Nutrition as a link between obesity and cardiovascular disease: how can we stop the obesity epidemic?

Marleen A. van Baak
Department of Human Biology, NUTRIM School for Nutrition, Toxicology and Metabolism, Maastricht University, Maastricht, The Netherlands

Summary
Overweight and obesity are associated with excess cardiovascular risk. To reduce cardiovascular risk at the population level, the prevention of overweight and obesity is key. This requires adoption of a healthy lifestyle, including less inactivity and more moderate-to-vigorous physical activity, and a healthy diet. Diet composition may facilitate weight gain prevention and weight loss. Effects of dietary fats, carbohydrates and proteins will be discussed in this context. Current evidence indicates that moderation of the intake of (saturated) fat, a moderate increase in protein content of the diet, a replacement of refined grain/high glucose index (GI) by whole-grain/low GI carbohydrates and limitation of the consumption of calorically-sweetened beverages are likely to facilitate weight control.

Keywords
Nutrition, obesity, prevention

Introduction
Cardiovascular disease (CVD) is worldwide a major cause of morbidity and mortality, although in many countries the prevalence has been decreasing over the last decades (1, 2). Overweight (body mass index [BMI] ≥ 25 to 29.9 kg/m²) and obesity (BMI ≥ 30 kg/m²) are associated with marked excess morbidity in terms of risk factor development and incidence of diabetes mellitus, CVD endpoints (including coronary heart disease, stroke, and heart failure), and other health conditions, including asthma, cancer, and degenerative joint disease (1). In contrast to the trends in CVD, the prevalence of overweight and obesity and especially that of type 2 diabetes mellitus is still increasing over time in many countries and this may hamper a further decline in CVD morbidity and mortality. Fortunately, stabilisation or a slowing of the rate of increase in recent years is suggested in some countries worldwide (3).

Obesity may affect the heart and vasculature through its influence on the known cardiovascular risk factors such as dyslipidaemia, hypertension, glucose intolerance, inflammatory markers, obstructive sleep apnea, and the prothrombotic state, as well as through yet-unrecognised mechanisms (4).

Cardiovascular health requires the presence of both favourable health behaviours (non-smoking, BMI <25 kg/m², physical activity at goal levels, and pursuit of a diet consistent with current guideline recommendations) and favourable health factors (untreated total cholesterol < 5.2 mmol/l, untreated blood pressure <120/<80 mmHg, and fasting blood glucose < 5.6 mmol/l) (5). To achieve improvements in cardiovascular health, improved cardiovascular health behaviours, in particular with regard to diet and weight, as well as an increase in physical activity and further reduction of the prevalence of smoking should be stimulated at the population level. Dietary factors may influence cardiovascular health both directly as well as indirectly by reducing body weight or preventing weight gain. In this paper the effects of diet on body weight and body composition will be reviewed.

Obesity: total body fat, fat distribution and ectopic fat
Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health. BMI provides the most useful population-level measure of overweight and obesity, as it is the same for both sexes and for all ages of adults. However, it does not correspond to the same degree of fatness in different individuals. Moreover, disease risk is not only dependent on percent body fat, but also on the localisation of the body fat. Visceral fat accumulation is associated with higher cardiometabolic disease risk. Although abdominal obesity is an important clinical tool for identification of individuals likely to possess metabolic abnormalities, the metabolic syndrome and diabetes appear considerably more important prognostic indicators of CVD risk than abdominal obesity (waist circumference) as such (6). The visceral fat mass surround-
ing the visceral organs and vasculature and the accumulation of fat in non-adipose cells, such as liver, heart, pancreas, kidney and skeletal muscle cells, may all contribute to the increased risk.

**Fat tissue function and dysfunction**

The normal function of subcutaneous fat tissue is that it stores surplus energy after a meal in the form of fat and releases it again when needed. When energy intake exceeds energy expenditure, subcutaneous fat mass increases. The storage capacity of the enlarged fat cells may decrease, for instance due to insulin resistance which will protect hypertrophied fat cells against lipid overload (7). Another mechanism may be that adipose tissue blood flow does not keep track with the increase in fat mass (8). A lower adipose tissue blood flow may hamper the clearance of circulating triglycerides (9) and increase the re-esterification of fatty acids in adipose tissue (10), which will lead to an impaired lipid buffering capacity. The postprandial increase in adipose tissue blood flow is also blunted in obesity (11). Circulating triglycerides that are no longer taken up by the subcutaneous fat cells postprandially will be deposited in other places (12), which will lead to enlargement of visceral (mesenteric, omental and retroperitoneal) fat stores, fat accumulation around the organs and blood vessels, but also ectopic fat accumulation in the liver, the heart, the skeletal muscle, and the pancreas (13). The level of subcutaneous fat mass at which fat mass loses its full buffering capacity may differ between individuals. Factors like age, gender, genetics, and ethnicity play a role (13). Although the visceral fat depots have normal functions in providing energy in times of shortage, in mechanical protection, and also serve a thermoregulatory role, increased amounts may be associated with organ dysfunction due to mechanical compression, local release of too large amounts fatty acids and of pro-inflammatory substances or other not fully elucidated mechanisms (13, 14). For instance, the putative physiological functions of human epicardial adipose tissue (EAT) include lipid storage for the energy needs of the myocardium, thermoregulation, whereby brown fat components of EAT generate heat by non-shivering thermogenesis, neuroprotection of the cardiac autonomic ganglia and nerves, and regulation of vasomotion and luminal size of the coronary arteries. Under pathophysiological circumstances (increased stores), EAT may play an adverse paracrine role in cardiac arrhythmias, in lipotoxic cardiomyopathy, and inflammation associated with coronary artery disease (15).

**Weight loss and cardiovascular disease**

Whereas the effect of weight loss on cardiovascular and diabetes risk factors and the metabolic syndrome has been clearly demonstrated (4, 16), evidence for the effect of intentional weight loss on cardiovascular disease and mortality is limited. In a recent overview key results of the Swedish Obese Subjects (SOS) trial, in which the long-term effects of bariatric surgery were compared with usual care, were summarised (17). Bariatric surgery was associated with a reduced number of cardiovascular deaths and with a lower number of total first time (fatal or non-fatal) cardiovascular events. However, there was no association with the magnitude of the weight loss after two years, suggesting that there is no straightforward dose-response relationship between weight loss and cardiovascular risk reduction. One of the suggestions of the SOS investigators is that following a relatively modest weight loss induced by bariatric surgery, there may be no further risk reduction attributable to greater, subsequent weight loss (17).

**Role of nutrition in weight management**

The main pillars of weight management are reducing (or not increasing) energy intake in relation to energy expenditure, improving diet quality, and increasing physical activity (PA). It is a matter of debate whether diet composition is important in weight management (18, 19). In the context of energy restriction, which is prescribed in most weight loss studies, dietary macronutrient composition is likely to be of minor importance. A recent large-scale study investigated weight loss maintenance over 2.5 years after a six-month weight loss programme (reduced calorie intake, consumption of the Dietary Approaches to Stop Hypertension [DASH] dietary pattern, 180 minutes of moderate-to-vigorous activity [MVPA per week]) with continuation of consumption of the DASH dietary pattern and a further increase in MVPA over the 2.5-year weight maintenance period (20). Over 1,000 individuals were included in the weight maintenance phase. A significant association between a higher Healthy Eating Index (21) and better weight loss maintenance was found. The investigators suggest that individuals who are adherent to recommendations concerning dietary pattern may also be more adherent to recommendations concerning caloric restriction and that weight loss can be maintained in the context of a dietary pattern consistent with current dietary guidelines (20). It may also be that adherence to this type of diet facilitates moderation in dietary intake.

Key population dietary goals for the prevention of cardiovascular disease include: limiting intake of total dietary fat, particularly saturated and trans fats, limiting intake of salt (sodium), carbohydrate, added sugars, and specifically sugar-sweetened drinks, and increasing intakes of fruit and vegetables and dietary fibre, in addition to limited or moderate alcohol intake, maintenance of healthy body weight and participation in physical activity.

For weight management the dietary focus is on maintaining energy balance to prevent weight (re)gain or to moderate dietary intake for weight loss. As indicated above, when a certain level of energy restriction is prescribed to attain weight loss, the exact dietary composition seems to be less important and people can select a diet that best fits their taste and possibilities. Since the long-term maintenance of weight loss and the prevention of weight gain in a more ad libitum situation are much more difficult to attain for many individuals, the question whether the diet composition will facilitate weight loss maintenance or weight gain prevention in the population is of much more importance. Diet composition can affect energy balance by either moderating energy intake, for instance by being more satiating and hunger suppressing, or stimu-
lating energy expenditure, for instance by increasing thermogenesis. From energy balance point of view, macronutrients are most influential and the role of different macronutrients in weight management, with a focus on prevention of weight (re)gain, will be discussed below. The review will focus on body weight (or BMI), because these parameters are mostly reported. However, it remains important to realise that not body weight as such, but body fat and body fat distribution are important for cardiovascular risk. The amount of total body fat and visceral adiposity are strongly correlated (shared variance of ~50%) (13). It is therefore likely that interventions that will reduce total adiposity will induce some (albeit variable) loss of abdominal fat. Studies tend to show that the greater the initial amount/proportion of visceral adipose tissue, the greater is the loss of visceral relative to subcutaneous adipose tissue in response to weight loss (13).

**Dietary fats**

The role of dietary fat content of the habitual diet has been extensively reviewed previously (22-25). In the large majority of the studies included in these reviews, the reduction in fat content was accompanied by an increase in carbohydrate content, leaving protein content unaffected. Moderate reductions of fat content of around 10% of total energy intake were associated with moderate weight loss or reduced weight gain under *ad libitum* conditions (25). The mean duration of most studies included in these reviews is relatively short (<6 months). In a more recent systematic review and meta-analysis only studies with longer follow-up and with no intention for weight loss were included (>6 months for trials, >12 months for observational studies) (26). Weight gain was consistently lower in the low fat arms than in the control arms. Studies with a reduction of fat intake between 5 and 15% of total energy intake showed the most consistent effects on body weight. Meta-analysis including all available studies suggested that diets lower in total fat were associated with lower relative body weight (by 1.6 kg, 95% confidence interval (CI) -2.0 to -1.2 kg, $I^2 = 75\%$, 57,735 participants) (26).

Although such a difference may seem minor from an individual perspective, its effect on public health should not be underestimated. Therefore, lowering of dietary fat intake remains key in weight management. It is likely that reduction of the fat content of the habitual diet increases the satiating capacity of the diet and will increase postprandial thermogenesis.

**Modification of type of fat**

The major groups of dietary fats are saturated fat (SFA), mono-unsaturated fat (MUFA) and poly-unsaturated fat (PUFA) fat. Although the type of dietary fat is important in cardiovascular risk reduction, its role in weight management is less evident. Postprandial does not seem to differ after consumption of isocaloric high SFA, high MUFA or high PUFA meals (27). No difference in postprandial thermogenesis between high SFA and high MUFA meals was found, although postprandial fat oxidation was increased after the high MUFA meal (28). Several animal studies and a very limited number of human studies suggest that PUFAs may reduce food intake and stimulate energy expenditure, but there is a clear lack of adequately designed longer-term human studies in this area (29, 30). Schwingshackl et al. (31) recently compared the effect of low and high MUFA diets on body weight in a meta-analysis. Duration of studies had to be at least six months. Dietary regimens with a high amount of MUFA (>12%) were compared to those with MUFA content ≤12%. Significant differences between high- and low-MUFA protocols could be observed with respect to fat mass [-1.94 kg (95% CI -3.72, -0.17), $p = 0.03$], but not for body weight [-0.82 kg (95% CI -1.87 to 0.22), $p = 0.16$]. However, these results are difficult to interpret because both weight loss studies with prescribed energy intake in both arms as well as studies in which weight was kept constant in both intervention arms were included. Moreover, low- and high-MUFA diets likely differed in many other dietary factors.

For the moment, there is no evidence that modification of the ratio between SFA, MUFA and PUFA in the context of an *ad libitum* diet will lead to better weight maintenance.

Tchernof and Després suggest in a recent review that fatty acid composition of the diet may have an impact on body fat distribution patterns above and beyond its impact on overall adiposity levels (13). The evidence for this statement is suggestive at the most and more studies are needed to further substantiate this hypothesis.

**Dietary carbohydrates**

As indicated above, studies that have compared high and low fat diets generally exchanged fat for carbohydrate, leaving protein content unaffected. This means that lowering fat and thereby increasing carbohydrates intake in *ad libitum* diets has a small, but beneficial effect on body weight. Based on a systematic review of the literature Hauner et al. (32) judged the evidence regarding the lack of a long-term effect of a change in carbohydrate intake on the development of obesity as probable.

This seems in contrast with data suggesting that low(er) carbohydrate diets induce more weight loss than higher carbohydrate diets in people who want to lose weight (33). On the other hand, another meta-analysis comparing low-fat with low-carbohydrate weight loss diets including a larger number of studies found no difference in weight loss between the two types of diets (34). Some low-carbohydrate diets were likely to be relatively high in protein and the beneficial influence of higher protein intake (see below) may be larger than the negative effect of higher fat intake.

**Modification of types of carbohydrates**

The major dietary carbohydrates are sugars (mono- and disaccharides), sugar alcohols (polys), oligosaccharides and polysaccharides (starches and non-starch polysaccharides). Different types of carbohydrates have different functional effects, therefore a classification based on functional properties, such as glycaemic...
index (GI), is also used. In addition the form in which carbohydrates are consumed, for instance in beverage or solid form, may also have distinctive effects.

**Sugars vs non-sugar carbohydrates**

We have previously reviewed the effects of intake of sugars vs. non-sugar carbohydrates with respect to body weight (25). Based on this review, we concluded that there was insufficient evidence that exchanging sugars for non-sugar carbohydrates in the context of a fat-reduced *ad libitum* diet or in the context of energy-restricted diets results in lower body weights. However, a lack of high quality randomised trials was acknowledged (25). Another narrative review by Ruxton et al. reached similar conclusions (35). Hauner et al. (32) concluded that the evidence for a specific contribution of mono- or disaccharides to the risk of obesity is insufficient.

**Sugar-sweetened beverages**

The effect of sugar-sweetened beverages (SSB) consumption on body weight has been heavily debated over the last decade. A number of reviews and meta-analyses have been published on this topic with varying conclusions. Van Baak and Astrup concluded that a limited number of randomised controlled trials support the positive association between BMI and SSB consumption that is found in observational studies, although not consistently (25). Gibson, on the other hand, concluded that there is little evidence from epidemiological studies that SSB are more obesogenic than any other source of energy (36). Wolff and Dansinger considered the evidence for SSB-related weight gain weak (37). In contrast, Olsen and Heitmann stated that a high intake of calorically sweetened beverages can be regarded as a determinant for obesity (38). Most recently, Malik et al. concluded that SSB intake is a significant contributor to weight gain (39), probably in part because of incomplete compensation for liquid calories at subsequent meals (39, 40). Hauner et al. (32) judged the evidence that a higher consumption of sugar-sweetened beverages is accompanied by an increased risk of obesity as probable.

A well-controlled randomised study by De Ruyter et al., published in 2012, addressed the question whether reduction of daily SSB intake by masked replacement of a SSB for a non-calorically sweetened beverage would reduce body weight in children. A total of 641 children aged 4 to 12 years were included, and 477 concluded the 18-month study. After 18 months the difference in body weight gain between the groups was 1 kg (95% CI for the difference, −1.54 to −0.48). Skinfold thicknesses, reflecting body fat, also increased significantly less in the non-SSB group (41). This important study strongly suggests that limiting calorically sweetened beverage consumption will lower body weight and fat mass in the population. Another study by Maersk et al. (42) showed that visceral fat and ectopic fat accumulation in liver and skeletal muscle and was higher in overweight subjects who drank 1 liter/day of SSB during six months compared to the consumption of an equal amount of aspartame-sweetened beverages, water or isocaloric semi-skimmed milk. Changes in total fat mass did not differ between groups.

**Glycemic index and glycemic load**

The glycemic index (GI) of a food is based on the average blood glucose response over 2 hours after consumption of an amount of this food that contains 50 grams of available carbohydrates in comparison to the blood glucose response after consumption of 50 grams of glucose (43). GI multiplied by carbohydrate amount is the glycemic load (GL). The GI of a diet is the weighted means of the GI of all foods eaten.

The glycemic index of foods introduced by Jenkins in 1981 (44). In 1999 Ludwig et al. (45) suggested that a high GI diet might lead to obesity, because consumption of a high GI meal induced hormonal and metabolic changes that increased hunger and subsequent food intake compared to a low GI meal. The importance of a low GI and/or low GL diet for weight control has been advocated since that time (46-49), and has been fuelled by the popular press. The popular belief that low GI diets are beneficial for body weight was not based on firm evidence, because high-quality randomised trials were lacking. Livesey et al. (50) concluded from a meta-analysis of GL studies that a reduction of dietary GI tended to lower body weight, but that the effect is modest and was most consistent with a GL reduction of at least 42 g d$^{-1}$. Based on a descriptive review of a similar selection of studies, Van Dam and Seidell, on the other hand, concluded that studies that have directly compared low- and high-GL diets do not consistently support the hypothesis that a low-GL diet supports weight loss (51). Thomas et al. (52) reported a mean difference of 1 kg body weight and fat mass in favour of low GI/GL diets in a meta-analysis of six studies. A clear distinction between low GI and low GL was not made. In 2009 we concluded, based on available evidence at the time, that there was no evidence that an *ad libitum* diet with a low GI caused a lower body weight than a diet with a high GI when total carbohydrate intake was not different. However, a clear need for more well-designed randomised controlled trials (RCTs) with GI differences between intervention groups of different magnitudes to investigate a potential dose–response relationship was indicated (25). Hauner et al. (32) judged the evidence regarding the relevance of GI or GL for the risk of obesity as possible at the most.

In 2010, results of the European Diogenes trial were published (53). The Diogenes trial was a large multi-centre study in eight European countries. The main questions were whether lowering the GI and increasing the protein content of the habitual *ad libitum* diet would better prevent weight regain in obese individuals who had lost at least 8% of their body weight by means of a low-calorie diet. Body weight regain over six months was 0.95 kg (95% CI, 0.33 to 1.57) lower in the groups that consumed the low GI diet compared to the high GI diet (53). This large study supports the idea that advising people to consume a low GI diet, despite all practical issues associated with such advice (54), may help them to better maintain a healthy body weight.
**Fructose**

The role of fructose consumption in the obesity epidemic has been heavily debated since Bray et al. (55) proposed a causal relationship between the increase in obesity in the US and the parallel increase in consumption of high-fructose corn syrup (HFCS)-sweetened beverages and the potential detrimental effects of high fructose intake in 1994. Although the debate originally focused on whether there was a difference between HFCS- and sucrose-sweetened beverages, it has now shifted more to the general obesogenic effect of calorically-sweetened beverages (56-60). Nevertheless, the discussion has continued whether fructose may have detrimental effects on body weight or body fat (distribution) independent of its caloric contribution.

We have recently reviewed the effects of fructose ingestion on appetite and postprandial energy expenditure (61). Potential mechanisms for a lower satiation after fructose- than glucose-containing meals could be the lower GI, the lower postprandial suppression of the orexigenic hormone leptin and lower increase in the satiety hormone leptin (62). In 2009, Moran reviewed acute preload studies comparing glucose, sucrose and fructose in either pure solutions or in mixed solutions/meals with respect to satiety (63). Intrinsic differences among the sugars were not found. Dolan et al. (64) reviewed long-term studies with dietary fructose intake up to 100 g/day. They concluded that there was no convincing evidence that such an amount of fructose intake compared to sucrose or glucose was associated with an increase in food intake. With respect to postprandial energy expenditure, studies suggest that the more pronounced increase in energy expenditure after fructose, sucrose or glucose-fructose mixture ingestion compared to glucose ingestion is due to the fructose component (61). The higher fructose-induced postprandial energy expenditure is probably due to the energy cost of fructose metabolism to glucose in the liver and continued gluconeogenesis.

A new and interesting hypothesis is that continuous exposure to fructose and sugar substitutes may cause loss of microbial genetic and phylogenetic diversity in the gut (65). This may lead to the generation of additional energy sources for the host, which may facilitate aberrant host–microbe interactions. This, in turn, might lead to disturbed energy regulation and altered gut transit times with subsequent enhancement of dietary energy extraction (65).

Thus, high fructose consumption may, from a mechanistic perspective, have both favourable as well as unfavourable influences on energy balance and body weight. Sievenpiper et al. (66) recently reviewed studies on the effect of fructose on body weight. Studies were usually small and of short duration. It was concluded that in studies where energy intake was controlled no weight differences were found between fructose and isocaloric amounts of other carbohydrates and that fructose overfeeding increased body weight, which was related to the increased calorie intake (66). Because there is also insufficient evidence that exchanging sucrose for non-sucrose carbohydrates (which are lower in fructose) in the context of a fat-reduced *ad libitum* diet or in the context of energy-restricted diets results in lower body weights (25, 61), there is currently insufficient evidence that high fructose consumption in an *ad libitum* diet, except in the form of sweetened beverages (see above), is associated with weight gain. However, high quality randomised trials of sufficient size and duration directly testing this are still needed to increase the evidence base.

Thernof and Després (13) suggested that fructose consumption stimulates deposition of triglycerides in non-adipose tissues and thus the accumulation of ectopic fat, independent of its impact on overall adipose tissue accretion. The study on which this statement is based showed that when overweight or obese men and women were given either glucose- or fructose-sweetened beverages providing 25% of energy requirements for 10 weeks changes in body fat were comparable [glucose: 3.2 ± 0.6 kg (not significant), fructose 2.8 ± 1.0 kg (p<0.05)], whereas the increase in visceral fat in the fructose treatment arm was 8.6 ± 3.0 cc (p=0.01) and in the fructose treatment 4.8 ± 2.1 cc (not significant) (67). No results of statistical tests comparing the changes in total fat mass and visceral fat in the glucose and fructose groups were reported, so it remains speculative whether these were robust differences. Ectopic fat accumulation was not reported. Moreover, the amount of fructose provided was extremely high (twice the recommended upper level of intake of fructose in the form of added sugar), making this study more a proof-of-concept study than a study reflecting normal dietary practices.

**Fibre**

In 2011 an extensive systematic review was published on dietary fibre, appetite and body weight (68). The different fibre structures were taken into account. More viscous fibre types (e.g. pectins, beta-glucans and guar gum) reduced appetite and acute energy intake more often than less viscous fibre types. For the effect on body weight 66 fibre/control comparisons were selected with an average duration of 11 weeks (range 3 to 15 weeks), so relatively short-term. All studies had to be *ad libitum* with respect to total energy intake. Overall, effects on body weight were relatively small, the mean effect size was -0.7 kg. However, this does not exclude the possibility that more weight loss would be achieved with prolonged study duration. High-quality randomised trials with a longer study duration are clearly needed. No clear dose-response was found and no association with specific fibre characteristics, suggesting that fibre intake may affect energy balance by mechanisms other than appetite alone. Potential additional mechanisms are via an effect on gut microbiota composition, short-chain fatty acid production and gastrointestinal hormone release (68).

**Whole-grain**

Based on a meta-analysis of prospective cohort studies, Ye at al. (69) concluded that higher intake of whole grain is associated with less weight gain during follow-up (8-13 years). A recent RCT showed that consumption of an energy-restricted diet with whole-grain wheat during 12 weeks resulted in a greater reduction in fat mass but no difference in body weight loss compared to a diet with refined wheat (70). Clearly, longer trials are necessary to show the full potential of whole-grain enriched diets on body weight and...
Van Baak: Diet and body weight

body composition. Brand-Miller and Buyken warn that whole-grain products are not always low GI, because many products advertised as whole-grain contain high amounts of finely milled endosperm and are thus high GI (48). A careful selection of whole-grain products with low GI is therefore warranted.

**Dietary proteins**

High protein diets are being advocated for better weight control because of their satiating and thermogenic capacity (71). The evidence has recently been reviewed in several narrative reviews and meta-analyses with differing inclusion criteria for studies (71-74). All reviews confirm the beneficial effects of higher compared to lower protein intake for weight loss or prevention of weight (re)gain. The meta-analysis by Wycherley et al. (73) included only weight-loss trials that compared isocalorically prescribed diets matched for fat intake but that differed in protein and carbohydrate intakes. Twenty-four trials that included 1,063 individuals were included with mean diet duration of 12.1 ± 9.3 weeks. The high protein diets produced more favorable changes in weighted mean differences for reductions in body weight (-0.79 kg; 95% CI -1.50 to -0.08 kg) and fat mass (FM; -0.87 kg; 95% CI -1.26 to -0.48 kg) and less reduction in fat-free mass (FFM; 0.43 kg; 95% CI 0.09 to 0.78 kg) (73). The meta-analysis by Santesso et al. (74) included both weight loss and weight maintenance trials. RCTs were included if the protein difference between arms was at least 5% of total energy intake, and attained by means of normal foods (no supplements). Study duration had to be at least four weeks. In total the meta-analysis on body weight included 38 studies with over 2,000 subjects. The overall weight change after three months was significantly lower in the high than in the low protein arm (mean difference -1.21 kg (95% CI -1.88 to -0.57)), and this was also true for waist circumference (mean difference -1.7 cm (95% CI -2.7 to -0.6)) (74). The Diogenes trial, which was not included in this meta-analysis because the difference in dietary protein content at six months was less than 5% of total energy intake (although the reported difference was 5.4% [53]), the weight regain was 0.93 kg less (95% CI, 0.31 to 1.55) in the groups assigned to the high-protein diet than in those assigned to the low-protein diet (p=0.003) (53). These data suggest that a moderate increase in dietary protein content by ~ 5% of energy intake is beneficial for weight control.

**Plant and animal protein**

In the meta-analyses discussed above type of protein was not addressed, but not all protein types may be equally beneficial for body weight control. Halkjaer et al. (75) studied the effect of dietary protein content on body weight and waist circumference changes in EPIC cohorts with a follow-up of 6.5 years, including almost 90,000 individuals in five European countries. Per 150 kcal/day of animal protein intake (~ 38 g/day) body weight increased 56 g/year, whereas the increase per 150 kcal of plant protein was 18 g/year. For waist change such differences were not found. In an analysis of the US cohort of the cross-sectional INTERMAP study including almost 1,800 individuals a higher BMI was associated with higher animal and lower vegetable protein intake (expressed as % of protein intake or energy intake) (76). No RCTs comparing the effects diets enriched in plant or animal protein on body weight and fat mass have been performed.

**What can we do to stop the obesity epidemic?**

In order to stop the obesity epidemic, prevention of unhealthy weight gain already from a young age is key. As discussed above, diet composition may play a role in facilitating the prevention of unhealthy weight gain. From this perspective, moderating (saturated) fat intake and increasing protein intake, increasing the intake of low GI and high-fibre carbohydrates and limiting the intake of sugar-sweetened beverage would be a good strategy. However, long-term changes in dietary habits are very difficult to attain and supporting policies will be needed to attain more healthy dietary habits in the population.

**Conflicts of interest**

None declared.

**References**