohydrates consumed as beverages as compared with carbohydrates consumed as solid foods. Although long-term randomized controlled trials of sugar-sweetened beverages are lacking, evidence from short-term blinded randomized controlled trials, medium-term non-blinded randomized trials, and long-term prospective cohort studies indicates that reduction of consumption of sugar-sweetened beverages is beneficial for weight management. Some data also support that reduction of solid foods high in free sugars can contribute to weight loss, but findings have been less consistent than for sugar-sweetened beverages. The high energy density and low content of micronutrients and fiber of many foods high in free sugars such as sugary candy, table sugar, cookies and cakes should be considered.

Dietary GI and glycemic load

Introduction

The GI of a food quantifies the strength of the blood glucose response after consumption of a fixed amount of available carbohydrates from that food as compared with the response after consumption of the same amount of available carbohydrate from a reference food (glucose or white bread) (Foster-Powell *et al.*, 2002). The glycemic load (GL) is the product of the GI of a food and the amount of carbohydrate that it contains (Foster-Powell *et al.*, 2002). The GL was conceived to reflect the total blood glucose-raising potential of the diet. The GL of a diet can thus be reduced by reducing the GI of the diet and/or by reducing the amount of carbohydrate consumed. It is important to clearly distinguish between the GI and the GL. First, the GL of a diet is strongly influenced by

its carbohydrate content, whereas a low-GI diet can be either high or low in carbohydrates. Second, physiological effects can be different for low-GI diets as compared with low-GL diets (Wolever *et al*., 1995). For example, in a study that evaluated four meals with different combinations of the GI (low or high) and carbohydrate content (low or high), the greatest contrast in effects on free fatty acid levels was found between the low-GI/high-carbohydrate meal and the low-GI/low-carbohydrate (that is, lowest GL) meal (Wolever *et al*., 1995).

Mechanistic studies of the GI and GL and energy balance

It has been postulated that consumption of high-GI foods can lead to excess energy intake through rapid rises and rapid subsequent declines in blood glucose concentrations and associated increases in levels of counter-regulatory hormones (Ludwig, 2002). This is supported by the observation that declines in blood glucose concentrations acutely increased voluntary food intake in time-blinded volunteers (Melanson *et al*., 1999). Several studies have reported beneficial effects of low-GI meals on self-reported hunger and short-term energy intake (Raben, 2002; Pereira *et al*., 2004), but overall findings have been mixed (Raben, 2002). In addition, a greater reduction in resting energy expenditure has been observed in 39 overweight adults after a 10% weight reduction as result of a high-GL hypocaloric diet than after the same weight reduction as a result of a hypocaloric diet with a lower GL (Pereira *et al*., 2004). No differences in lean or fat mass were detected and the authors suggested that low postprandial circulating concentrations of metabolic substrates may have caused this difference possibly through neuroendocrinological adaptations to conserve energy (Pereira *et al*., 2004). It cannot be fully excluded that other differences between the diets including substantial differences in protein, fiber and micronutrients may have contributed to the observed effects.

It is plausible that the effects on energy balance differ for different types of low-GI foods. For example, it has been reported that having some low-GI foods (for example, spaghetti) for breakfast reduced the glycemic response to a subsequent lunch as compared with high-GI white wheat bread, whereas having other low-GI foods for breakfast (for example, white wheat bread with added vinegar) did not (Liljeberg *et al*., 1999). The authors suggested that the 'second-meal effect' for the former foods might have resulted from the prolonged elevation of postprandial glucose concentrations and avoidance of a between-meal fasting. Furthermore, the effect of foods with a low-GI as a result of slow absorption of starches in the intestines may be different from that of foods with a low GI as a result of high fructose content. For example, slowly absorbed starches may reach the lower part of the ileum and stimulate the secretion of gut satiety hormones such as glucagon-like peptide-1 (McMillan-Price and Brand-Miller, 2006).

Cohort studies of the GI and GL

The association between the dietary GI or GL and changes in body weight has been examined in two cohort studies, and lower values were associated reductions in body weights (Spieth *et al*., 2000; Ma *et al*., 2005). However, the limited control for other dietary factors (Spieth *et al*., 2000; Ma *et al*., 2005) and substantial loss to follow-up (Spieth *et al*., 2000) complicate the interpretation of these results.

Intervention studies of the GI and weight change

Table 4 presents data on intervention studies that examined the dietary GI in relation to body weight and body fatness (Slabber *et al*., 1994; Tsihlias *et al*., 2000; Bouche *et al*., 2002; Wolever and Mehling, 2003; Sloth *et al*., 2004; Carels *et al*., 2005; Raatz *et al*., 2005). These trials had a duration ranging from 5 weeks (Bouche *et al*., 2002) to 12 months (Carels *et al*., 2005), and included only dietary advice (Slabber *et al*., 1994; Bouche *et al*., 2002; Carels *et al*., 2005; Raatz *et al*., 2005), provision of key foods (Tsihlias *et al*., 2000; Wolever and Mehling, 2003) or provision of foods that provided much of the total energy intake (Sloth *et al*., 2004; Raatz *et al*., 2005). The presented intervention studies tested effects of slowly absorbed carbohydrates rather than fructose-rich low-GI foods. Effects of the dietary GI on body weight may be mediated by effects on satiety/satiation and energy intake. Therefore, we did not include studies in which energy intakes were fixed. In the study by Raatz *et al*. (2005) the energy intake was fixed in the first phase of the study, but not in the second 'free-living' phase. Although the dietary advice in the Slabber *et al*. (1994) intervention had a specific deficit in energy intake as a target, the characteristics of the trial (no foods provided 12-week duration) implied that the energy intake of the participants could still vary widely.

In one of the studies, the low-GI intervention resulted in a statistically significant reduction in weight as compared with the control intervention (Slabber *et al*., 1994). This study consisted of a randomized parallel trial comparing a low-GI diet ('low insulin response' diet) with a control diet ('balanced diet'), where about half of the participants volunteered to subsequently switch the other diet resulting in a cross-over study (Slabber *et al*., 1994). Although the same trend was observed in the parallel study and the cross-over study, differences in weight loss were only statistically significant in the latter. The used cross-over study approach may result in selection bias, because volunteering to switch to the other diet may depend on the experience with the previous diet. Another limitation of this study is that it is not reported how the diets changed as a result of the provided advice. Differences in diets other than the GI may have occurred, for example the 'low-insulin response' advice also included the instruction not to use any snacks. In a French study, dietary advice to consume low-GI foods did not lead to a lower body weight but resulted in a 0.5 kg lower fat mass as compared with dietary advice to eat high-GI foods (Bouche *et al*., 2002). Fiber intake also differed substantially

Table 4 Intervention studies of low GI diets and body weight

Reference/country	*Participants*[a]	*Trial design*[a]	*Duration*	*Intervention*	*Control*	*Compliance*	*Results*
(Slabber *et al.*, 1994) South Africa	$n=30$ F age 35 ± 6 years, BMI 35 ± 4. No loss to follow-up. $n=16$ participants volunteered to switch to the other diet after completion	Parallel design with minimization and cross-over study	12 week (2×12 weeks for cross-over study): counseling	Only carbohydrate foods with low insulin response, carbohydrate foods in separate meals, no snacks	'Balanced diet'. Both advised intervention and control diet were hypocaloric (4200–5000 kJ per day)	Diet records. Difference in GI not reported	Parallel: intervention diet −9.3 kg, control −7.4 kg, difference 1.9 kg (95% CI −0.7, 4.6; $P=0.14$). Cross-over: intervention diet −7.4 kg, control −4.5 kg, difference 2.9 kg (95% CI 0.1, 5.8; $P=0.04$)
(Tsihlias *et al.*, 2000) Canada	M/F type 2 diabetes High GI: $n=22$, age 63, BMI 28. Low GI: $n=26$ age 62, BMI 28. An additional $n=7$ (high GI) and $n=4$ (low GI) were lost to follow up and not included in analyses	Randomized parallel	6 months: breakfast cereals (10–15% total energy intake) provided and meal plans	Low-GI cereals provided	High-GI cereals provided	Diet records: low GI reported 10 point lower GI and 27 g per day higher fiber intake as compared with high GI	No statistically significant differences in body weight (high GI ~1 kg more weight loss than low GI)
(Bouché *et al.*, 2002) France	$n=11$ months, age 46, BMI 28. No loss to follow-up	Randomized cross-over study	2×5 week and 5 week washout: counseling	Foods with GI <45 recommended	Foods with GI >60 recommended	Diet records: Low GI 30 point lower GI and 12 g per day higher fiber intake	No statistically significant difference in body weight. Low GI lost −0.52 kg body fat, high GI −0.02 (difference 0.50 kg $P<0.05$)
(Wolever and Mehling, 2003) Canada	M/F impaired glucose tolerance; low GI: $n=13$ age 55, BMI 30; high GI: $n=11$ age 59, BMI 29	Randomized parallel	4 months: monthly counseling and key foods provided	Instructed $\geqslant1$ low-GI food at each meal	Instructed $\geqslant1$ high-GI food at each meal	Diet records: Low GI decreased GI 4.3 points and increased fiber 12 g per day. No significant changes for high GI	High GI: −0.49 kg, low GI −0.19 kg (difference 0.30 kg, $P<0.05$)
(Sloth *et al.*, 2004) Denmark	F low GI: $n=23$, age 29, BMI 27.6; high GI: $n=22$, age 31, BMI 27.6; another $n=6$ (low GI) and $n=4$ (high GI) lost to follow-up not included in primary analysis	Randomized parallel, participants blinded with regard to study aim	10 weeks: test foods provided (~49% of total energy)	Low-GI test foods (GI 103)	High-GI test foods (GI 79)	Test food diaries (>95% used), urinary lithium recovery from the provided bread (low GI 74%, high GI 82%, $P>0.05$), diet records	Low GI: −1.9 (SE 0.5) kg, high GI −1.3 (SE 0.3) kg (difference 0.6 kg, $P=0.31$) body weight (intention to treat: difference 0.4 kg, $P=0.57$). Fat mass: low GI −1.0 (0.4) kg, high GI −0.4 (0.3) kg (P difference 0.20)
(Carels *et al.*, 2005) US	$n=40$ F/M. Low GI, age 43.4, BMI 38.0; high GI, age 43.5, BMI 37.2. An additional $n=13$ was lost to follow up and not included in the analysis	Randomized parallel	20 week with weekly group sessions and 12 months follow-up	Behavioral weight loss program + GI education and popular book on GI	Behavioral weight loss program only	Test of difference in GI knowledge, session attendance, diet records: five-point GI difference achieved	After 20 weeks: low GI 7.1 kg weight loss, controls: 8.2 kg weight loss. Difference not statistically significant, also not after 12 months follow-up

Table 4 *Continued*

Reference/country	*Participants*[a]	*Trial design*[a]	*Duration*	*Intervention*	*Control*	*Compliance*	*Results*
(Raatz *et al.*, 2005) US	F/M adults. Low GI, $n=10$, BMI 37.7. High GI, $n=9$, BMI 34.6. 31% lost to follow-up in feeding phase. During the free living phase $n=4$ of the low GI and $n=1$ of the high-GI group lost. No intention to treat analysis	Randomized parallel	12-week feeding phase (all foods provided) + 24-week free-living phase with counseling	Feeding phase: hypocaloric (3138 kJ per dcay deficit), low GI. Free living: advised to continue this diet	Feeding phase: hypocaloric (3128 kJ per day deficit), high GI. Free living: advised to continue this diet	Diet records: no significant difference in GI between groups after free-living phase	Feeding phase: low GI −9.95 kg, −6.9 kg fat mass. High GI −9.3 kg, −4.5 kg fat mass. Additional weight change in free-living phase: −1.8 kg for low GI and −1.6 kg for high GI. No significant differences between groups

Abbreviations: BMI, body mass index (kg/m); F, female; GI, glycemic index; M, male.
Values are means (s.d.) unless reported otherwise.
[a]None of the studies reported on blinding of outcome assessors or allocation concealment.

between the diets, and given the magnitude of the effect other modest differences between the intervention diets may also have been responsible. In a Danish study, almost half of the foods were provided, allowing better control of differences between the diets, and recovery of lithium from the provided breads was used to monitor compliance (Sloth *et al.*, 2004). Despite the substantial differences in the GI of the diets, no statistically significant effects on body weight or fat mass were observed although a small beneficial effect could not be excluded either. In the studies by Raatz *et al.* (2005) ('free living phase' of the study) and Carels *et al.* (2005) low-GI dietary advice did not have effects on body weight as compared with the control interventions, but achieved differences in dietary GI were small. In two Canadian studies, provision of key low-glycemic foods resulted in modest differences in dietary GI, but did not result in a lower body weight over 4 or 6 months as compared with the provision of high-GI foods (Tsihlias *et al.*, 2000; Wolever and Mehling, 2003). In contrast, weight loss tended to be somewhat larger for the high-GI as compared with the low-GI diet. A larger randomized intervention study that evaluates substantial differences in the dietary GI in the absence of other dietary differences with the control group would be of interest. In addition, it may be warranted to distinguish further between different types of low-GI foods. However, the currently available data provides little support for an important role of the dietary GI in weight management.

Intervention studies of the GL and weight change

Four studies aimed to test the effects of low-GL diets on body weight (Table 5). The effect of low-GL dietary advice on body weight was tested in 16 obese adolescents (Ebbeling *et al.*, 2003). The low-GL advice resulted in a substantially larger reduction in fat mass as compared with the conventional control diet. Given the very small resulting differences in dietary GI and carbohydrate intake between the intervention and control diet, effects on body fat may also have resulted from other beneficial characteristics of the recommended foods (non-starchy vegetables, fruits, legumes, nuts, dairy) or a greater acceptation of the *ad libitum* approach by the adolescents (Ebbeling *et al.*, 2003). The same low-GL advice resulted in greater changes in GI, carbohydrate intake, and GL in a trial in young adults, but did not result in a statistically significant greater reduction in body fat or fat mass (Ebbeling *et al.*, 2005). In a substantially larger 12-week Australian trial, four diets were compared: (A) a high-GI/high-carbohydrate diet (highest GL), (B) a low-GI/high-carbohydrate diet, (C) a high-GI/high-protein diet and (D) a low-GI/high-protein diet (lowest GL) (McMillan-Price *et al.*, 2006). No significant differences in weight loss or decrease in fat mass were found, although the percentage with at least 5% weight loss was greater for diets B and C than for the other diets. Also, in a subgroup analysis in women, more fat mass was lost for diets B and C than for the other diets.

Table 5 Randomized intervention studies of low GL diets and body weight (all parallel design)[a]

Reference/ country	*Participants*[a]	*Duration*	*Intervention*	*Control*	*Compliance*	*Results*
(Ebbeling *et al.*, 2003) US	Obese adolescents M/F. Low glycemic load (GL): $n=8$, age 17, BMI 35, fat mass 39 kg; high GL: $n=8$, age 15, BMI 37, fat mass 49 kg ($P=0.03$ vs low GL); $n=2$ lost to follow-up but included in intention to treat	12 months: 12 counseling sessions during 0–6 months and 2 during 6–12 months	Low to moderate GI foods, balanced consumption of carbohydrates with fat and protein at each meal/ snack; *ad libitum*	Reduced fat and hypocaloric (250–500 kcal per day deficit)	Diet records (follow-up): low GL 10 g per 1000 kcal lower GL, 3 en% lower carbohydrate and 3 point lower GI than control group	BMI decreased 1.8 ($P=0.02$) and fat mass 4.2 kg ($P=0.01$) for low GL as compared with control diet
(Ebbeling *et al.*, 2005) US	F/M. Low GL: $n=11$, age 30, BMI 34.0. High GL: $n=12$, age 27, BMI 27.2. An additional $n=6$ (low GL) and $n=5$ (high GL) lost to follow up	Ebbeling *et al.* (2003)	Low glycemic load: see Ebbeling *et al.*(2003)	Reduced fat and hypocaloric (250–500 kcal per day deficit)	Diet records. Low vs high GL: 24 g per 1000 kcal lower GL, 7 point lower GI, 12 en% lower carbohydrate	Low GL: weight −7.8 kg, fat mass −16.5%. High GL: weight −6.1 kg ($P=0.89$ vs low GL), fat mass −15.7% ($P=0.97$). Similar for intention to treat analysis
(McMillan-Price *et al.*, 2006) US	F/M, age 18–40 BMI $\geqslant 25\ kg/m^2$ A. High GI/ high carb: $n=32$, B. Low GI/high carb: $n=32$, C. High GI/high protein: $n=32$, D. Low GI/high protein: $n=33$. $n=5$, 2, 1 and 5 withdrew, but included in intention to treat	12 weeks: counseling and provision of key foods each week	All eating plans were hypocaloric (~1400 kcal for women and 1900 kcal for men), but participants were told to 'eat to appetite' and accordingly eat more or less than eating plan. Diet A had the highest GL (diet records: 129 g) and diet D the lowest GL (59 g)		Diet records and monitoring of 10 h glucose and insulin responses indicated that substantial contrasts in GI and GL existed between the diets. Fiber intake was substantially higher for diet B than for the other diets	Diet A: weight −3.7, fat −2.8 kg; diet B: weight −4.8, fat −4.5 kg; diet C: weight −5.3, fat −4.3 kg; diet D: weight −4.4, fat −3.7 kg $P=0.17$ for differences in weight and $P=0.08$ for differences in fat mass
(Maki *et al.*, 2007) US	F/M, age 18–65 waist $\geqslant 87$ cm for women and $\geqslant 90$ cm for men. Low GL: $n=43$, control diet: $n=43$. $n=10$ and 7 lost to follow-up, but all except 1 for both groups included in intention to treat for weight (last observation carried forward)	36 weeks starting with 12–24 weeks weigh loss phase followed by weight maintenance. Counseling at 14 visits and written information	*'Ad libitum* reduced GL'. first phase: 2 weeks with elimination of high carbohydrate foods. Second phase: addition of low-GI foods	'Portion-controlled low-fat diet'. Reduction of high-fat foods, portion sizes, and energy density aiming at deficit of 500–800 kcal per day	FFQ (for GI and GL) and diet records. Low GL vs control (week 36): 55 g lower carbohydrate, 23 g lower sucrose/fructose, 3 point lower GI, 33% lower GL	Low GL: weight −4.9, fat −2.2, fat-free mass −2.1 kg. Control: weight −2.5, fat −1.3, fat-free mass −0.9 kg $P=0.09$ for difference in weight, $P=0.33$ for difference in fat, $P=0.004$ for difference in fat-free mass
(Das *et al.* 2007) US	F/M, age 24–42 BMI 25–30 $kg\,m^{-2}$. Low GL: $n=17$. High GL: $n=17$. $n=3$ and 2 lost to follow-up	1 year: 6 months, where foods were provided followed by 6 months with counseling and self-selected foods	Low GL with 30% caloric restriction. Lower GI foods and 40 en% carb, 30 en% fat, 30 en% protein	High GL with 30% caloric restriction. Higher GI foods and 60 en% carb, 20 en% fat, 20 en% protein and higher GI foods	Provided foods for high GL vs low GL had a 63% higher GI 161% higher GL. Caloric restriction (doubly labeled water) at 3 months, 6 months and 12 months were 21%, 16%, and 17% for high GL and 28%, 18% and 10% for low GL	Low GL: weight −10.4% (6 months) and −7.8% (12 months). High GL: weight −9.1% (6 months) and −8.0% (12 months). No significant differences between diet groups (also not in body fat %)

Abbreviations: BMI, body mass index ($kg\,m^{-2}$); en%, energy percent; F, female; FFQ, food frequency questionnaire; GI, glycemic index; GL, glycemic load; M, male. Values are means.
[a]Das *et al.* reported the blinding of outcome assessors. None of the other studies reported on blinding of outcome assessors or allocation concealment.

Despite a substantially lower GL for diet D as compared with diet A, according to diet records (−54%) and 10-h incremental area under the glucose (−38%) and insulin (−45%) curve on profile days, no substantial or significant difference in loss of fat mass was observed. Thus, although results from this study could be seen as supportive for a low-GI /high-carbohydrate/high-fiber diet and a high-protein diet for weight loss, the unexpected results for the diet that combined a low-GI and high protein intake, the sex differences in results and the limited duration warrant a cautious interpretation. In a US study, a reduced GL diet was compared with a portion-controlled low-fat diet (Maki *et al*., 2007). Weight loss and loss of fat mass was greater for the low-GL diet as compared with the control diet after 12 weeks ('weight loss phase'), but these differences did not remain significant after 36 weeks ('weight maintenance phase'). Finally, another US study in 34 participants combined a goal of 30% caloric restriction with a low or high-GL diet (Das *et al*., 2007). No significant differences in weight loss or energy intake measured with the doubly labeled water method were found after either the 6-month phase in which all foods were provided or the subsequent 6-month phase where the participants selected the foods themselves. In summary, studies that have directly compared low- and high-GL diets do not consistently support this hypothesis that a low-GL diet supports weight loss.

Conclusion on GI and GL

Current evidence from studies on low-GI and low-GL diets is too limited to warrant specific recommendation with regard to these concepts for the prevention of obesity. Caution with regard to the health effects of high fructose intake is warranted, whereas other low-GI foods such as legumes that also have other beneficial nutritional properties could be recommended as part of a diet for weight control.

Dietary fiber

Introduction

A higher fiber content contributes to a lower energy density of foods (Slavin, 2005). In addition, viscous fibers form a viscous gel in contact with water and have been suggested to reduce energy intake through increased feelings of fullness (Pasman *et al*., 1997). These types of fiber may also increase gastrointestinal transit time, slow glucose absorption and lead to a more gradual increase in blood glucose levels (see glycemic index section) (Slavin, 2005).

Intervention studies of 'fiber' supplements and body weight

Guar gum is a viscous galactomannan fiber that is commonly used in the form of supplements in attempts to lose weight (Pittler and Ernst, 2001). In a meta-analysis published in 2001, the results of 11 randomized double-blind trials of guar gum intake and body weight were pooled (Pittler and Ernst, 2001). The results did not suggest a difference in effect on body weight as compared with placebo treatment (weighted mean difference −0.04 kg; 95% confidence interval −2.2 to 2.1). In a 14-month randomized intervention study with 11 obese women, adding 20 g of guar gum supplements per day to an *ad libitum* diet after completion of a very low-calorie diet did not reduce weight as compared with controls (Pasman *et al*., 1997). Timing of the intake of fiber supplements in relation to meals may be relevant (Pasman *et al*., 1997). Also, fiber supplements may not have appreciable effects in isolation, but rather improve adherence to hypocaloric diets. Ryttig *et al*. (1989) examined the effects of a fiber supplement in combination with a hypocaloric diet in a series of double-blind, randomized trials of 3- to 12-month duration in overweight persons (Rossner *et al*., 1987; Rigaud *et al*., 1990). The addition of the fiber supplements to a hypocaloric diet led to a statistically significant 1–2 kg greater weight loss as compared with a placebo in combination with the hypocaloric diet. An effect of similar magnitude was observed for adding viscous glucomannan fiber supplement to a hypocaloric diet in 5-week placebo-controlled double-blind randomized study (Birketvedt *et al*., 2005). In summary, although results for 'fiber' supplements on body weight have been mixed there is some evidence that these supplements may increase adherence to hypocaloric diets and thus lead to a small additional weight loss. The role of different types of fiber as well as the timing of fiber intake requires further study in this context.

Weight loss interventions with high-fiber foods

In a randomized trial in obese men and women that received an energy-restricted diet (target 500 kcal per day deficit) for 48 weeks additional advice to increase consumption of vegetables, fruit and whole grains was associated with a ~10 g per day reported higher fiber intake, but not with greater weight loss (Thompson *et al*., 2005). In a 2-year randomized trial, the effect of a 'Mediterranean-style' diet high in fiber-rich foods was tested in 180 persons with the metabolic syndrome (Esposito *et al*., 2004). The intervention group received individualized dietary advice from a dietician (monthly session in the 1st year, bimonthly in the second year) and participated in group sessions with education on reducing calories, personal goal setting and self-monitoring. Aims included increasing consumption of fruits, vegetables, legumes, nuts, whole grains and olive oil combined with less than 30% of energy from fat and 50–60% from carbohydrates. The control group did not receive individualized advice, but only general recommendations based on the same goals for macronutrient intakes. Weight loss after 2 years was 4.0 kg for the intervention and 1.2 kg for the control group (difference 2.8 kg, 95% confidence interval 0.5–5.1). The 16 g per day greater increase in fiber intake as well as other characteristics of the recommended foods or

the educational program may have contributed to this greater weight loss.

Intervention studies of high-fiber foods not primarily aimed at weight loss

In the Women's Health Initiative, a modest self-reported increase in fruit, vegetable and fiber intake was observed in the intervention group and this was not associated with a substantial long-term effect on body weight (Howard *et al.*, 2006). Other trials that were not aimed at weight loss generally did not find an effect of increased consumption of fruits and vegetables on body weight (Rolls *et al.*, 2004). For example, in a 1-year trial in 201 men and women specifically aimed at fruit and vegetable consumption, fruit (diet records +2.8 serving per day), vegetable (+1.4 serving per day), juice (+2.5 serving per day) and fiber intake (+5.5 g per day) increased substantially more in the intervention as compared with the control group (Smith-Warner *et al.*, 2000). These changes were supported by increased plasma carotenoid concentrations, but no appreciable difference in weight change was found between the intervention (+0.3 kg) and control group (+0.4 kg). It has been suggested that concomitant increases in juice consumption, a high-caloric beverage, may have reduced possible beneficial effects of the fruits and vegetable interventions on body weight (Rolls *et al.*, 2004). An alternative explanation that is consistent with the results from prospective cohort studies is that effects of higher consumption of fiber-rich foods on body weight are modest and only apparent after several years.

Cohort studies of high-fiber foods and long-term weight change

The association between fiber intake and weight change has been examined in several large prospective cohort studies with detailed adjustment for potential confounders. In a study of men, a 10 g per day increase in fiber intake was associated with a 2.25 kg lower weight gain over 8 years after correction for measurement error in the assessment of fiber intake (Koh-Banerjee *et al.*, 2004). Similar results have been obtained in women, younger adults, and a Mediterranean population (Ludwig *et al.*, 1999; Liu *et al.*, 2003; Bes-Rastrollo *et al.*, 2006a). Higher consumption of whole grains (Liu *et al.*, 2003; Koh-Banerjee *et al.*, 2004) and fruits and vegetables (He *et al.*, 2004; Bes-Rastrollo *et al.*, 2006a) was also associated with a modestly lower long-term weight gain. These findings may reflect a dietary pattern rather than fiber intake per se, and the possibility that confounding by unmeasured or imprecisely measured factors contributed to these associations cannot be excluded.

Conclusion on dietary fiber

The currently available evidence does not support a major effect of fiber intake on weight loss, but evidence is consistent with modest long-term effects of higher consumption of fiber-rich foods on body weight gain. An important reason to attempt weight loss is the prevention of morbidity associated with excess adiposity including type 2 diabetes, coronary heart disease and stroke (Willett *et al.*, 1999). Consumption of a diet high in fruits, vegetables and whole grains is associated with reduced risk of these diseases (Appel *et al.*, 1997; de Lorgeril *et al.*, 1999; Jacobs and Gallaher, 2004) and should therefore be included in diets for long-term weight management. *Ad libitum* intervention studies that specifically examine the effects of whole grain consumption on body weight appear to be lacking and this topic warrants further research.

General discussion

Although weight gain is due to an imbalance between energy intake and energy expenditure, this equation is deceivingly simple in the context of obesity prevention and treatment under realistic conditions. Complex feedback mechanisms appear to stimulate regaining lost weight (Hirsch *et al.*, 1998) and potent environmental influences stimulate over-consumption of ubiquitously available foods and a sedentary lifestyle (Egger and Swinburn, 1997). The optimal macronutrient composition of diet for weight management may also differ by individual characteristics. First, the response to diets may differ by genetic susceptibility of individuals (Memisoglu *et al.*, 2003), although a recent study of 26 candidate genes did not identify important modifiers of the effects of a high or low carbohydrate weight loss diet (Sorensen *et al.*, 2006). Second, findings from two recent randomized intervention studies suggest that insulin sensitivity or glucose-induced insulin secretion can modify the weight loss in response to low-carbohydrate or low-GL diets (Cornier *et al.*, 2005; Pittas *et al.*, 2005). Larger studies are needed to test the hypothesis that characteristics related to a person's glucose homeostasis may affect the optimal macronutrient composition for weight management. Finally, the carbohydrate content of a diet that allows long-term adherence may to a large extent depend on individual preferences. For prevention of weight gain, individuals should be able to maintain a dietary pattern that prevents excess energy intake for decades and the degree of adherence to weight loss interventions is a strong predictor of weight loss (Heshka *et al.*, 2003; Dansinger *et al.*, 2005).

This overview is limited to dietary carbohydrates in relation to obesity. However, many other factors should be considered in the design of weight loss interventions. Self-monitoring of diet and activity, structural approaches providing foods, meal replacements or menus and recipes, increased physical activity, and longer length of treatment have been shown to contribute to greater weight loss (Perri *et al.*, 1989; Foster *et al.*, 2005). Although, the achieved weight loss of long-term interventions may appear small, ~5% loss of body weight as a result of dietary changes and

increased physical activity has been associated with a major decrease in incidence of type 2 diabetes and other metabolic disturbances (Tuomilehto *et al*., 2001; Knowler *et al*., 2002). The high prevalence of overweight and obesity indicates that energy imbalance is a population-wide phenomenon in many societies across the world. In addition to interventions aimed at individuals, rigorous changes in the social and physical environment including the food supply that reduce stimuli to overeat and facilitate greater physical activity will be needed to target the epidemic of obesity.

Although more randomized longer-term trials of diet and body weight have been conducted in recent years, many caveats exist in the current evidence and further research efforts to address this topic that is of pivotal importance for public health is strongly recommended.

Conclusions and recommendations

Carbohydrates are among the macronutrients that provide energy and can thus contribute to excess energy intake and subsequent weight gain. If energy intake is strictly controlled, macronutrient composition of the diet (energy percentages of fat and carbohydrates) does not substantially affect body weight or fat mass (Golay *et al*., 1996). However, an important issue is whether among free-living individuals, macronutrient composition of the diet increases the likelihood of passive over-consumption. There is no clear evidence that altering the proportion of total carbohydrate in the diet is an important determinant of energy intake. However, there is evidence that sugar-sweetened beverages do not induce satiety to the same extent as solid forms of carbohydrate and that increases in sugar sweetened soft drink consumption are associated with weight gain. Thus, there is a justification for the recommendation to restrict the use of beverages high in free sugars in order to reduce the risk of excessive weight gain and to treat obesity. Solid foods high in free sugars tend to be energy dense, and there is some evidence from intervention studies that reduction of solid foods high in free sugars can contribute to weight loss. Thus, the current recommendation to restrict free sugars to no more than 10 percent of total energy is consistent with appropriate diets for the prevention of obesity. A high content of dietary fiber in whole-grain cereals, vegetables, legumes and fruits is associated with relatively low energy density, promotion of satiety, and in observational studies a lesser degree of weight gain than among those with lower intakes. Although it is difficult to establish with certainty that dietary fiber rather than other dietary attributes are responsible, it is considered appropriate to recommend that whole grain cereals, vegetables, legumes and fruits are the most appropriate sources of dietary carbohydrate. The currently available evidence is considered to be insufficient to recommend carbohydrate-containing foods likely to reduce the risk of obesity or promote weight loss on the basis of their GI.

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Conflict of interest

During preparation and peer-review of this paper in 2006, the authors and peer-reviewers declared the following interests.

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