

# How are components of dietary intake, dietary composition, foods, and nutrients related to obesity and weight gain?

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## Current evidence and recommendations

A report on diet, nutrition, and the prevention of chronic diseases was published after the joint World Health Organization (WHO)/Food and Agriculture Organization of the United Nations (FAO) Expert Consultation held in 2002 [1]. A summary of the risk factors in relation to prevention of excess weight gain and obesity is presented in Table 4.1 [2]. Lifestyle factors listed as obesity-promoting factors (with the strength of evidence) included high intake of energy-dense foods (convincing) and high-sugar drinks (probable). The review found evidence that protective factors against obesity were a high intake of energy-dilute foods (non-starch polysaccharides/fibre) (convincing)

and foods of low glycaemic index (GI) (possible). Correspondingly, energy-dense foods (foods high in fat and/or sugar) and sugary drinks were considered to be probable determinants of obesity by the World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) in the second WCRF/AICR expert report, published in 2007 (Table 4.2) [3]. Recent WHO guidelines, from 2015, which focus on reducing the risk of noncommunicable diseases in adults and children, including prevention and control of unhealthy weight gain, strongly recommend reducing the intake of free sugars to less than 10% of total energy intake [4]. Another probable risk factor for weight gain, overweight, and obesity, which did not appear in the WHO/FAO Expert Consultation report

but was mentioned in the second WCRF/AICR expert report, referred to fast foods, defined as foods that “are consumed often, in large portions, and are energy-dense” [3]. The only dietary factor that was considered by WCRF/AICR to decrease the risk of weight gain, overweight, and obesity, by promoting appropriate energy intake, was intake of low-energy-dense foods, i.e. wholegrain cereals and cereal products, non-starchy vegetables, and dietary fibre.

## Dietary scores and dietary patterns

An analysis of three cohorts in the USA indicated that better diet quality, i.e. higher Alternate Mediterranean Diet (aMED), Alternate Healthy Eating Index-2010 (AHEI-2010), and Dietary

**Table 4.1. Factors that might promote or protect against overweight and weight gain**

Strength of evidence <sup>a</sup>	Decreases risk	No relationship	Increases risk
Convincing	Regular physical activity High intake of dietary non-starch polysaccharides/fibre		Sedentary lifestyles High intake of energy-dense foods <sup>b</sup>
Probable	Home and school environments that support healthy food choices for children Breastfeeding		Heavy marketing of energy-dense foods <sup>b</sup> and fast-food outlets Adverse social and economic conditions (in developed countries, especially for women) High-sugar drinks
Possible	Foods with low glycaemic index	Protein content of the diet	Large portion sizes High proportion of food prepared outside the home (developed countries) “Rigid restraint/periodic disinhibition” eating patterns
Insufficient	Increased eating frequency		Alcohol consumption

<sup>a</sup> Strength of evidence: The totality of the evidence was taken into account. The World Cancer Research Fund schema was taken as the starting point but was modified in the following manner: randomized controlled trials (RCTs) were given prominence as the highest ranking study design (RCTs not a major source of cancer evidence); associated evidence was also taken into account in relation to environmental determinants (direct trials were usually not available or possible).

<sup>b</sup> Energy-dense foods are high in fat and/or sugar; energy-dilute foods are high in non-starch polysaccharides/fibre and water, such as fruits, legumes, vegetables, and wholegrain cereals.

Source: Reproduced with permission from Swinburn et al. (2004) [2].

**Table 4.2. Factors that modify the risk of weight gain, overweight, and obesity**

Strength of evidence	Decreases risk	Increases risk
Convincing	Physical activity	Sedentary living <sup>a</sup>
Probable	Low-energy-dense foods <sup>b</sup> Being breastfed <sup>d</sup>	Energy-dense foods <sup>b,c</sup> Sugary drinks <sup>e</sup> Fast foods <sup>f</sup> Television viewing <sup>g</sup>
Limited – suggestive		
Limited – no conclusion	Refined cereals (grains) and their products; starchy roots, tubers, and plantains; fruits; meat; fish; milk and dairy products; fruit juices; coffee; alcoholic drinks; sweeteners	
Substantial effect on risk unlikely		None identified

<sup>a</sup> Sedentary living comprises both high levels of physical inactivity and low levels of physical activity (in terms of intensity, frequency, and duration).

<sup>b</sup> The direct epidemiological evidence for low-energy-dense foods is from wholegrain cereals (grains) and cereal products, non-starchy vegetables, and dietary fibre. The direct epidemiological evidence for energy-dense foods is from animal fat and fast foods. These are interpreted as markers of the energy density of diets, based on compelling physiological and mechanistic evidence.

<sup>c</sup> Some relatively unprocessed energy-dense foods (which tend to be eaten sparingly), such as nuts, seeds, and some vegetable oils, are valuable sources of nutrients.

<sup>d</sup> The evidence relates principally to obesity in childhood, but overweight and obesity in children tend to track into adult life: overweight children are liable to become overweight and obese adults.

<sup>e</sup> The evidence relates to all drinks containing added caloric sweeteners, notably sucrose and high-fructose corn syrup. Fruit juices are also sugary drinks and could have similar effects, but the evidence is currently limited.

<sup>f</sup> Fast foods characteristically are consumed often, in large portions, and are energy-dense.

<sup>g</sup> Television viewing is here identified as a sedentary activity. It is also associated with consumption of energy-dense foods. The evidence relates specifically to childhood and adolescence, and is taken also to apply to adults.

Source: Reproduced with permission from WCRF/AICR (2007) [3].

Approaches to Stop Hypertension (DASH) scores, was associated with less weight gain during adult life [5]. This finding was in agreement with the results obtained from European cohorts using similar indices [6, 7]. A systematic review found that 13 of 21 epidemiological studies reported a

negative association between adherence to the Mediterranean diet and overweight/obesity or weight gain [8]. In turn, increased frequency of consumption of fast-food products was linearly associated with lower Mediterranean Diet and Healthy Eating Index scores [9]. In today’s environ-

ment, both the increased availability of and the portion sizes of fast-food products may contribute to rising obesity rates [10, 11].

Dietary patterns derived a posteriori by using dimension-reduction techniques such as factor or cluster analysis also showed that adherence

to a healthy dietary pattern (high intake of whole grains, fruits and vegetables, and reduced-fat dairy products) was associated with smaller gains in body mass index (BMI) and waist circumference (WC), whereas adoption of a dietary pattern typical of developed countries (also called the meat–sweet diet) may lead to weight gain [12–17]. A diet characterized by higher intakes of vegetables and wholemeal cereal products resulted in a lower risk of becoming overweight or obese (odds ratio [OR], 0.69; 95% confidence interval [CI], 0.54–0.88) in children followed up for 2 years [18]. The first study to prospectively investigate the association between dietary patterns at the nutrient level and weight change corroborated the previous findings that a healthy dietary pattern is associated with less weight gain and also highlighted combinations of nutrients that may be responsible for such associations at the food level [19].

### The nutrition transition

The nutrition transition in developing countries leads to dietary intakes of micronutrient-poor, energy-dense foods, which may be important determinants of overweight/obesity and important for child development [20]. In low- and middle-income countries (LMICs), consumption of fruits and vegetables was observed to be lower in groups with low socioeconomic status compared with those with high socioeconomic status; this may be due to a lack of knowledge of the health benefits of fruits and vegetables, their high cost, and limited access to fresh-food markets in groups with lower socioeconomic status [21]. In addition, groups with high socioeconomic status were observed to have a higher intake of protein (due to increased intake of animal foods accompanying the nutrition transition), a lower intake of carbohydrates and fibre (attributable to a higher intake

of processed foods replacing traditional, carbohydrate-rich foods), and a higher intake of fat (associated with increased prosperity and supermarket expansion) [21]. Nutrient-dense foods are often more expensive than the energy-dense alternatives [22].

### Foods

One of the most consistent results with regard to obesogenic dietary factors pertains to the high energy density of some foods, i.e. an energy content of more than about 225–275 kcal per 100 g (941–1151 kJ per 100 g). *Energy-dense foods* have been rated as probable [3], convincing [1], or suggestive [23] obesity-promoting factors by three comprehensive reports and reviews on nutrition and obesity/weight gain. A study based on a prospective cohort from five European countries indicated an increase in WC of 0.09 cm/year (95% CI, 0.01–0.18 cm/year) per 1 kcal/g (4.2 kJ/g) dietary energy density, but did not observe a significant association of energy density with weight gain [24].

*Fast foods* are energy-dense, micronutrient-poor foods that are often high in saturated and trans-fatty acids, processed starches, and added sugars [25]. Several observational studies have indicated an increased risk of being obese, greater weight gain, higher BMI, and higher rates of overweight/obesity in those consuming fast-food products compared with non-consumers, in both developed regions [9, 26–28] and developing regions [29–31]. Consumption of a fast-food product (including hamburgers, cheeseburgers, and French fries) more than once per week by adults in Spain increased the risk of being obese by 129%, compared with non-consumers, after controlling for energy intake and several lifestyle factors [9]. In a cohort of participants aged 18–30 years in the USA, more frequent consumers (more than twice

per week) gained an extra 4.5 kg of body weight over a 15-year period compared with less frequent consumers (less than once per week) of fast-food products [26]. Also, an increase of 5 BMI units (kg/m<sup>2</sup>) was observed in children and adolescents in China who consumed processed foods frequently [29]. A recent analysis of the European Prospective Investigation into Cancer and Nutrition (EPIC) study using biomarkers of dietary exposure to industrially processed foods reported that a high blood level of industrial trans-fatty acids may increase the risk of weight gain, particularly in women [32].

In contrast, the evidence is not straightforward for beverages that may be a significant source of additional energy intake, including sugary drinks and alcoholic drinks.

Both the WHO/FAO report and the WCRF/AICR report indicated the probable role of *sugary drinks* (also called sodas, soft drinks, high-sugar drinks, or sugar-sweetened beverages) in obesity development [1, 3]. Some [33–37] but not all later meta-analyses and reviews [38–42] concluded that there is a significant positive association between intake of this food group and risk of obesity. Several factors are likely to contribute to these discrepant findings, including methodological differences between studies (different outcomes [overweight, weight gain, obesity]; varying exposure [types of beverages]; types of studies included [interventional and/or observational]; adjusted or not for energy intake and physical activity; different populations considered [age groups, sex, geographical regions that may vary in the composition of sugary drinks and the level of intake]), reporting and publication bias, and conflict of interest with the food industry [43]. Nevertheless, evidence supporting the obesogenic effect of sugary drinks of poor nutritional quality is growing, with increasing relevance

in children, especially in low-income socioeconomic groups [44] and in LMICs [45]. A meta-analysis of 22 cohort studies showed that each increment of one sugary drink per day was associated with an increase of 0.05–0.06 BMI units (kg/m<sup>2</sup>) in children per year and an additional weight gain of 0.12–0.22 kg in adults per year [34]. A meta-analysis of five cohort studies indicated a 55% (95% CI, 32–82%) higher risk of being overweight in children who consume sugary drinks daily [46].

In the above-mentioned studies, the main methodological difference that may cause the discrepancies may be related to adjustment for energy intake. Because sugary drinks are believed to be an additional non-compensated energy source, an ad libitum strategy (energy intake not controlled or adjusted for) was proposed to be a better measure of the association of the intake of sugary drinks with obesity and/or weight gain. Indeed, an ad libitum strategy resulted in significant positive associations in meta-analyses of both experimental and observational studies [33]. Other authors claim that adjustment for energy intake should be taken into consideration; these studies generally observed no significant association [37]. Moreover, more pronounced genetic predisposition to obesity was observed with higher consumption of sugary drinks [47].

Discrepant results have been found also for *alcoholic drinks*. A recent review summarizing the metabolic effect of intake of energy-containing beverages concluded that observational studies have shown a positive association, a negative association, or no relationship between intake of alcohol or sugary drinks and body weight [48]. For alcohol intake, both the WHO/FAO report and the WCRF/AICR report ranked the evidence as insufficient to draw any conclusion in relation to body weight gain or obesity. Longer inter-

vention studies and more detailed assessment of energy balance and other possible confounding lifestyle factors are still warranted to ascertain the obesogenic effect of these beverages. Also, better exposure assessment, with the possible use of validated biomarkers of intake (discussed later in this chapter), would be a valuable asset in judging the evidence, especially from existing well-powered epidemiological studies.

*Sweets and desserts* is another food group that may be characterized by high sugar content and high energy density. Suggestive evidence was found that high intake of sweets and desserts is a risk factor for weight gain [23]. In an analysis in the EPIC-Potsdam cohort, each increment of 100 g per day in intake of sweets was shown to be associated with the likelihood of a short-term weight gain in men (OR, 1.48; 95% CI, 1.03–2.13) [49]. Also in cohorts in the USA, each portion of sweets and desserts was significantly associated with an increase of 0.19 kg (95% CI, 0.07–0.30 kg) in weight per 4-year period [50].

Intake of *meat in general*, which is a significant dietary source of high-quality protein and specific fatty acids, was ranked by Fogelholm et al. as a probable risk factor for weight gain [23]. Higher intake of *red and processed meat* was positively associated with both BMI (mean difference between groups with high and low intake, 1.37 kg/m<sup>2</sup> [95% CI, 0.90–1.84 kg/m<sup>2</sup>] for red meat and 1.32 kg/m<sup>2</sup> [95% CI, 0.64–2.00 kg/m<sup>2</sup>] for processed meat) and WC (mean difference between groups with high and low intake, 2.79 cm [95% CI, 1.86–3.70 cm] for red meat and 2.77 cm [95% CI, 1.87–2.66 cm] for processed meat), based on a meta-analysis of 18 observational studies [51]. However, as stated in the WCRF/AICR report, the energy density of meat depends on the amount of fat it contains and how it is cooked, whereas the fatty acid composition of meat de-

pends on its origin, processing, and animal feed. The quality of meat may differ according to the socioeconomic status of the consumer [52].

Sufficient evidence does not exist for establishing an association between body weight and intake of *fish*, a major source of omega-3 polyunsaturated fatty acids [3, 23]. No significant association was observed between fish intake and 5-year change in body weight in the EPIC study [53]. Additional evidence from a recent meta-analysis of randomized controlled trials (RCTs) that studied the effect of *fish or fish oils* on body composition found that participants in supplemented groups lost 0.59 kg more body weight, 0.49% more body fat, and 0.24 kg/m<sup>2</sup> more BMI compared with the control group and that their WC decreased by 0.81 cm more than the control group [54].

Results from two independent meta-analyses of RCTs suggested a potential beneficial effect of intake of *total dairy products* on weight loss (mean difference between groups with high and low intake, –0.61 kg [95% CI, –1.29 to 0.07 kg] [55] and –0.14 kg [95% CI, –0.66 to 0.38 kg] [56]) and improved body composition. However, this effect was significant only when dairy products were used as components of energy-restricted weight-loss diets or short-term interventions [56]. A systematic review of prospective cohort studies concluded that the protective effect of consumption of dairy products on the risk of overweight and obesity is suggestive but not consistent [57]. Subsequent findings from the Framingham Heart Study indicated a 0.10 ± 0.04 kg smaller annual weight gain in participants who consumed dairy products more frequently, probably attributable to yogurt intake [58]. Three prospective cohorts in the USA indicated a 0.82 lb (~0.37 kg) lower 4-year weight associated with yogurt consumption [50].

*Legumes* (i.e. beans, chickpeas, lentils, lupins, soybeans) could be



consumed as a plant-based alternative to animal protein. They have a lower energy density than animal protein and are good sources of fibre and microelements. Replacing energy-dense foods with legumes has been shown to have a favourable effect on obesity prevention [59] and short-term weight loss [60–62] in adults. Longer-term interventions with specific legume sources did not confirm these findings [63, 64]. The effect of legume consumption on weight control in children remains to be evaluated.

For *refined cereal products*, most reviews state that insufficient evidence exists for an association between intake and obesity [3, 35, 36], with a suggestion of an adverse effect by Fogelholm et al. [23]. *Wholegrain cereals and foods*, due to their low energy density and high fibre content, were indicated by several reports as having a protective effect against obesity and weight gain [3, 23, 35, 36]. A meta-analysis of prospective cohorts indicated a reduction of weight gain in those who consumed whole grains more frequently by 0.4–1.5 kg during 8–13 years of follow-up [65], whereas RCTs found only a small effect of wholegrain intake on the percentage of body fat (weighted difference, –0.48%; 95% CI, –0.95% to –0.01%, per g/day) [65a].

The group of *non-starchy vegetables* has similar characteristics in terms of fibre content and energy density. High-fibre/low-energy-density foods as a group were evaluated by WCRF/AICR as a probable obesity-preventive factor [3]. A meta-analysis of eight RCTs indicated that the change in body weight was 0.68 kg lower in the group with high intake of *fruits and vegetables* compared with the group with low intake [66]; however, not all studies [67] supported this inverse association, particularly in children [68]. When fruits and vegetables were considered separately, a meta-analysis of prospective cohort

studies indicated that intake of fruits and intake of vegetables were each associated with a 17% reduced risk of adiposity, whereas intake of combined fruits and vegetables was associated with a 9% reduced risk of adiposity (OR, 0.91; 95% CI, 0.84–0.99), but only intake of fruits was inversely associated with weight change [69]. A negative association with long-term weight change was also observed for higher consumption of *nuts* in three prospective cohorts (–0.26 kg 4-year weight change per one-serving increment per day in the intake of nuts) [70]. A protective effect of nuts against weight gain has been also supported by several intervention studies [71].

In a meta-analysis of three prospective cohorts, a 4-year weight loss was observed for consumption of vegetables (–0.22 lb, or –0.10 kg), whole grains (–0.37 lb, or –0.17 kg), fruits (–0.49 lb, or –0.22 kg), and nuts (–0.57 lb, or –0.26 kg) [50]. However, it should be kept in mind that GI differs for different types of fruits and vegetables. For example, potatoes – similarly to refined carbohydrates characterized by high GI – could be positively associated with higher weight; however, sufficient evidence is still lacking [3, 23] to discourage intake of starchy vegetables in relation to obesity prevention. Nevertheless, the above-mentioned meta-analysis of cohorts in the USA [50], as well as an observational study from Denmark [72], indicated a 4-year weight gain of 1.28 lb (0.58 kg) and a 5-year increase in WC in women of 0.1 cm (per 60 kcal/day, or 250 kJ/day) in relation to higher intake of potatoes. These results require confirmation based on well-established cohorts.

## Macronutrients

*Fat* is characterized by the highest energy density of all macronutrients (37 kJ/g, or 8.8 kcal/g). However, at the macronutrient level, according to the WHO/FAO report and a system-

atic review [1, 23], no sufficient or consistent evidence exists for fat or specific fatty acids and their ratios to be listed as determinants of obesity [73]. Long-term supplementation of the Mediterranean diet with unsaturated fat from olive oil or nuts improved cardiovascular health and was associated with a lower risk of obesity, as shown in the Prevención con Dieta Mediterránea (PREDIMED) trial [74, 75]. A recent systematic review evaluated four RCTs and two meta-analyses that investigated intake of fat and fatty acids in relation to body weight and composition [76]. The study concluded that there was probable evidence for a moderate positive association between total fat intake and body weight. A subsequent comprehensive meta-analysis of RCTs with a follow-up of 6–96 months showed that reduction of dietary fat intake ( $\leq 30\%$  of energy from fat) led to greater weight loss (–1.5 kg; 95% CI, –2.0 to –1.1 kg) and reductions in BMI (–0.5 kg/m<sup>2</sup>; 95% CI, –0.7 to –0.3 kg/m<sup>2</sup>) and WC (–0.3 cm; 95% CI, –0.6 to –0.02 cm) than in the control group with usual fat intake [77], but no significant association between total fat intake and measures of body fatness was found based on the evidence from 25 cohort studies [77]. This meta-analysis included only RCTs that compared a lower fat intake versus usual or moderate fat intake in subjects from the general population without any intention to reduce body weight. However, another meta-analysis based on 53 studies that compared the long-term effect ( $\geq 1$  year) of low-fat and higher-fat dietary interventions on weight loss found no effect of lowering fat intake on long-term weight loss [78].

Nevertheless, at the level of the overall dietary composition, interaction of macronutrients is more likely to have an impact on obesity control. In their meta-analysis of 23 RCTs, Hu et al. [79] compared the effects of low-fat diets ( $\leq 30\%$  of energy from

fat) versus low-carbohydrate diets ( $\leq 45\%$  of energy from carbohydrates) and found that the two types of diets resulted in comparable reduction in weight and WC. However, compared with participants following low-fat diets, those following low-carbohydrate diets experienced a slightly but statistically significantly lower reduction in total cholesterol and low-density lipoprotein cholesterol but a greater increase in high-density lipoprotein cholesterol and a greater decrease in triglycerides. Following a *low-carbohydrate* diet for at least 6 months reduced body weight by 2.1–14.3 kg and WC by 2.2–9.5 cm and led to similar or greater abdominal fat loss compared with an isoenergetic low-fat intervention [80].

With respect to the type of carbohydrate, increased intake of dietary *sugars* may be associated with an increase in body weight by 0.75 kg (95% CI, 0.30–1.19 kg) and decreased intake with a comparable weight decrease, by 0.80 kg (95% CI, 0.39–1.21 kg), as suggested by a meta-analysis of 30 trials of adults with ad libitum diets. Isoenergetic exchange of free sugars (from a diet high in fructose or sucrose) with other carbohydrates (i.e. starch or fibre) did not result in a change in body weight, suggesting that energy intake rather than the type of carbohydrate is a determinant of weight change [46]. On the basis of these outcomes, WHO concluded that the strength of evidence is moderate for the association between added sugar (including in the form of sugary drinks) and body weight gain/obesity, and suggested that longer trials (> 8 weeks) with increasing or decreasing intake of sugars should be conducted in free-living individuals to confirm this association and set the threshold of intake [4]. Special attention should be paid to fructose and fructose-containing sugars, for which mechanistic data suggest their potential effect on increased

energy intake and reduced energy expenditure (failure to stimulate leptin production) and their effect on lipid and carbohydrate metabolism (stimulation of de novo lipogenesis) [81], but also on inducing signalling and inflammatory pathways [82].

A probable obesity-protective effect of *fibre* (in both adults and children) and of low GI (in women only) has been advocated by two reviews [23, 35]. The WHO/FAO report also suggested a possible anti-obesogenic effect of *low-GI foods* [1]. As shown by a European trial, lowering the GI of a diet and increasing its protein content in an ad libitum setting led to a weight regain that was 0.95 kg lower (95% CI, 0.33–1.57 kg) compared with a high-GI diet in obese individuals after the loss of more than 8% of their initial weight. That study found an additive effect of a high-protein and low-GI diet on body weight maintenance during the 6 months after the weight loss [83, 84]. In a meta-analysis of six RCTs, a greater decrease in fat mass and BMI was observed in participants assigned to a low-GI diet compared with controls [85]. A recently published study investigated the effect of changes in intake of protein foods and glycaemic load on long-term weight gain [86]. The study, based on three prospective cohorts in the USA, showed that protein foods were not interchanged with each other but rather replaced with carbohydrate-rich foods and that an interaction between changes in intake of protein foods and glycaemic load and long-term weight gain was present. The study found that an increase in intake of protein foods that were positively associated with weight gain (i.e. unprocessed red meat and processed meat) together with a concomitant increase in glycaemic load augmented the weight gain, whereas a higher intake of protein foods associated with weight loss (i.e. nuts, seafood, and plain yogurt) generally reduced the amount of weight loss when there was a concurrent increase

in glycaemic load and increased the amount of weight loss when there was a concurrent decrease in glycaemic load.

However, the existing epidemiological evidence in relation to *protein* intake in terms of obesity prevention is not clear. In 2004, WHO concluded that there is no relationship between obesity and the protein content of the diet [1]. Later studies suggested an inverse association between protein intake and BMI ( $-4.54$  kg/m<sup>2</sup> per g/kg body weight) and WC ( $-2.45$  cm per g/kg body weight) [87] or no association for total protein intake, increased body weight for animal protein intake, and decreased body weight for plant protein intake (per  $\sim 38$  g/day) [88]. This was confirmed by Freisling et al., who investigated nutrient patterns based on the EPIC cohort [19]. The study indicated that a pattern characterized by higher intakes of plant food sources (characterized by higher intakes of folate, vitamin C, and  $\beta$ -carotene) was negatively associated with weight gain ( $-22$  g/year for men and  $-18$  g/year for women), whereas a pattern characterized by higher intakes of total protein, vitamin B<sub>2</sub>, phosphorus, and calcium was associated with a weight gain of  $+41$  g/year (95% CI,  $+2$  to  $+80$  g/year) in men and  $+88$  g/year (95% CI,  $+36$  to  $+140$  g/year) in women. However, another study based on the EPIC cohort concluded that a diet with the highest consumption of protein (> 22% of energy from protein) was associated with a 23–24% higher risk of overweight or obesity in models adjusted for energy intake, and that isoenergetic replacement of 5% of energy from carbohydrate (especially fibre) or fat by 5% of energy from protein was positively associated with weight gain after 5 years, regardless of the type of protein (animal protein or plant protein) [89].

Given the possible mechanisms of the effect of proteins on body weight related to satiety control, studies in an ad libitum setting are more likely

to observe their potential anti-obesity effect. Proteins, similarly to fibre, are believed to induce greater satiety signals by affecting gastric kinetics and release of gut hormones [90, 91]. However, this effect may depend on the type (casein vs whey) and form (liquid or solid) of macronutrient ingested, and it still needs to be elucidated whether this effect is maintained in the long term [92]. More consensus exists in the literature for the effect of protein intake on weight loss and/or maintenance. Based on two meta-analyses of experimental studies, high-protein diets resulted in greater reduction of weight/WC/fat mass and preservation of lean body mass compared with low-protein diets with similar dietary fat content [93, 94]. This effect, in turn, is believed to be attributable to greater diet-induced thermogenesis, affecting energy balance and alterations in protein turnover. Adverse health outcomes may be observed with excessive protein intakes [95].

### Biomarkers of exposure

Despite the fact that the field of metabolomics is growing, to date few validated biomarkers of dietary exposure have been used to validate dietary intakes. Some examples are urinary nitrogen (biomarker of protein intake), urinary sucrose and fructose (intake of sugars), fatty acid profiles of plasma phospholipids, erythrocytes, and adipose tissue (intake of dietary fats/fatty acids), plasma vitamins (surrogate of intake of fruits and vegetables), plasma alkylresorcinols (intake of whole grains), urine methylhistidine (meat intake), trimethylamine *N*-oxide (fish intake), and urine polyphenols (intakes of red wine, citrus, tea, soy, and olive oil), which are discussed in reviews [96–99]. More recently, the application of stable carbon isotope (<sup>13</sup>C) analysis of alanine in red blood cells was suggested as a validation marker of intake of sugary drinks and sugars [100], and a spe-

cific plasma fatty acid (elaidic acid) was suggested as a biomarker of industrial trans-fatty acids [101].

### Conclusions

Taken together, the evidence indicates that adherence to a healthy diet characterized by increased intake of low-GI foods and/or fibre (wholegrain products, non-starchy vegetables, and nuts) and avoidance of energy-dense foods (fast foods, sweets, and desserts), simple carbohydrates (including sugary drinks), low-quality processed meats, and refined cereal products should be implemented for obesity prevention. More studies are required to ascertain the effect of intake of legumes, fish, different types of dairy products, and specific fatty acids on weight and in relation to obesity prevention. To ensure better estimation of true dietary intakes, the use of exposure biomarkers is warranted.

## Key points

- Energy intake as part of energy balance plays a major role in weight gain and obesity management.
- In an ad libitum free-living setting, specific macronutrients may reduce energy intake by affecting satiety signalling.
- As part of a healthy diet, foods that are micronutrient-dense, are high in fibre, have a low GI, and/or have a low energy density (fruits and non-starchy vegetables, wholegrain products, nuts, and seeds) help to maintain a healthy body weight.
- The following may be obesity-promoting factors: energy-dense, micronutrient-poor fast foods that are high in saturated and industrial fatty acids and/or refined starches and sugars, low-quality processed meats, sweets and desserts, and sugary drinks.

## Research needs

- Well-designed longer observational and intervention studies, especially in children and adolescents, are needed to establish the link between intake of fish, different types of dairy products, fruits, vegetables, legumes, specific fatty acids, energy density, and interaction between nutrients as a part of diet and obesity and weight gain.
- Detailed, appropriate, and standardized assessment of potential confounders (including baseline BMI, weight gain during follow-up, energy intake from different dietary sources, and socioeconomic status) and outcomes (obesity and adiposity measures) should be considered.
- Measurement of validated biomarkers of dietary exposure should be used in order to better control for measurement error and reporting bias in dietary intake assessment.

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