Turkish Journal of Endocrinology and Metabolism, (2003) 4 : 141-148 **REVIEW**

Dietary Fat & Obesity: Still an Important Issue

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The role of a reduction in dietary fat for weight loss and maintenance should be assessed by evidence based principles giving most weight to randomised clinical trials. Four meta-analyses have examined weight changes on ad libitum fat-reduced diets in intervention trials lasting up to a year, and they all demonstrate a 3-4 kg larger weight loss on the fat-reduced than on the normal-fat diet in normal weight and overweight subjects. The analyses also show a dose-response relationship, i.e. the reduction in percent energy as fat is positively associated with weight loss. Weight loss is also positively related to initial weight - a 10% reduction in dietary fat is predicted to produce a 4-5 kg weight loss in an individual with a BMI of 30 kg/m2. The outcome of the meta-analysis of trials with long-term follow up included only 6 studies, and none of the trials had an active intervention throughout the period.

Short-term trials clearly demonstrate that the non-fat diet components are at least as important for body weight regulation as the fat content. Sugar in beverages is less satiating and more obesity-promoting than sugar in solid foods, and replacement of energy from fat by sugar derived from sweetened beverages is not likely to produce weight loss. Protein is more satiating and thermogenic than carbohydrates, and a fat-reduced diet with a high protein content (20-25 % of energy) may increase the efficacy of fat-reduced diets markedly. Whereas the glycemic index of the carbohydrate may play a role for cardiovascular risk factors, there is very little evidence to support that low glycemic index foods facilitate weight control. The evidence linking particular fatty acids to body fatness is weak. If anything, monounsaturated fat may be more fattening than polyunsaturated and saturated fats, and no ad libitum dietary intervention study has shown that a normal-fat, high MUFA diet is equivalent or superior to a low-fat diet in the prevention of weight gain and obesity. The current evidence strongly supports a diet with reduced content of fat and sugar-rich beverages, and more carbohydrates rich in fibre and grain (whole grain foods, fruit and vegetables) and protein (lean meat and dairy products) as the best choice for the prevention of weight gain, obesity, type 2 diabetes and cardiovascular disease. The use of a normal-fat, high monounsaturated diet needs more evidence from randomised ad lib dietary intervention trials before it can be recommended to the public.

Key words: Low-fat diets, Weight loss, Obesity

The currently recommended diet

In order to prevent cardiovascular disease, cancer, obesity and type 2 diabetes it is recommended that dietary fat should be reduced from the current 35-45% of the total energy content in most Western diets to below 30% (1, 2). However, observational epidemiology does not support that this reduction in total fat content is a prerequisite for primary and secondary prevention of cardiovascular disease, because monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA) are less atherogenic than saturated fat and even carbohydrate (3). This has been translated into the public health recommendations by Willett and co-workers that the total fat content of the diet is unimportant, and that trans fat and saturated fat just needs to be replaced by MUFA and PUFA. They conclude that recommending a reduction in total dietary fat is misleading and unnecessary, and they point at starchy carbohydrates with a high glycemic index

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as posing a greater risk of producing weight gain, and obesity, and increasing cardiovascular risk (4).

The present review examined the evidence in favour of a fat-reduced diet (25-30% energy from fat) versus a normal-fat (30-40%) high-MUFA diet for the prevention of weight gain and obesity, type 2 diabetes and to some extent cardiovascular disease.

The evidence-based principle was used to assess the strength of the existing documentation to substantiate whether one of the diets is superior to the other (5). Notably, meta-analysis of randomised controlled trials is recognised as being the strongest evidence, followed by experimental studies, and finally by observational epidemiological studies and personal opinions.

How does dietary fat influence energy balance ?

A link between dietary fat content and obesity must be exerted through an effect of the ingested fat on energy balance, and a positive energy balance can be promoted by overconsumption of energy, e.g. due to a lower satiating effect per Joule of a high-fat vs. a low-fat diet. Moreover, energy from fat could be more effectively absorbed from the intestine than carbohydrate and protein, and fat may also reduce energy expenditure, e.g. by a lower thermogenic effect of fat compared to carbohydrate and protein. All evidence points at that fat exerts its effect on energy balance by affecting spontaneous energy intake, and the relation between dietary fat and body fat should therefore be studied under *ad libitum* conditions, where the studied individuals have free access to food.

There is a robust series of studies showing that most of the fattening effect of dietary fat is linked to the higher energy density of fatty foods than carbohydrate and protein rich foods (For review see Rolls et al, ref. 6)

The 4 meta-analyses of randomised clinical trials on fat-reduced versus normal-fat diets

We are aware of 4 meta-analyses of controlled trials comparing low-fat diets with normal-fat diets as a control under *ad libitum* conditions. In a systematic review and meta-analysis based on 28 intervention trials Bray and Popkin found that a reduction of 10% in the proportion of energy from fat was associated with a reduction in weight of 16 g/d. This corresponds to a weight loss of 2.9 kg over 6 months (7). Our own first meta-analysis included a total of 1728 individuals, and 13 studies were randomised, controlled trials. The control groups were either advised to continue their regular diet or to consume a diet with a fat content comparable to that of the background population. The low-fat interventions produced a weight loss of 2.4 kg more than in the control groups (95-% CI, 1.9–2.9; $P < 0.0001$) in the fixed effects analysis, and 2.5 kg more (1.5–3.5; $P<0.0001$) in the random effects analysis. In a simple correlation analysis the major determinant of the weight loss difference was pre-treatment body weight ($r = 0.52$, $P < 0.05$). There was a dose-response relationship between the reduction in % dietary fat intake and weight loss after adjustment for pre-treatment body weight, ($r = 0.66$, $P < 0.005$). With no change in % dietary fat intake, no weight change occurred (8).

The third meta-analysis included 37 dietary intervention studies, and found weight loss in the intervention groups to be 2.8 kg larger than in the control groups, and there was a highly significant relation between reduction in dietary fat and weight loss (9). For every 1% decrease in energy from fat there was a 0.28 kg decrease in body weight.

The fourth meta-analysis was from my own group, and we now included new trials and excluded any trial in which the intervention group was instructed to increase physical activity. We included16 trials (duration of 2 ± 12 months) with 19 intervention groups, which gave a total of 1910 individuals participating in studies. Weight loss was not the primary aim in 11 studies. Before the interventions the mean proportion of dietary energy from fat in the studies was 37.7% in the low-fat groups, and 37.4% in the control groups. The low-fat intervention produced a mean fat reduction of 10.2% (8.1 - 12.3). Low-fat intervention groups showed a greater weight loss than control groups (3.2 kg, 1.9 - 4.5 kg; $P <0.0001$), and a greater reduction in energy intake (1138 kJ/day, 564 - 1712 kJ/day, $P< 0.002$). A pre-treatment body weight 10 kg higher than the average was associated with a 2.6 kg greater difference in weight loss (10). These 4 meta-analyses thus consistently show that a reduction in dietary fat without restriction of total energy intake causes reduction in caloric intake and weight loss in a

dose-dependent fashion and may produce a modest, but clinically relevant, weight loss in overweight subjects.

The 5th meta-analysis: does fat reduction work in the long term ?

Pirozzo et al. (11) have conducted a meta-analysis to determine the effectiveness of fat-reduced diets in achieving sustained weight loss when used for the expressed purpose of weight loss in obese or overweight subjects. The analysis included six trials, and they conclude that low-fat diets are as efficacious as other weight-reducing diets for achieving sustained weight loss but not more so. Hill and Astrup (12) have expressed some concerns about the conclusions drawn from the meta-analysis by Pirozzo et al. (11). The major problem is the very few trials that met the inclusion criteria set by the authors. Several trials supportive of low fat diets in weight management did not meet these criteria. This suggests that despite the tremendous interest and debate about the best diets to recommend for long-term weight loss, there are surprisingly few studies that address this issue. Second, there are some important differences in study design among the six studies. For example, two studies were of only 3-4 months duration, 3 trials lasted only 6 months, and one was of 18 month in duration. It is very difficult to compare a study where intervention was 3 months to one where intervention was 18 months. While the authors aimed to assess the effectiveness of the different diets on sustained weight loss, none of the studies had active intervention during the follow-up period. Thus, the questions addressed is not whether low fat diets can sustain weight loss but whether a few months of low-fat eating can lead to sustained weight loss. To answer the first question, studies would have to continue active intervention (fat-reduced versus normal-fat) for sustained periods of time. This was not done in any of the six studies included in this meta-analysis, but can be found in other trials (13, 14).

Does 3-5 kg weight loss really matter ?

A sustained weight loss of 3-5 kg in obese at high risk for diabetes or cardiovascular disease is sufficient to reduce the incidence of type 2 diabetes by 40-60 % (15-17), and reduce the incidence of cardiac events by ~40 % (13, 14, 18), and increasing physical activity amplifies the effect (9). Type 2 diabetes is associated with an almost 10 year reduction in life expectancy, mainly due to increased cardiovascular mortality, and its prevention therefore has substantial health benefits.

In addition, typical weight loss of 3-5 kg produced by *ad libitum* low-fat diets is more likely an underestimation of the true effect. Obviously, adherence to the low-fat diets can be difficult in a "toxic high-fat, soft drink environment". There is good evidence to demonstrate the necessity of some sustained intervention therapy in order to counteract the tendency to fall back into usual dietary habits. Consequently, compliance and diet adherence become key issues to consider when assessing the efficacy of fat-reduced diets in long-term weight management.

A number of the trials have provided some evidence to support that incomplete dietary compliance tends to underestimate the real effect of a fat reduction. Swinburn et al. found that weight loss on an *ad libitum* low-fat diet was 3.3 kg after one year (19). However, if the subjects in the intervention group was stratified according to compliance assessed by attendance at the monthly meetings and completion of the diet diaries one gets a better idea about the efficacy of the low-fat diet to produce weight loss. While those is the less compliant group lost only about 1 kg, the more compliant group lost almost 6 kg after one year (19). Moreover, it is evident that many people think that they are consuming a low-fat diet but are not aware of many of the foods they eat are high-fat. Such factors will contribute to underestimate the real efficacy of low-fat diets. The follow-up in this trial clearly shows that unless the intervention is reinforced regularly the patients will inevitably relapse. In this aspect, dietary treatment does not differ from other medical treatment: it only works as long as it is taken!

The role of different carbohydrates: a role for fibre and whole grain foods

Glycemic index of foods

In Willetts suggestion for a new "inversed" food pyramide it is stressed that the carbohydrate rich foods should predominantly be whole, grain fibre

rich, with a low glycemic index (GI) (4). The long-term effects of a diet containing low or high GI foods on body weight have been very poorly investigated (20, 21), and the interpretation of the current body of evidence is conflicting (22). In the majority of the published studies a low GI diet has been found to produce favourable effects on risk factors of diabetes and cardiovascular diseases compared to a high GI diet. Since most of the intervention studies have used diets aiming at energy balance or energy reduction the effects on body weight are, however, still unclear, and recent evidence suggests that GI of composed meals are unpredictable based on the tables providing GI values for individual foods (23).

Complex versus simple carbohydrates

The role of different types of carbohydrate in the regulation of body weight has not been investigated as thoroughly as the role of the total dietary fat content. A few recent studies have illuminated this area with regard to carbohydrate structure (e.g. simple/complex carbohydrates, sucrose/starch). The largest and most recent is the CARMEN multicentre trial, which involved a total of 316 overweight subjects in 5 different countries (24). In this study, the impact of 6 months' *ad libitum* intake of low-fat diets, rich in either simple or complex carbohydrates, on energy intake, body weight and blood lipids was investigated. The results showed that both low-fat diets reduced body weight by 1.6 kg and 2.4 kg, respectively, compared with the normal-fat control diet. The slightly lower weight loss on simple carbohydrates than on complex carbohydrates did not reach statistical significance. Furthermore, no detrimental effects on blood lipids were observed during either of the two carbohydrate diets. According to this study, the type of carbohydrate (simple sugars vs. complex carbohydrates) does not seem to have much importance for body weight regulation and risk factors as previously suggested.

As we alluded to above, the low energy density of carbohydrates as compared with fat is important. One gram of carbohydrate (17 kJ/g) provides less than half the calories of one gram of fat (37 kJ/g). This means that a smaller amount of calories is consumed in a carbohydrate rich meal than in a fat-rich meal of similar weight. A starch and fibre rich diet is often comprised of a surprisingly large volume of foods. In one long-term study using such a diet, the volunteers actually had problems consuming the large volume of food, especially the diets composes for the volunteers with the highest energy requirements.

A role for whole grain and fibre ?

A decreased energy availability of a high fibre diet might also play a role. The ingestion of 64 g compared with 34 g dietary fibre/day for 10 weeks in lean healthy males resulted in a 5.7% lower protein utilisation and in a 3.0% lower fat utilisation (25). Total energy utilisation was 2.9% lower, equal to 400 kJ/d (25). A theoretical calculation showed that if the fibre intake in a typical American diet was increased from 18 g/d to 36 g/d the amount of metabolisable energy would be reduced by 540 kJ/d (26).

A long-term, randomised dietary intervention trial in patients with cardiovascular disease has shown that a modest 6% point reduction in dietary fat, combined with increases in fish, fruit, vegetables, pulses and nuts, is associated with a weight loss of 4 kg over one year and a reduction in cardiac events and mortality by ~40% (13). In a recent trial that enrolled 1000 patients the control group was instructed to follow the National Cholesterol Education Program Step 1 Prudent Diet, which recommends < 30% of energy from fat, and less than 10% from saturated fat (14). The intervention group was instructed to follow the same diet and in addition to consume at least 250-300 g of fruit, 125-150 g of vegetables, 25-30 g of walnuts or almonds, and 400-500 g of whole grains, legumes, rice, maize or wheat. Together this achieved a 3% point reduction in total fat content, together with a significant increase in alpha-linolenic acid. The cardio-protective effect previously reported was confirmed, and the intervention group spontaneously reduced their energy intake, resulting in a weight loss of 3 kg over 2 years. These trials suggest the more emphasis in future dietary intervention trials should focus more on a combination of a fat reduction, and increased intake of whole grain and fibre rich foods.

Sucrose versus artificial sweeteners

It has been speculated that the removal of sucrose (carbohydrate) from the diet will increase the relative dietary fat content, which would then result in increased energy intake and body weight in the long term. The number of long-term inter-

vention studies without caloric restriction is small, and none have lasted more than 3 weeks (27, 28). These intervention studies suggest that an increased intake of artificial sweeteners decreases energy intake and body weight compared to sucrose. We investigated the effect of 10 week supplementation with either sucrose or artificial sweeteners on *ad libitum* food intake and body weight in 2 groups of overweight subjects. About 80% of the supplements were given as drinks and 28% of the caloric intake came from sucrose in the sucrose group. Similar food items and volumes were given to the two groups. An increase in total energy intake (2.6 MJ/d), body weight (1.6 kg) and fat mass (1.3 kg) was seen in the sucrose group after 10 weeks, whereas a decrease in body weight and fat mass (1.0 kg and 0.3 kg) was seen in the artificial sweetener group (21). One likely reason for the increased energy intake and body weight in the sucrose group is that about 70% of the sucrose came from fluids. Calories from fluids have been shown to be less satisfying than solid foods, and it is easier to overconsume energy from drinks than from solids (29). That sucrose from fluids may be fattening was also suggested by a recent observational, prospective study in children, reporting that those with a high intake of sugar sweetened drinks were at an increased risk of becoming overweight (30). It may therefore be advisable for overweight subjects to choose drinks and foods containing artificial sweeteners rather than sucrose in order to prevent weight gain.

Protein

There is some concern that a high protein intake in infant formulas and during growth may increase the susceptibility to weight gain and obesity. However, a new study suggests that a high protein intake may be associated with a higher BMI due to a positive relationship with the size of the fat-free mass, not with the amount of body fat (31). There is also a large body of experimental data to suggest that protein has a higher satiating power per calorie than carbohydrate and fat in adults. The impact on obesity and risk factors of replacing carbohydrate with protein in *ad libitum* low-fat diets has been addressed in only one clinical trial. Two fat reduced diets (30% of total energy), a high carbohydrate diet (protein 12% of total energy) and a high-protein diet (protein 25% of total energy) were compared in 65 obese patients (32). Weight loss after 6 months was 5.1 kg in the high carbohydrate and 8.9 kg in the high protein groups, and more subjects lost >10 kg in the high protein group (35%) than in the high carbohydrate group (9%). The protein rich diet had no adverse effect on blood lipids, homocysteine levels (33), renal function (34) or bone mineral density (35). Replacement of some dietary carbohydrate by protein in *ad libitum*, low-fat diets may improve weight loss. More freedom to choose between protein rich and complex carbohydrate rich foods may encourage obese subjects to choose more lean meat and dairy products, and hence improve adherence to low-fat diets in weight reduction programmes.

Effects of different types of fat on energy balance

Although the same quantities of different types of fat contain almost the same amounts of energy, differences may exist in their potential to influence energy balance. Thus, energy expenditure as well as satiety, both of which influence the energy balance of *ad libitum* low-fat diets and weight maintenance diets, have shown to be affected by the quality of fat.

It is known from animal studies that rats fed a diet rich in safflower oil (PUFA) demonstrate less accumulation of body fat than rats fed a diet rich in beef tallow (SFA) (36, 37). This is probably due to a higher diet induced thermogenesis, an elevated fat oxidation and a higher sympathetic activity (36, 38). MUFA also seems to increase body weight more than PUFA (37). Other studies also report differences in fat accumulation, body fat distribution and oxidation rates as a result of diets varying in fatty acid composition, chain length and saturation (39).

In humans, in a cross-sectional, observational study, strong positive associations between the intake of monounsaturated fats (MUFA) and different indices of adiposity were found, whereas high intakes of polyunsaturated fats (PUFA) and saturated fat (SFA) were only weakly related to adiposity (40). Similarly, in a cohort of women, all lipids other than vegetable fat were positively related to BMI. Furthermore, the strongest positive association between a nutrient and BMI was found to be the intake of trans fatty acids (41). That MUFA might

be more fattening is also suggested by a study from Willett's own group (42).

A study on the effect of high-fat meals, differing in fatty acid composition, on post-ingestive satiety in lean subjects found that MUFA induced a lower level of satiety and a larger subsequent energy intake than PUFA and SFA (43). Intestinal infusions of linoleic acids concordantly result in a lower subsequent food intake than oleic and stearic acids. However, the different effects on energy expenditure, appetite and *ad libitum* energy intake were not confirmed in a recent study performed with overweight subjects, suggesting that differences exists between subject groups (44).

Together, these preliminary reports suggests that some differences between fatty acids are apparent, but until clinical trials based on longer term interventions have been conducted some caution should be taken in recommending specific fat types in preference to others, e.g. replacement of PUFA with MUFA in diets for individuals susceptible to weight gain and obesity, despite the apparently more neutral effects of MUFA reported in some studies in relation to insulin resistance, type 2 diabetes, cardiac heart disease and cancer. We are aware only of the trial reported by Wolever et al. (45) in which he randomised subjects to 3 different ad lib diets, one normal-fat high MUFA diet, and two different fat-reduced diets, either with high or low glycemic index. After 16 weeks body weight and insulin resistance were increased in the high-MUFA diet as compared to the fat-reduced diets. (46).

Conclusions

Ad libitum consumption of diets with a reduced fat content (25-30 % of energy), and high in protein and fibre-rich, and whole grain carbohydrates, contributes to the prevention of weight gain in normal weight subjects, and causes a spontaneous weight loss of 3-4 kg in overweight subjects (Table 1). The modest weight loss has proven sufficient to reduce the incidence of type 2 diabetes and cardiac events among subjects at high risk.

Because type 2 diabetes is associated with an increased cardiovascular mortality and a 10 year reduced longevity, the prevention of this disease will substantially justify the use of low-fat diets for the prevention of cardiovascular disease. A Mediterranean fat-reduced diet may leave room for plenty of fruits, vegetables, and fish, and such a diet has been shown to reduce total mortality by 45 to 60% in individuals with IHD (2).

Table 1. Eidence for the importance of various dietary factors for body weight regulation and obesity using the evidence based principles. Category A is evidence based on randomised clinical trials (1A, meta-analyses; 1B, at least one trial). Category B is evidence based on non-randomised trials and mechanistic studies. (IIA, evidence from at least one non-randomised controlled clinical trial; IIB, at least one other trial quasi-experimental design). (**+** and **+** indicates positive and negative effects on body weight, and numbers of symbols the strength of the effect).

Dietary factor	Association with obesity		Level of evidence
	Short term (<6 months)	Long term (>6 months)	
Fat (energy density)	+++	+	A (1A)
Dietary fibre	÷		A (1B)
Types of carbohydrate in solid foods/glycemic index	0	0	A (1B)
Sugar-sweetened Soft-drink/fruit juices	++	?	A (1B)
Artificial sweeteners	÷	?	A (1B)
Fruit and vegetable	?	?	A (1B)
Protein	÷	(÷)	A (1B)
The high MUFA-diet Willett-diet)	+	?	A (1B)
Palatability	?	?	-
Calcium	÷		B (11a)
Capsaicin/etc.			B (11b)

The inverted food pyramide proposed by Willett et al. is so far not backed up by randomised clinical trials that support its efficacy for weight control. Whereas it is very likely the an increased consumption of whole grain and more fibre rich foods may contribute to the prevention of weight gain and obesity, we are sceptical about the recommendation of increased intake of fat (MUFA and PUFA) from plant oils, nuts etc. which clearly poses the risk of producing weight gain. Preliminary evidence supports that this might be the case (47), and that the weight gain is accompanied by the expected increased risk of complications.

In summary, we desperately need more long-term, randomized clinical trials to study the impact of diet composition on weight loss, on maintenance of weight loss and on primary prevention of weight gain. Further, we know that weight management is not simply a function of the type of diet eaten, but depends on amount of physical activity performed. Most studies of diet composition have not also included efforts to increase physical activity. Until we have more well-designed studies to examine

the long-term impact of diet composition on body weight, we should not throw the baby (the fat-reduced diet) out with the bathwater. We agree with Willett that many of the previous studies have many short-comings, and we have listed some of the key points to take into consideration in the design of future trials (Table 2).

Table 2. Shortcomings of most previous randomised dietary intervention trials.

1) The lack of similar attention, food provision and number of visits in the intervention and control groups
2) The lack of compliance assessment by use of biological markers
3) The lack of standardisation of the non-fat dietary component
4) The lack of detailed description of other lifestyle changes in the intervention group
5) More focus on gene-nutrient interaction?

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References

1. National Institutes of Health: The practical guide: Identification, evaluation, and treatment of overweight and obesity in adults. NIH Publication no. 00-4084. U.S.A 2000.
2. Eurodiet core report: Nutrition & diet for healthy lifestyles in Europe: science & policy implications. *Public Health Nutrition* **4(2A)**: 265-273, 2001.
3. Willett WC. Is dietary fat a major determinant of body fat? *Am J Clin Nutr* **67**: 556S-562S, 1998.
4. Willett WC, Stampfer MJ. Rebuilding the food pyramid. *Scienctific American* **297:** 64-71, 2002.
5. Eccles M, Freemantle N, Mason J. North of England evidence based guidelines development project: methods of developing for efficient drug use in primary care. *BMJ* **316:** 1232-1235, 1998.
6. Rolls BJ, Hammer VA. Fat, carbohydrate, and the regulation of energy intake. *Am J Clin Nutr* **62**(5 Suppl): 1086S-1095S, 1995.
7. Bray GA, Popkin BM. Dietary fat intake does affect obesity. *Am J Clin Nutr* **68:** 1157-1173, 1998.
8. Astrup A, Ryan L, Grunwald GK, Storgaard M, Saris W, Melanson E, Hill JO. The role of dietary fat in body fatness: evidence from a preliminary meta-analysis of ad libitum low fat dietary intervention studies. *British Journal of Nutrition* **83(suppl 1)**: S25-S32, 2000.
9. Yu-Poth S, Zhao G, Etherton T, Naglak M, Jonnalagadda, Kris-Etherton PM. Effects of the National Cholesterol Education Programs step I and step II dietary intervention programs on cardiovascular disease risk factors: A meta-analysis. *Am J Clin Nutr* **69:** 632-646, 1999.
10. Astrup A, Grunwald GK, Melanson EL, Saris WHM, Hill JO. The role of low-fat diets in body weight control: a meta-analysis of *ad libitum* intervention studies. *Int J Obes* **24**: 1545-1552, 2000.
11. Pirozzo S, Summerbell C, Cameron C, Galsziou P. Should we recommend low-fat diets for obesity? *Obes Rev In press.*
12. Hill JO, Astrup A. What diets should we be recommending for obesity? *Obes Rev In press.*
13. Singh RB, Rastogi SS, Verma R, Laxmi B, Singh R, Ghosh S. Randomised controlled trial of cardioprotective diet in patients with recent acute myocaridal infarction: result of one-year follow up. *BMJ* **304:** 1015-1009, 1992.
14. Singh RB, Dubnov G, Niaz MA, et al. Effect of an Indo-Mediterranean diet on progression of coronary artery disease in high risk patients (Indo-Mediterranean Diet Heart Study): a randomised single-blind trial. *Lancet* **360**(9344): 1455-1461, 2002.
15. Tuomiletho J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, Keinänen-Kiukannniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Uusitupa M. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* **344:** 1343-1350, 2001.
16. Knowler WC, Barrett-Connor E, Fowler SE et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* **346**: 393-403, 2002.
17. Sjöström L, Togerson JS, Hauptman J, Boldrin M. XENDOS – a landmark study: xenical in the prevention of diabetes in obese subjects. In Abstracts from the Satellite Symposium New Frontiers in Weight Management, 9th International Congress on Obesity, Sao Paolo, Brazil, 2002.
18. Ornish D, Brown SE, Scherwitz LW, Billings JH, Armstrong WT, Ports TA, McLanahan SM, Kirkeeide RL, Brand RJ, Gould KL. Can lifestyle changes reverse coronary heart disease? *Lancet* **336**: 129-133, 1990.
19. Swinburn BA, Metcalf PA, Ley SJ. Long-term (5-year) effects of a reduced-fat diet intervention in individuals with glucose intolerance. *Diabetes Care* **24:** 619-624, 2001.
20. Pi-Sunyer FX Glycemic index and disease. *Am J Clin Nutr* **76**(1): 290S-298S, 2002.
21. Raben A. Should obese patients be counseled to follow a low-glycaemic index diet? No. *Obes Rev* **4:** 245-256, 2002.
22. Pawlak DB, Ebbeling CB, Ludwig DS. Should obese patients be counseled to follow a low-glycaemic index diet? Yes. *Obes Rev* **4:** 235-244, 2002.
23. Møller BK, Flint A, Pedersen D, Raben A, Tetens I, Holst JJ, Astrup AA. Prediction of Glycemic Index. *Int J Obes. Submitted to the European Congress on Obesity* 2003.
24. Saris WHM, Astrup A, Prentice AM, Zunft HJH, Formiguera X, Verboeket-van de Venne WPHG, Raben A, Poppitt SD, Seppelt B, Johnston S, Vasilaras TH, Keogh GF. Randomized controlled trial of changes in dietary carbohydrate/fat ratio and simple *vs.* complex

carbohydrates on body weight and blood lipids: the CARMEN study. *Int J Obes* **24:** 1310-1318, 2000.

25. Miles C. The metabolizable energy of diets differing in dietary fat and fiber measured in humans. *J Nutr* **122:** 306-311, 1992.
26. Baer DJ, Rumpler WV, Miles CW, Fahey Jr GC. Dietary fiber decreases the metabolizable energy content and nutrient digestibility of mixed diets fed to humans. *J Nutr* **127:** 579-586, 1997.
27. Tordoff MG, Alleva M. Effect of drinking soda sweetened with aspartame or high-fructose corn syrup on food intake and body weight. *Am J Clin Nutr* **51**:963-969, 1990.
28. Porikos KP, Hesser MF, van Itallie TB. Caloric regulation in normal-weight men maintained on a palatable diet of conventional foods. *Physiology & Behaviour* **29:** 293-300, 1982.
29. Di Meglio DP, Mattes RD. Liquid versus solid carbohydrate: effects on food intake and body weight. *Int J Obes* **24:** 794-800, 2000.
30. Ludwig DS, Peterson KE, Gortmaker SL. Relation between consumption of sugar-sweetened drinks and childhood obesity: a prospective, observational analysis. *Lancet* **357:** 505-508, 2001.
31. Hoppe C, Mølgaard C, Juul A, Michaelsen KF. Protein intake in infancy is related to body size but not to adiposity in 10-y old children. *Int J Obes* **25(suppl 2):** S64, 2001.
32. Skov AR, Toubro S, Rønn B, Holm L, Astrup A. Randomized trial on protein versus carbohydrate in ad libitum fat reduced diet for the treatment of obesity. *Int J Obes* **23:** 528-536, 1999.
33. Haulrik N, Toubro S, Dyerberg J, Stender S, Skov AR, Astrup A. Effect of protein and methionine intakes on plasma homocysteine concentrations: a 6-mo randomized controlled trial in overweight subjects. *Am J Clin Nutr* **76:** 1202-6, 2002.
34. Skov AR, Toubro S, Bülow J, Krabbe K, Parving HH, Astrup A. Changes in renal function during weight loss induced by high *vs.* low-protein low-fat diets in overweight subjects. *Int J Obes* **23:** 1170-1177, 1999.
35. Skov AR, Haulrik N, Toubro S, Mølgaard C, Astrup A. Effect of protein intake on bone mineralisation during weight loss: a 6-month trial. *Obes Res* **10:** 432-8, 2002.
36. Shimomura Y, Tamura T, Suzuki M. Less body fat accumulation in rats fed a safflower oil diet than in rats fed a beef tallow diet. *J Nutr* **120:** 1291-1296, 1990.
37. Dulloo AG, Mensi N, Seydoux J, Girardier L. Differential effects of high-fat diets varying in fatty acid composition on the efficiency of lean and fat tissue deposition during weight recovery after low food intake. *Metabolism* **44:** 273-279, 1995.
38. Matsuo T, Shimomura Y, Saitoh S, Tokuyama K, Takeuchi H, Suzuki M. Sympathetic activity is lower in rats fed a beef tallow diet than rats fed a safflower oil diet. *Metabolism* **44**: 934-939, 1995.
39. Hill JO, Peters JC, Lin D, Yakubu F, Greene H, Swift L. Lipid accumulation and body fat distribution is influenced by type of dietary fat fed to rats. *Int J Obes* **17:** 223-236, 1993.
40. Doucet NA, White MD, Després J-P, Bouchard C, Tremblay A. Dietary fat composition and human adiposity. *Eur J Clin Nutr* **52:** 2-6, 1998.
41. Colditz GA, Willett WC, Stampfer MJ, London SJ, Segal MR, Speizer FE. Patterns of weight change and their relation to diet in a cohort of healthy women. *Am J Clin Nutr* **51:** 1100-1105, 1990.
42. van Dam RM, Stampfer M, Willett WC, Hu FB, Rimm EB. Dietary fat and meat intake in relation to risk of type 2 diabetes in men. *Diabetes Care* **25** (3): 417-424, 2002.
43. Lawton CL. Delargy HJ, Brockman J, Smith FC, Blundell JE. The degree of saturation of fatty acids influences post-ingestive satiety. *Brit J Nutr* **83:** 473-482, 2000.
44. Flint A, Jørgensen BH, Raben A, Toubro S, Astrup A. No differences in appetite and energy expenditure after intake of polyunsaturated, monounsaturated or trans-fatty acids. *Obes Res: In press.*
45. Wolever TMS, Jenkins DJA, Vuksan V, Jenkins AL, Wong GS, Josse RG. Beneficial effect of low-glycemic index diet in overweight NIDDM subjects. *Diabetes Care* **15:** 562-564, 1992.
46. Wolever TMS, Mehling C. High-carbohydrate-low-glycaemic index dietary advice improves glucose disposition index in subjects with impaired glucose tolerance. *Brit J Nutr* **87:** 477-487, 2002.
47. Wolever TMS, Mehling C. Long-term effect of varying the source of dietary carbohydrate on postprandial plasma glucose, insulin, triacylglycerol, and free fatty acid concentrations in subjects with impaired glucose tolerance. *Am J Clin Nutr* **77:** 612-621, 2003.