Dietary Fat Is Not a Major Determinant of Body Fat

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The percentage of energy from fat in diets has been thought to be an important determinant of body fat, and several mechanisms have been proposed. Comparisons of diets and the prevalence of obesity between affluent and poor countries have been used to support this relationship, but these contrasts are seriously confounded by differences in physical activity and food availability. Within areas of similar economic development, regional intake of fat and prevalence of obesity have not been positively correlated. Randomized trials are the preferable method to evaluate the effect of dietary fat on adiposity and are feasible because the number of subjects needed is not large. In short-term trials, a modest reduction in body weight is typically seen in individuals randomized to diets with a lower percentage of calories from fat. However, compensatory mechanisms appear to operate, because in randomized trials lasting ≥1 year, fat consumption within the range of 18% to 40% of energy appears to have little if any effect on body fatness. The weighted mean difference was −0.25 kg overall and +1.8 kg (i.e., less weight loss on the low-fat diets) for trials with a control group that received a comparable intensity intervention. Moreover, within the United States, a substantial decline in the percentage of energy from fat during the last 2 decades has corresponded with a massive increase in the prevalence of obesity. Diets high in fat do not appear to be the primary cause of the high prevalence of excess body fat in our society, and reductions in fat will not be a solution. *Am J Med.* 2002;113(9B):47S–59S. © 2002 by Excerpta Medica, Inc.

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Excess body fat is the largest nutritionally related problem in the United States and many other affluent countries. Excess adiposity can account for approximately 30% to 40% of coronary heart disease,[1,2] many cancers of several types,[3] most cases of adult onset diabetes,[4] and a substantial proportion of disabling osteoarthritis.[5] Whereas genetic factors influence which individuals within a population will develop excessive adiposity, diet and lifestyle factors clearly make critical contributions to the present high rates of excessive body fat in our population. Evidence for this is provided by the dramatic changes in prevalence of overweight in migrants from countries with minimal adiposity who come to the United States; for example, the prevalence of obesity was 3-fold higher in Japanese men living in San Francisco compared with those in Japan.[6] Also, the major increases in adiposity within many populations over short periods of time, including the general US population,[7] cannot be explained by genetic factors. Among the aspects of lifestyle often said to be responsible for these high rates of adiposity has been the fat content of diet, that is, the percentage of calories from fat. Indeed, a reduction in obesity has often been a primary justification for recommendations to reduce the percentage of calories from fat.

Diet composition, in principle, could affect body fat content by virtue of effects that include a putative greater efficiency of metabolism of fat calories, hence more energy available per fat calorie for deposit in the organism; a tendency to partition fat calories preferentially to storage in adipose tissue without affecting net energy expenditure; hedonic effects related to greater palatability of high-fat foods; a higher caloric density of high-fat foods, which could lead to greater caloric intake if food intake is regulated by volume or weight (as opposed to calories per se).

In this review, we will first consider possible mechanisms by which diet composition might influence body fatness and will then examine empirical evidence, updated from an earlier overview,[8] for an effect of dietary fat composition on adiposity.

BIOCHEMICAL AND PHYSIOLOGIC CONSIDERATIONS

The potential effects of diet composition on body fat can be reduced to several biochemical/physiological considerations. First, because of differences in the energy costs

of digesting and disposing of (to storage or metabolism) fatty acids and carbohydrate, the calories available for storage as fat or glycogen may not be equivalent to their chemical caloric content by bomb calorimetry.[9,10] In addition, hexoses and fatty acids may be cycled from 1 physical form to another (glucose to glycogen to glucose; free fatty acid to triglyceride to free fatty acid). Such "futile cycles" consume adenosine triphosphate and can be invoked intermittently, changing the net caloric value of a foodstuff from meal to meal.[11–13] Thus, any arguments concerning the contributions of dietary composition to energy balance and body fat content must consider the metabolic state of the subject(s) in which the studies are conducted. Growth and overall energy balance will have significant effects on net energy storage (and its chemical composition) resulting from the ingestion of any foodstuff.

Second, glucose and other carbohydrates can be converted to fatty acids and glycerol by the liver. This process is active in humans and sensitive to the relative proportion of fat in the diet.[14,15] Because fatty acids synthesized in this fashion are more saturated than those in an ordinary diet, because of the liver's inability to synthesize linoleic acid, there could be consequences of such interconversion for atherogenesis. Simple sugars appear to induce endogenous fatty acid synthesis to a greater degree than do complex carbohydrates.[15] Although the glycerol backbone of triglyceride can be converted to glucose, net glucose synthesis from fatty acids is not possible. Hence, the pathways for fatty acid disposal are more limited than those for carbohydrates.

Third, the body has limited storage capacity for glucose polymers (approximately 70 g of glycogen in liver and skeletal muscle of an adult) but nearly unlimited capacity to store fatty acids (as triglycerides).[16] Thus, "excess" carbohydrates in a meal will be preferentially oxidized or converted to fat. The nearly 10-fold higher caloric density of adipose tissue versus tissue glycogen is presumably among the reasons for "selection" of fat as the primary long-term storage form of energy.

Fourth, because of the metabolic immediacy of need for glucose to support nervous system activity, the limited storage capacity for glycogen, and lack of free fatty acid interconvertibility to glucose, humans are constrained to eat carbohydrate as part of their diet. Thus, fat has been viewed as a passive dietary constituent,[17–23] and it is not surprising that overfeeding of fat is not compensated for by increases in fat oxidation in relatively short-term experiments.[24–29]

MEDIUM-TERM METABOLIC STUDIES

In addition to the short-term effects of dietary composition, body fat content is regulated by complex and as yet incompletely understood processes that are clearly sensitive and responsive to the mass of body fat stores.[30,31] The operation of this system is apparent in the changes in hunger and energy expenditure that occur with experimental weight perturbation.[32,33] For reasons related to the importance of body fat stores for reproductive function and growth, the defense of fat stores is apparently stronger against loss than gain of body fat.[34] These regulatory processes may influence the effects of specific dietary components on body composition.[35] Further, due to the existence of these regulatory mechanisms, the use of extrapolations from metabolic studies of only a few days to predict the effects of dietary composition on body weight is likely to be misleading.

In metabolic studies lasting several weeks or months, the effects of diet composition on body composition in adult humans[36–39] are modest. One small, but well-controlled study[40] examined the effects on ad libitum caloric consumption and body weight of 2-week dietary treatments in which 15% to 20%, 30% to 35%, or 45% to 50% of food energy was derived from fat. Efforts were made to minimize potential confounding effects of palatability. When compared with caloric intake on the 30% to 35% fat diet, subjects on the higher- and lower-fat diets over- and underconsumed calories by +15.4% and −11.3%, respectively, resulting in weight changes of approximately +0.3 kg and −0.4 kg. If the caloric density of the weight gained and lost is assumed to be 5 kCal/g, the 300-g weight gain accounts for only 1,500 of the 5,068 extra kCal ingested on the high-fat diet. Conversely, the 400-g weight loss on the low-fat diet accounts for only 2,000 kCal of the 3,710-kCal deficit. Thus, whatever effects diet composition may have on net energy balance in this context, weight change in either direction is not well explained by composition effects on energy intake.

In another study conducted in a clinical research center setting, 13 adults and 3 children were placed on isoenergetic liquid formula diets of precisely known composition with extremes of composition (including 15% carbohydrate and 70% fat or 85% carbohydrate and 0% fat).[36] Under these highly controlled conditions, dietary fat composition did not affect energy requirement to maintain body weight for 15 to 56 days.

As indicated earlier, short-term overfeeding experiments indicate that excess dietary calories as fat are not oxidized to the same extent as excess carbohydrate calories.[24,25,27–29] As the medium-term experiments described here show, these differences do not, however, appear to carry over to circumstances in which diet composition is manipulated in the context of isocaloric feeding. The latter experiments are more relevant to the situation that obtains in most clinical circumstances and suggest that isocaloric change in diet fat content is not likely to have a substantial effect on body weight.

LONG-TERM RANDOMIZED TRIALS

Although the effects of dietary fat reduction on body weight in short-term studies have been modest, these could potentially be important if they were cumulative over periods of years. Thus, long-term studies are critical. Longer term randomized trials of fat reduction and body weight are few, and most data are secondary observations from studies in which body weight was not the primary outcome. Most were pilot studies of fat reduction for the prevention of cancer or cardiovascular disease (**Table 1**).[41–46] The only double-blind, longer-term study of fat reduction appears to be the National Diet-Heart Study[42] conducted among 900 individuals; foods with variable fat content were provided to participants. The difference in fat intake between groups was 30% compared with 35% of energy, and after approximately 1 year, the difference in weight was only 0.8 kg. Although the difference in fat intake was not large, this is similar to the difference between current US diets and US dietary goals.

Three longer term trials of fat reduction were pilot studies for interventions targeting breast cancer. In the Women's Health Trial[41] fat intake was to be reduced from approximately 38% to 20% of energy. Reported compliance was nearly perfect by 6 months and decreased only modestly by 24 months. Women in the low-fat group lost 3.2 kg of body weight by 6 months; however, some of this was regained so that by 24 months they had lost only 1.9 kg, and the difference between the intervention and control group was 1.8 kg. This study strongly suggests that weight losses on low-fat diets are not cumulative over time and indeed seem to be in part transient. In a trial of fat reduction in the prevention of skin cancer,[45] the reduction in body fat on a low-fat diet relative to the control diet was only about 1 kg.

The study of Kasim et al[44] included only overweight women and, thus, presumably those who might be susceptible to higher fat diets. Fat intake was reduced to 17.6% of energy at 1 year, therefore providing a major contrast in diets. This study included more detailed data on body composition than most other investigations (**Table 2**).[44] The difference in weight change between intervention and control groups (2.6 kg) was somewhat greater than in the other studies. However, lean mass as well as fat mass was lost so that the difference in change between treatment groups in percent of body fat at 1 year was only 0.7%, and no effect was observed on the waist/hip circumference ratio. Thus, despite a very large contrast in diet, the change in adiposity was minimal. Importantly, the maximal difference in body weight was seen at 3 months, with no subsequent divergence between groups.

The weighted mean difference between the low-fat and control groups for the randomized trials lasting ≥1 year (Table 1) is −0.25 kg. In none of these studies did the effect of dietary fat reduction approach a 5% weight loss, which is generally considered to be clinically significant.

A major limitation of most long-term studies of dietary fat reduction is that the fat-reduction and control groups did not receive a comparable intensity of dietary instruction and motivation. The intervention groups were generally given state-of-the-art individual and group instruction and support to increase consciousness about dietary fat, sometimes including the provision of scales to weigh food and control portion sizes. Thus, changes in body weight, to the extent that they occurred, could have been the result of greater attention to intake of total calories rather than just fat per se. To determine whether dietary fat reduction per se reduces body fatness, an appropriate control group would receive a similar intensity of dietary instruction and counseling but directed at the reduction of carbohydrate or total calories. In such a study reported by Jeffery et al,[46] participating women, who were initially moderately obese, received either counseling to reduce fat to 20 g/day or to reduce overall energy intake to 5,000 kJ/day. Both groups lost weight initially, but after 6 months they also gained weight in parallel and by 18 months there was no significant difference between groups. In another study in which both treatment arms received similar intensity of interventions, McManus et al[47] randomized 101 overweight persons to a diet with 35% of fat (mainly unsaturated fat), or diet with 20% of energy from fat. Mean weight loss (5 kg) was similar in the 2 groups at 6 months among those returning for follow-up, but after 18 months, the low-fat group regained much of the weight lost (**Figure 1**).[47] Long-term weight loss and participation rates were substantially higher for those on the higher-fat diet (**Figures** 1 and **2**). Thus, a higher fat composition of the diet may lessen weight regain after weight loss, possibly because of enhanced diet satisfaction. The weighted mean difference for the effect of fat reduction among the 4 studies in Table 1 that included a control group with comparable intensity of intervention[42,46,49] was +1.8 kg, that is, the control group tended to lose slightly more weight than the low-fat group. This is similar to the results of a recent meta-analysis by the Cochrane Collaborative[49] of long-term randomized trials of low-fat diets in which the control group was assigned overall caloric reduction. The weighted mean difference was +3.7 kg (95% confidence interval, −1.8 to 9.2) for studies lasting ≥18 months, again consistent with greater weight loss with lower carbohydrate/higher fat diets.

A major concern in any long-term study of dietary change is that compliance may deteriorate with time so that the lack of a substantial effect on body weight could simply be the result of a lack of difference in diets. In general, studies of fat reduction have been hindered by a lack of a well-documented measure of compliance. How-

Table 1. Long-term Trials of Fat Reduction and Body Weight

Study	Length of Trial (mo)	N	Energy from Fat (%)	Greatest Weight Loss (kg)	Change in Weight at End of Trial	Weight Loss Difference (kg)	Comments
National Diet-Heart Study[42]	12–20	Int 450	30	−2.8	−2.3		The only double-blind study
		Cont 450	35	−2.3	−1.5	−0.8	
NCI feasibility trial for low-fat diet to reduce breast cancer risk[41]	24	Int 171	20	−3.2	−1.9		A somewhat large difference at 6 mo became smaller with time
		Cont 105	38	−0.4	−0.1	−1.8	
Low-fat diet for women with breast dysplasia[43]	12	Int 100	21	−2.0	−1.0		
		Cont 106	37	0	0	−1.0	
Effect of low-fat diet on lipoprotein metabolism[44]	12	Int 34	17	—	−3.4		Weight differences reflect changes in lean as well as fat mass, because there were no differences between groups in changes in percentage of body fat, BMI, or waist–hip ratio.
		Cont 38	36	—	−0.8	−2.6	
Effect of low-fat diet on incidence of actinic keratosis[45]	24	Int 38	21	−3.0	−2.0		No significant differences in weight at any time during the 24 mo
		Cont 38	40	−1.0	−1.0	−1.0	
Randomized trial of counseling for fat vs. caloric restriction in treatment of obesity[46]	18	Int 39	26	−4.6	+0.4		Fat counseling ≤20 g/day, calorie reduction = 1,000–1,200 kcal/day; 33% of original participants failed to finish trial. Adherence to both fat and calorie reduction regimen was poor after 6 mo.
		Cont 35	33	−3.7	+1.8	−1.4	
Treatment of dyslipidemia[48]	12	Int 78	27	—	−2.9		Additional subjects on intermediate levels of fat experienced no difference in weight loss. The lowest fat group experienced a large increase in plasma fasting triglycerides, indicating compliance with low fat intake.
		Cont 59	22	—	−2.9	0.0	

BMI = body mass index; Cont = control group; Int = intervention group; NCI = National Cancer Institute.

Table 2. Randomized Trial of a Low-Fat Diet in 72 Women

		Baseline	12 Mo	Δ
Dietary fat (% energy)	LF	36.3	17.6	—
	Cont	35.6	33.8	—
Weight (kg)	LF	66.8	63.4	−3.4
	Cont	72.7	71.9	−0.8
% Body fat	LF	31.8	30.3	−1.5
	Cont	35.1	34.3	−0.8
Waist–hip ratio	LF	0.74	0.73	−0.01
	Cont	0.77	0.76	−0.01
HDL-C (mmol/L)	LF	1.56	1.44	−0.12
	Cont	1.47	1.56	+0.09

Cont = control subjects; HDL-C = high-density lipoprotein cholesterol; LF = subjects on low-fat diet.

Maximal weight change seen at 3 months.

Adapted from *Am J Clin Nutr.*[44]

ever, depressed levels of high-density lipoprotein (HDL) cholesterol and increased levels of fasting triglyceride consistently occur on low-fat diets.[50] Although depression of HDL cholesterol is not specific to fat reduction (such change can also result from reduced physical activity, cigarette smoking, abstinence from alcohol, and weight gains) on a group basis, circulating HDL cholesterol does appear to be reasonably sensitive to changes in dietary fat. Thus, it is notable that the dietary intervention studies by Kasim et al[44] and Lee-Han et al[51] both demonstrated depressions of HDL that were maintained over time. Using the data on changes in HDL at 12 months in the Kasim et al study[44] (Table 2) and the Mensink and Katan[50] meta-analysis of metabolic studies on dietary fat and blood lipids, it can be back-calculated that the difference in fat intake at 12 months was approximately 20% of energy, which is similar to the reported difference in these studies. In addition, in the study of Knopp et al[48] a substantial elevation in serum triglyceride levels was seen in the lowest-fat-intake group (**Table 3**), which is consistent with known metabolic effects of low-fat diets. Thus, these studies do not support the notion that failure to observe a substantial weight loss on long-term low-fat diets is simply the result of noncompliance.

The importance of long-term, as opposed to short-term, trials has been noted but deserves emphasis. Bray and Popkin[52] conducted a meta-analysis of fat reduction studies without regard to duration and concluded that a 10% reduction in the proportion of energy from fat was associated with a 16-g/day reduction in body weight. Over a period of 1 year, this would predict a weight loss of 6 kg if fat intake were reduced by 10% of energy, which is highly incompatible with all studies that have lasted for ≥1 year (Table 1). Thus, the conflation of the far more numerous short-term studies with the longer term trials leads to a completely misleading result. For this reason, not only the meta-analysis of Bray and Popkin, but also meta-analyses by Astrup et al[53,54] and Yu-Poth et al[55] are irrelevant to the long-term effects of dietary fat on body weight because they relied mainly on studies lasting <1 year. These meta-analyses are further flawed by inclusion of nonrandomized studies,[52–54] double-counting of multiple reports from the same study,[52–55] failure to distinguish studies with a control group of comparable intensity,[52–55] inclusion of studies that combined physical activity and other interventions with fat reduction,[52,53,55] use of short-term results instead of long-term results that were available,[52–55] and failure to include other informative studies.[52–54]

WEIGHT LOSS TRIALS

As noted earlier, a hypothesized reason to expect lower body fat on a diet with a lower percentage of calories from fat is the difference in metabolic efficiency of processing fat compared with carbohydrate or protein. Several studies of weight loss are germane to this proposed mechanism.[56–58] In the largest of these studies, Powell et al provided 5,000-kJ diets to women randomized to 10%, 20%, 30%, and 40% of energy from fat. No significant differences were seen in weight change, although the magnitude of reduction was actually somewhat less on the lowest fat intake (**Table 4**).[56] The studies by Alford et al[57] and Lehmann et al[58] also found no effect of dietary fat composition on weight loss. These data provide further evidence that, under realistic circumstances, the theoretical differences in metabolic efficiency associated with different levels of fat intake do not account for important differences in rates of weight loss.

A weight loss study by Astrup[35] has been frequently cited to support the notion that a low-fat diet reduces weight regain after a major loss. In the initial period, groups assigned to the calorie-counting or selection of low-fat foods lost similar amounts of weight, but after 2 years the amount of weight regain was less in the low-fat group. However, only 28 participants were seen at 2 years, and the results were only marginally significant in 1 analysis and nonsignificant in 2 other analytic comparisons.

INTERVENTION TRIALS

The long-term randomized trials of dietary fat reduction published thus far are particularly inconsistent with the hypothesis that body fat as a percentage of weight is proportional to percent of energy intake from fat.[17,59] The lack of major effects is notable because, with the exception of the National Diet-Heart Study[42] and the studies of Jeffery et al[46] and McManus et al,[47] the designs of the other trials were biased in favor of finding an effect of fat reduction.

In addition to the lack of an appropriate control group in many studies, other issues complicate what would seem to be a simple hypothesis to test. One of the issues is

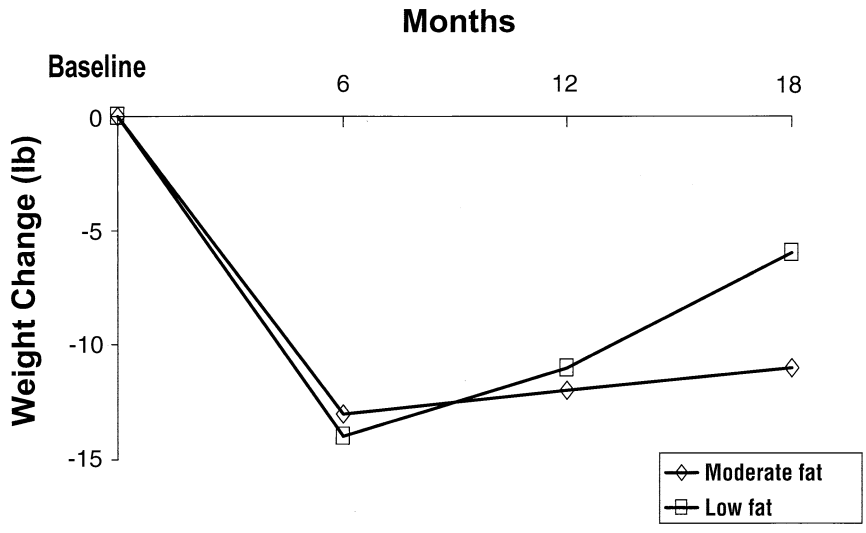

Figure 1. Weight loss for study subjects in a weight loss trial comparing a moderate-fat with a low-fat diet both restricted in energy. (Adapted from *Int J Obesity*.[47])

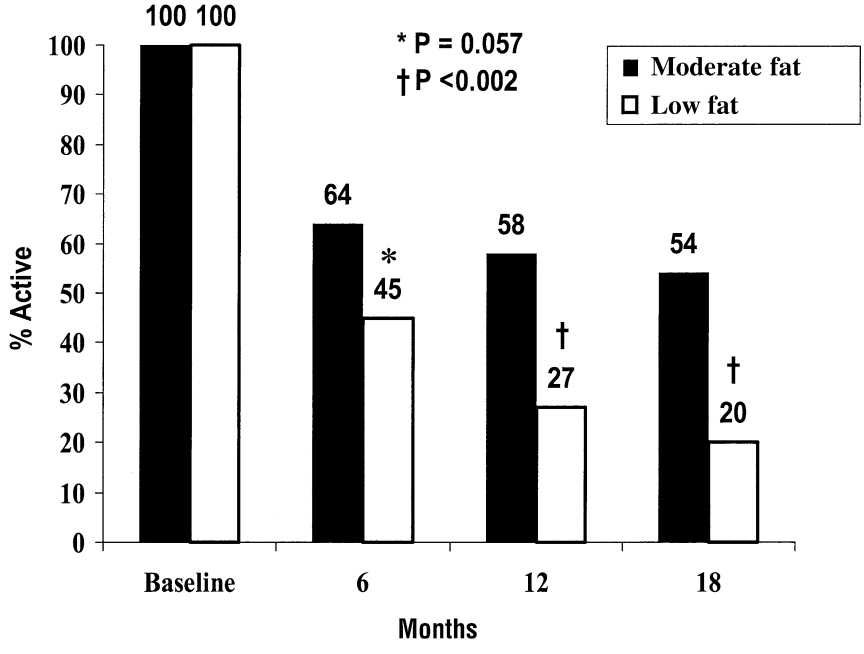

Figure 2. Participation rates for study subjects in a weight loss trial comparing a moderate-fat with a low-fat diet both restricted in energy. (Reprinted with permission from *Int J Obesity*.[47])

that dietary fat reduction may be confounded by differences in fiber or in energy density of the resultant diet. For example, in most of the fat-reduction trials, subjects were generally counseled to consume high amounts of fruits and vegetables as well as whole grains and legumes. In a recent trial of fat reduction among elderly individuals,[60] subjects continuing a baseline higher fat diet (35% energy from fat) were compared with an isocaloric low-fat diet. No weight loss was observed over a 12-week period, again arguing against any important difference in efficiency of energy utilization. However, when subjects were allowed to eat the low-fat diet ad libitum for another 12 weeks, a modest weight reduction was observed. This diet was exceptionally high in fiber and had a low energy density so that subjects complained of fullness and abdominal discomfort on the isocaloric low-fat diet. Thus, in this study, and potentially others, low-fat diets might be confounded by high fiber content or low energy density. It might be argued that this is simply a desirable and inevitable consequence of a low-fat diet and thus should not be con-

Table 3. Body Weight Change After 1 Year

	Fat Intake (% Energy)			
	27	−26	25	22
Weight change (kg)	−2.9	−3.5	−2.4	−2.9
TG change (mmol/L)	+9.5	+3.1	+21.7	+38.7

TG = triglyceride level.
Data from 270 hypercholesterolemic adults.
Reprinted with permission from *JAMA*.[48]

Table 4. Weight Change on 1,200-Kcal Diets Over 12 Weeks (n = 35 Women)

% Energy from Fat	Baseline	Δ (kg)
10%	95.0	−4.5
20%	88.2	−6.8
30%	101.4	−6.9
40%	85.0	−6.8

Reprinted with permission from *Am J Health Promot.*[56]

trolled for in the study design. However, low energy density is not an inevitable characteristic of low-fat diets, because many of the low-fat foods presently being promoted in our commercial food supply are based on fat replacement with sugar or highly refined carbohydrates and often have an energy value similar to their high-fat counterparts. On the other hand, in the Mediterranean tradition, abundant quantities of vegetables are consumed along with whole grains and copious amounts of olive oil, thus providing a high-fat, high-fiber, and high-volume diet. Because there is not an inevitable relation between the percentage of fat and energy density of diets, it is important to distinguish between these effects in the design of studies to assess the impact of the percentage of energy from fat on body weight. Whether the energy density of the diet has an important effect on long-term body fat is, of course, an important question itself. Short-term studies suggest that this may be important.[41,60–64] However, the contrasts between short- and long-term studies of dietary fat indicate the need for long-term studies of energy density and body weight before any conclusions can be drawn.

Given the evidence from randomized trials lasting 1 or 2 years that reductions in dietary fat have no or only small effects on body weight, some have argued that the low-fat diets are beneficial for preventing initial weight gains, even if they do not induce weight loss. However, this position is not supported by direct evidence. Moreover, there is no apparent reason why the mechanisms discussed initially relating to the effects of dietary fat should operate differently for preventing weight gain. Finally, despite the limitations of ecological comparison, we would expect to see higher rates of obesity in countries with higher fat intake if this were true, but when areas with similar levels of economic development are examined, this effect is not observed (see below). Thus, the contention that the fat composition of diets is specifically important for initial long-term weight gain is unsupported.

Subtle aspects of the diets being compared could potentially confound randomized trials of dietary fat composition on body weight. Studies in animals consuming "cafeteria-style" diets suggest that palatability, flavor, and texture may influence over- or undereating.[65] More subtle aspects of palatability may be difficult to control in any particular circumstance, but attempts to do so should be made. The relative palatability of the diets may be specific to the study population.

BETWEEN-POPULATION (ECOLOGICAL) STUDIES

The observation that the prevalence of overweight in affluent countries with high-fat intakes tends to be higher than in poorer regions of the world with low-fat diets has frequently been mentioned to support a relation between dietary fat and body fat. Because such observations are exceedingly confounded by the availability of food and levels of physical activity, such comparisons can be completely misleading. For example, Bray and Popkin[52] have used **Figure 3** as evidence to support a relation between fat intake and body fat. However, it can be readily appreciated that the countries with low fat intake and low body fat are poor developing countries that are not comparable to affluent Western nations in innumerable ways in addition to dietary fat content. The individual countries, however, are of interest because the data for South Africa and Kuwait make the point that a high prevalence of overweight can be achieved, once above the level of severe poverty, on diets that would be considered low fat by

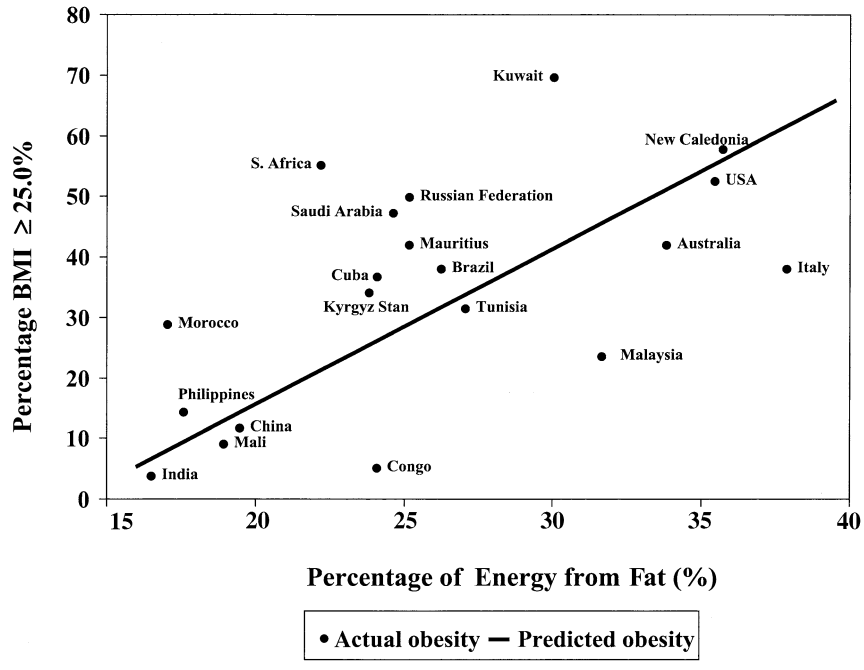

Figure 3. Relation between the percentage of the population that is overweight and the proportion of energy from fat. BMI = body mass index. (Reprinted with permission from *Am J Clin Nutr.*[52])

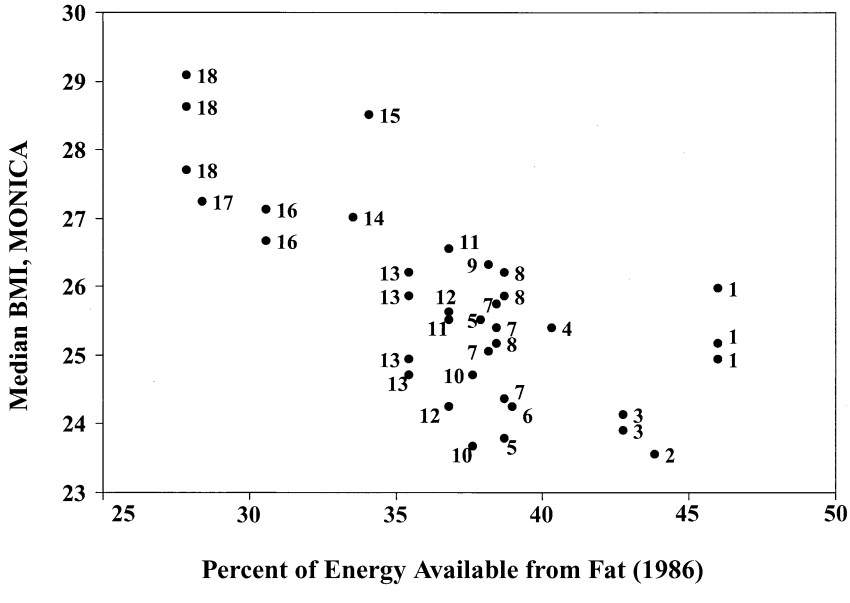

Figure 4. Median body mass index (BMI) of women (European surveys from 1982 to 1986) versus percent of energy available from fat (Food and Agriculture Organization/Interlink Computerized Storage 1986). 1 = Belgium; 2 = Denmark; 3 = Switzerland; 4 = United Kingdom; 5 = France; 6 = Iceland; 7 = West Germany; 8 = Finland; 9 = Spain; 10 = Sweden; 11 = Hungary; 12 = Italy; 13 = East Germany; 14 = Czechoslovakia; 15 = Malta; 16 = Poland; 17 = Yugoslavia; 18 = USSR. MONICA = Multinational Monitoring of Trends and Determinants in Cardiovascular Disease. (Reprinted with permission from *Eur J Clin Nutr.*[66])

Western standards. Comparisons among countries within regions of the world with similar degrees of economic development are more informative. Among European countries, for men, no association was observed between the national percentage of energy from fat and median body mass index, even though fat intake varied from approximately 25% to 47% of energy intake.[66] However, for women a clear inverse relation was observed (**Figure**

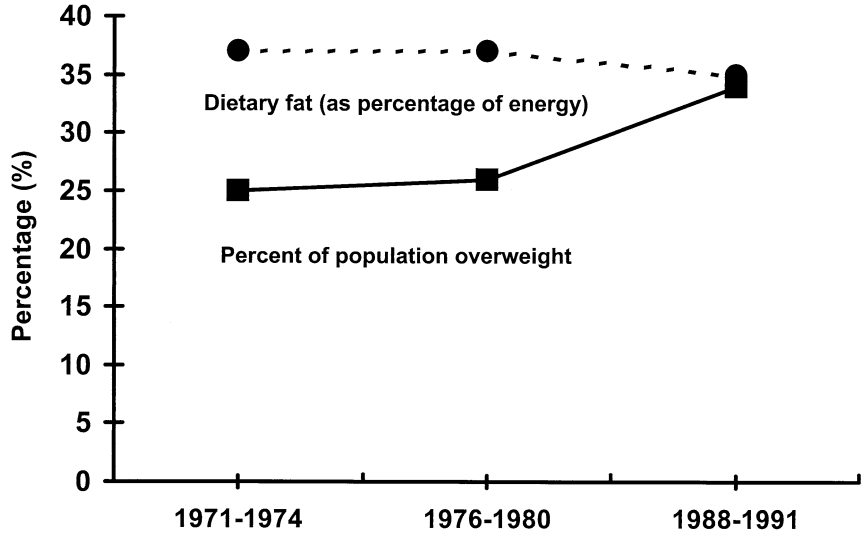

Figure 5. Changes in dietary fat (percent of energy) and percent of population that is overweight. (Reprinted with permission from *Am J Clin Nutr*.[8] Data from National Research Council,[3] *JAMA*,[68] and *MMWR*.[69])

4).[66] In a study among 65 counties in China, no correlation was found between dietary fat intake, which ranged from approximately 8% to 25% of energy, and body weight.[67] Ecological studies such as these have many limitations, including variable quality of dietary data in some studies and confounding by such unmeasured variables as activity levels, smoking, and cultural attitudes toward body fat. Nevertheless, the failure to observe any clear, positive association between dietary fat intake and obesity among areas with roughly similar degrees of affluence weighs against an important causal relationship. Time trends in dietary and body fat within countries making a transition from poverty or agrarian lifestyles to greater affluence are likely to be confounded by changes in food availability and level of physical activity, because higher fat intake typically accompanies newly gained affluence. Thus, in such circumstances, correlations across time are generally not informative regarding the causal role of dietary fat and obesity. However, in the United States and several other northern European countries, fat intake and affluence have been disassociated by conscious efforts to reduce fat intake. Thus, it is notable that as fat intake as a percentage of total energy intake has declined over the last 25 years, the prevalence of obesity has dramatically increased in the United States (**Figure 5**).[3,68,69] Such evidence weighs against the hypothesis that reducing the percentage of energy from fat will lead to a reduction in energy intake and, therefore, obesity.

WITHIN-POPULATION CORRELATIONS

Numerous cross-sectional studies, reviewed by Lissner and Heitmann,[66] have been conducted to examine the correlation between dietary fat and body fatness within populations. Results have been inconsistent; positive associations have been seen in some studies,[40,61,70–78] but not in others.[61,72,76,78,79] Unfortunately, most cross-sectional studies within populations are also prone to confounding that is almost uniquely intractable. In most populations studied, both dietary fat and the desirability of avoiding overweight have become strongly linked with general health consciousness in recent years. The confounding is particularly problematic, because health-conscious persons do have awareness and influence over the primary determinants of body weight, specifically the amount of calories they eat and their levels of physical activity, both of which are measured imperfectly in free-living populations and thus difficult to control for statistically. Therefore, it should not be surprising that the fat composition of the diet is positively associated with body fat in some studies. Unlike many other health-related parameters, body fatness is readily apparent to the individual, who may alter dietary intake in an unpredictable direction because of weight or weight gain. Prospective studies are generally considered a substantially stronger epidemiologic design, as compared with cross-sectional studies. However, they are similarly susceptible to severe confounding when individuals are aware of the dependent variable, here weight status, and also have conscious control over its primary determinants, physical activity and total energy intake, as well as the percentage of energy from fat. Relatively few prospective studies of dietary fat and weight change have been published,[41,74,77,78,80] and the findings are inconsistent. The study of Colditz et al[74] provided indirect support for confounding of the association between diet and body weight by health consciousness. In this large prospective cohort, weight gain was

weakly positively associated with intake of animal fat (generally viewed as unhealthy) but weakly negatively associated with intake of vegetable fat (generally viewed as healthier), even though there is little reason to believe that these fats would be metabolically distinct in relation to weight gain.

Because of the serious potential for confounding that is extremely difficult to control, both cross-sectional and prospective studies are likely to be unhelpful in assessing the relationship between the fat composition of diets and body fat.

GENETIC VARIATION IN RESPONSE TO DIETARY FAT

The possibility exists that humans, like different strains of animals, vary in their genetic susceptibility to effects of dietary fat on body fat content so that some will gain weight on high-fat diets but others will not. The storage of energy in the body is dictated by 3 processes: energy intake, energy expenditure, and the partitioning of calories between lean tissues and fat. Some of the biochemical/neuroendocrine mechanisms underlying these processes are alluded to above. It is clear that there are potent genetic influences on each of these elements.[81,82] Naturally occurring and/or transgenic exemplars of derangements in single components of this triad have been identified and confirm the validity of this model.[83] In rodents, single gene obesities affecting all of these phenotypes (e.g., *ob* and *db*) have been identified. In addition, about 70 unique quantitative trait loci (QTLs) for aspects of body composition have been mapped.[84–90] Some of these loci appear to affect susceptibility to weight gain on high-fat diets because of both palatability and direct metabolic effects.[89,90] In humans, there is also evidence for genetic effects on food preference and palatability.[91]

One recent study suggests that a family history of obesity might be an indicator of susceptibility to major weight gain on high-fat diets.[92] However, this analysis was based on very small numbers, and the finding was not reproduced in the much larger Nurses' Health Study (Coakley, unpublished data, 1998). Although it is possible that susceptible individuals exist, the lack of any substantial overall effect of fat reduction on body weight in the longer term randomized trials suggests that the susceptible subgroup is not large or that other persons are susceptible to weight gain on high-carbohydrate diets.

ALTERNATIVE HYPOTHESES

The failure of dietary fat to explain the prevalence and increases in excess body fat in our population indicates the need to consider alternative causes. Abundant evidence clearly supports a central role of physical activity in the regulation of body fatness. Numerous cross-sectional studies indicate an equilibrium between physical activity and body fatness, and intervention studies demonstrate that increased physical activity at least stabilizes body weight and may lead to modest reductions.[93] It has been noted that the magnitude of physical activity in these intervention studies was small in relation to the levels of activity typical of nonindustrialized countries so that the full potential impact of higher activity levels has not been adequately addressed in such investigations.[93]

The glycemic index of a diet has also been proposed as a factor that might influence food intake, and thus long-term weight control. After consuming a meal high in rapidly absorbed carbohydrate, serum glucose and insulin rapidly increase, which may be followed by a period of reactive hypoglycemia and hunger.[94] After a single meal with a high glycemic index, increased snacking was observed compared with a lower glycemic index meal.[94] Because both a higher percentage of calories from carbohydrate and its rapidity of absorption will increase the glycemic index of diet, it is conceivable that the reduction in percentage of energy from fat in the US diet may have contributed to the overall increase in energy intake by this mechanism. Higher dietary glycemic load has been associated with adult-onset diabetes[95,96]; effects of the glycemic index of ingested calories on body weight deserve to be examined in long-term randomized trials.

The availability and other characteristics of food and the social context of food consumption are also likely to have important impacts on body fatness, but these are difficult to study in free-living populations. The food industry has invested greatly in research on texture, color, sweetness, saltiness, and flavor of food, as well as on its packaging and promotion, all of which have been designed to enhance consumption. It seems likely that these efforts have contributed to overweight, although these contributions are difficult to quantify. A national character that values quantity and abundance over quality and presentation may further aggravate the situation. Finally, the almost ubiquitous presence of food in our life and the convenience with which it is obtained and eaten is likely to contribute further to overconsumption, but again quantification of such subjective factors is probably impossible.

CONCLUSIONS

In short-term studies a modest reduction in body weight is typically seen in individuals assigned to diets with a lower percentage of calories from fat. However, compensatory mechanisms appear to operate, such that in the longer term, fat consumption within the range of 18% to 40% of energy appears to have little if any effect on body fatness. The nature of these compensatory mechanisms is presently unknown. The possibility that individuals vary in their susceptibility to high-fat or high-carbohydrate diets deserves further examination. Nevertheless,

diets high in fat are not the primary cause of the high prevalence of excess body fat in our society, nor are reductions in dietary fat a solution. Other means will be needed to reduce substantially the prevalence of obesity; reduction in total calories ingested and enhancement of physical activity appear to be the most effective physiological alternatives. However, long-term studies of other dietary characteristics, such as energy density and glycemic index, deserve further examination in long-term studies.

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