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Biomedical Rationale for a Wellness Approach to Obesity: An Alternative to a Focus on Weight Loss

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The direct medical hazards of obesity, although real, have been overstated. Because current remedies for obesity have little long-term effectiveness, no controlled clinical trial has demonstrated improved longevity after weight loss. In contrast, advances in drug therapy for diabetes, hypertension, and high cholesterol allow obese persons affected by these conditions to live healthier lives. Furthermore, weight cycling may cause much of the cardiovascular risk associated with obesity. Repeated loss and regain of weight increases human deaths from heart disease, and in obese laboratory animals weight cycling increases blood pressure, enlarges the heart, damages the kidney, increases abdominal fat deposits, and promotes further weight gain. Additional health risks in obesity may be caused by hazardous treatments for obesity, as illustrated by heart disease caused by diet pills. Obese patients often lack full access to medical services owing in part to social stigma and low self-esteem, which impair self-care activities, and the bias of health professionals. These barriers, along with the prevalence of poverty among the obese, may contribute to the association of obesity with poor health. Medical beliefs about obesity are shaped by expert panels that are highly selective in the data they consider. Experts included on government consensus panels have been disproportionately drawn from the ranks of diet clinic directors, which might explain the congruence between panel recommendations and the economic interests of the diet industry. One remedy is a wellness approach focused on healthy lifestyle, positive attitude to health and self-care, and a disregarding of predetermined weight standards in favor of preventing further weight gain and reducing risk factors. Medical conditions common in obese patients, including

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hypertension, type-2 diabetes, hyperlipidemia, and sleep apnea, are dealt with directly and aggressively rather than relying on weight loss as the primary treatment. This new approach should improve the physical and mental well being of obese patients.

In this review, we address the prevailing view of obesity as a major threat to public health and find that this paradigm is based on incomplete consideration of the evidence. In particular, life expectancy is reduced more by underweight than by overweight. Although many diseases are more common in obese patients, in many cases a direct causal link cannot be made. Weight loss alone has limited effectiveness as a treatment for chronic medical conditions, whereas lifestyle enhancement can improve health independent of the loss of body fat. Repeated loss and regain of weight may make a significant contribution to obesity-associated disease. Also, obese persons are stigmatized and often have low socioeconomic status, which contributes independently to disease and reduced life expectancy. We advocate a wellness approach focused on healthy lifestyle and treating disease in the obese, rather than treating obesity as a disease.

Body Weight, Risk Factors, and Disease

What are the health hazards of obesity? In looking to the medical literature, there are hundreds of studies we can turn to for information. How can we decide which studies provide the best information? Epidemiologists and statisticians rank different types of medical studies according to their validity, reliability, and generalizability (Table 1; Hill, 1966). The gold standard for guiding medical practice is the controlled clinical trial. In the case of obesity, a controlled trial would require a group of obese persons to be divided into two groups: one to be cured of their obesity by some form of treatment, and a comparison group that would not be treated. This type of study is impossible, of course, because there are no effective treatments for obesity. Next to controlled trials, the most trustworthy source of information is the prospective study. A well-known example is the Framingham study, in which 5,000 residents of the Boston suburb were weighed and given medical exams in 1948 and their health was followed for the next 30 years (Lissner et al., 1991). The largest of these controlled trials involved 1.8 million Norwegians, who were weighed and examined and then followed for 10 years (Waaler, 1984). Prospective studies inform us about the predecessors of disease, and factors such as body weight that can predict whether someone stays alive and healthy or sickens and dies prematurely. Dozens of prospective studies have examined the long-term health consequences of obesity, and these are summarized in Table 2. Prospective studies are the best source of information on the relationship between body weight and health and are the focus of this article.

Table 1. Hierarchy of Medical Studies

Type of study	Design	Available for obesity?
Controlled clinical trial	Obesity is reversed by an effective treatment. Health outcomes compared between treated and untreated groups.	Not possible, because all therapies lack long-term effectiveness.
Prospective study	Group is monitored for many years, and the relationship between initial body weight and later health outcomes is determined.	Yes. Nearly every prospective epidemiological has included body weight.
Retrospective case-control study	Persons with a particular disease are compared to healthy controls matched for age, gender, and background.	Yes.
Cross-sectional survey	Groups of people are surveyed, and the number of diagnoses reported by people of different body weights is recorded.	Yes. This is the type of study mainly considered by obesity experts.

Retrospective studies compare persons having a particular disease (the cases) with other people who are healthy (the controls). These studies attempt to reconstruct the cause of a disease by comparing the medical histories of its sufferers compared to healthy controls. For example, using a case-control design it was found that people with pulmonary hypertension are 23 times more likely to have a history of taking diet pills than are matched controls (Abenhaim et al., 1996). The retrospective design is most commonly used for relatively uncommon disorders, such as pulmonary hypertension, where population-based prospective studies are impossible.

The weakest type of medical study is the cross-sectional survey. Cross-sectional studies are also the least difficult to carry out, requiring no more than a questionnaire or a single medical exam. Typically, participants are asked their height and weight and what diseases their doctor has told them they have. Obese persons usually report more medical diagnoses, particularly diabetes, hypertension, high cholesterol, heart disease, arthritis, and gallstones. Compared to prospective studies, there are many problems and confounding factors with cross-sectional studies. One example is diagnostic bias. Doctors are trained to expect certain diseases in obese persons and may diagnose them more readily. For whatever reason, cross-sectional studies generally paint a much more unfavorable picture of the health of obese persons than controlled prospective studies. In this report we have focused on prospective studies that do not rely on a doctor's diagnosis, but rather use the simplest and most verifiable measure of health: age at the time of death.

Table 2. Population Characteristics and Outcome of Epidemiological Studies of Obesity and Total Mortality

Study population	Relative hazard of obesity	Likely prevalence of weight loss practices	Reference
Young nurses	Exceptionally high	Very high	Manson et al., 1995
Holders of individual life insurance policies	Very high	Very high	Lew, End, & Wilber, 1979
Harvard alumni	Very high	High	Lee, Manson, Hennekens, & Paffenbarger, 1993
Residents of affluent Boston suburb (Framingham)	High	High	Garrison, Feinleib, Castelli, & McNamara, 1983
Neighbors and relatives of American Cancer Society volunteers	High	High	Lew et al., 1979
Residents of Finland	Moderate	Moderate	Rissanen et al., 1989; Rissanen et al., 1991
White women in Charleston, South Carolina	Moderate	Moderate	Stevens et al., 1992
Black women in Charleston, South Carolina	None	Low	Stevens et al., 1992
Civil servants in rural eastern Finland	None (Women) Low (Men)	Low	Tuomilheto et al., 1987
German construction workers	Inverse	Low	Brenner et al., 1997
Dutch civil servants	None (Women) Low (Men)	Low	Tuomilehto et al., 1987
Black Kaiser Permanente subscribers	None (Women) U-shaped* (Men)	Low	Wienpahl, Ragland, & Sidney, 1990
San Francisco longshoreman	Inverse relation	Low	Borhani, Hechter, & Breslow, 1963
Residents of villages in rural Italy	None	Very low	"Incidence and Prediction of Coronary Heart Disease," 1982
Residents of villages in rural Scotland	Inverse relation	Very low	Garn, Hawthorne, Pilkington, & Pesick, 1983
Elderly populations	Inverse relation	Very low	See text discussion.
Residents of American Samoa	None	Very low	Crews, 1989
Residents of Micronesia	Inverse relation	Very low	Vandenbroucke et al., 1984

Residents of Fiji	Inverse relation	Very low	Hodge, Dowse, Collins, & Zimmet, 1996; Collins, Dowse, Cabealawa, Ram, & Zimmet, 1998
New Zealand Maori	None	Very low	Salmond, Beaglehole, & Prior, 1985
Native Americans of the Pima tribe	Inverse relation (women) Inverse up to BMI of 40 (men)	Very Low	Hanson et al., 1995

Note: Studies are ranked according to the degree of relative risk associated with obesity. The incidence of weight loss behavior is based either on direct report or on the characteristics of populations known to be associated with a high prevalence of dieting practices.
*Highest mortality at body mass index (BMI) < 20; lowest mortality at BMI of 28 (moderately overweight). Risk increase only for BMI > 40.

Even though cross-sectional studies are the least reliable (Table 1) and are seldom relied upon when other information is available, obesity experts rely primarily on these health surveys. For example, reviews of the health consequences of obesity focus almost entirely on the fact that certain diseases are more common in obese people than in lean ones (Akram et al., 1997; Bray, 1996; Pi-Sunyer, 1993). Thus, we will briefly discuss each of these conditions in turn. We will first discuss the evidence that the disease is more common among the obese, then we will explore possible disease processes that might logically link obesity to the pathology, and finally we will address the question of whether weight loss is an effective treatment for the condition.

Type-2 diabetes is probably the condition most strongly linked to obesity. In type-1 diabetes, the pancreas fails to produce enough insulin. Without frequent injections, the patient will die. In contrast, insulin levels are normal or even high in type-2 diabetes, but blood sugar is elevated because insulin is unable to carry out its functions. Type-2 diabetes does not lead to as severe a set of complications as type-1, and the biggest danger of the disease is as a risk factor for coronary heart disease. Type-1 diabetes usually begins before age 40, and decreases life expectancy by an average of 8 years (Bale & Entmacher, 1977). Type-2 usually occurs later in life, and reduces life expectancy by only 2 to 4 years. Diabetics over the age of 70 have the same life expectancy as nondiabetics of the same age.

The link between obesity and type-2 diabetes is undeniable. One oft-cited statistic is that 80% of persons with type-2 diabetes are obese (Bray, 1996; Pi-Sunyer, 1993). Less often mentioned is the fact that in the demographic group with the highest incidence of type-2 diabetes, women in their 50s, the overall prevalence of obesity is about 60% (Flegal, Carroll, Kuczmarski, & Johnson, 1998). In

one study cited by the World Health Organization (Akram et al., 1997), diabetes was 40 times more common in women with a body mass index (BMI; kg body weight per meter of height squared) of 30 relative to lean women with a BMI less than 22. Although most studies have not documented such an extreme risk, an association does exist and has been verified in prospective studies, wherein obese persons are found to be more likely to develop diabetes (Edelstein et al., 1997). However, a relationship between obesity and subsequent development of diabetes was not found in all studies. In a study of a multiethnic population in Israel, there was no increase in risk of diabetes except when BMI was greater than 31 (Modan et al., 1986).

Does excess body fat lead directly to type-2 diabetes? Studies have consistently shown that the disease is genetic in origin. If one identical twin over the age of 50 has type-2 diabetes, there is a 91% chance that the second twin will also develop it (Barnett, Eff, Leslie, & Pyke, 1981). Although it is true that identical twins share their environment and diet while growing up, by the sixth decade of life the effect of childhood environment is probably minimal. Furthermore, there was little effect of BMI on the age of onset for diabetes, as the first twin to be diagnosed had an average BMI of 23.8 while the second twin, who stayed free of diabetes up to 15 years longer, had an average BMI of 24.9. Given that diabetes type-2 is a genetic disease and that most of its victims are obese, it follows that the genes causing diabetes must also facilitate weight gain. There is now excellent evidence that this is the case.

Excess levels of insulin are the first abnormality to appear in future diabetics, followed by excessive weight gain. This was shown in a prospective study in which levels of insulin were found to predict the subsequent rate of weight gain during a 17-year follow-up (Sigal et al., 1997). People with a family history of diabetes are heavier than those lacking this genetic endowment, and this high-risk group also shows more weight gain over time (Lapidus, Bengtsson, Lissner, & Smith, 1992). Also, people with diabetes in their family have higher insulin levels, independent of their body weight (Ishikawa, Pruneda, Adams-Huet, & Raskin, 1998). This is consistent with the idea that a diabetes-inducing "thrifty gene" promotes obesity and weight gain (Groop & Tuomi, 1997). As suggested by the epidemiologist Peter Bennett, "Insulin resistance, therefore, may be the key defect that *independently* [italics in original] leads to obesity, hypertension, and diabetes, and accounts for the well-known associations among obesity, serum insulin levels and glucose intolerance. Insulin resistance, rather than obesity, may be the principal determinant of diabetes" (Bennett, 1986).

Bennett's model for the development of diabetes is illustrated in Figure 1. Genetic factors initiate the disease process, leading to insulin resistance and a compensatory increase in insulin production by the pancreas. High levels of insulin lead to weight gain, which can further exacerbate insulin resistance. After many years, the system decompensates and blood glucose rises. Dietary factors may also

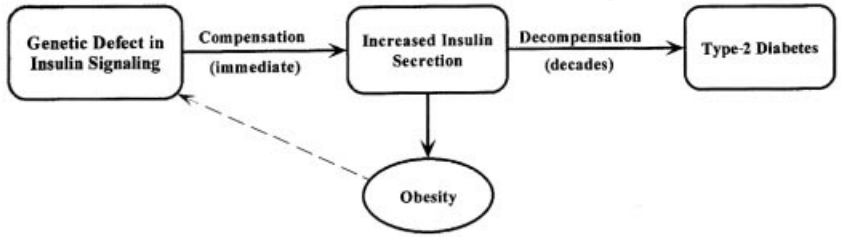


Fig. 1. Hypothetical model, based on current human genetic studies, for the relationship between genetic defects in insulin signaling, circulating insulin, obesity, and the development of diabetes.

contribute to the development of diabetes. In one study, nutritional habits were surveyed in a population followed prospectively for 20 years (Feskens et al., 1995). Future diabetics ate more saturated fat and took in fewer vegetables and less vitamin C. Thus although genetic factors predominate, lifelong dietary habits can modify genetically determined risk.

How effective is weight loss as medical treatment for diabetes? Obviously, blood glucose levels fall within hours of skipping a meal, so there can be an immediate apparent benefit. Simply because blood glucose falls in the short run, however, does not mean that the chronic disease of diabetes has been reversed. Many studies have looked at the short-term benefits of weight loss programs, usually while the participants are still on a restrictive regimen. Many authors have reviewed the apparent risk factor improvements that take place during the initial phase of weight loss and in early maintenance (Akram et al., 1997). Here we will consider only those few studies that included at least a 6-month follow-up. For type-2 diabetics, the critical factor to monitor is glycosylated hemoglobin, which provides a picture of the prevailing glucose levels over several weeks. A review of all the controlled trials of weight loss in type-2 diabetes showed that there were initial improvements immediately after the weight loss program, but follow-up at 6 to 18 months showed a deterioration back to starting values, even when weight loss persisted (Ciliska, Kelly, Petrov, & Chalmers, 1995). In 21 experimental groups where there was follow-up, persisting benefit was found only in 3, despite maintained weight losses of 3 to 9 kg. A 1-year follow-up study of a behavior modification weight loss program showed that diabetics were actually worse off for having lost weight after 1 year. Overall, it appears that existing very-low-calorie or behavioral programs have no beneficial effect at 1 year of follow-up, even when weight loss is maintained. In a prospective study of the relationship between weight change and mortality in type-2 diabetics, those who lost weight had a higher, not lower, risk of death (Chaturvedi, Fuller, & the WHO Multinational Study Group, 1995). For moderately overweight diabetics (BMI < 26), successful weight loss led

to a tripling of the death rate. For severely obese diabetics (BMI > 29), there was a small but significant (16%) reduction in death rate associated with weight loss. Why are diabetics who are losing weight more likely to die? One possibility is that weight loss occurs as diabetes progresses and worsens. Thus those that are losing weight may be those with the most severe disease. However, if diabetics with severe disease lose weight even as they continue to deteriorate, the question remains whether weight loss is best treatment for type-2 diabetes.

Can weight loss prevent diabetes? Most prospective studies suggest that weight gain precedes the onset of type-2 diabetes. However, other studies do not show this. In an Israeli prospective study, formerly obese persons had a higher incidence of diabetes (14%) than currently obese subjects who had gained weight (6%; Modan et al., 1986). In every category of current BMI, weight losers had a higher risk of developing diabetes than those who gained weight or stayed stable. Among the Pima Indians, who have the highest rate of type-2 diabetes in the world, weight gain is not related to the development of the disease (Charles et al., 1993). Despite poor results from weight reduction trials in diabetics, weight loss is still usually considered the cornerstone of diabetes treatment. As noted in the *New England Journal of Medicine* (Wood & Bierman, 1986), "Tradition, as opposed to scientific evidence, has had a remarkable influence on the prescription of dietary therapy for diabetes."

Hypertension is two to three times more common in obese women and men than in the leanest members of the population (Akram et al., 1997). Hypercholesterolemia, on the other hand, is only weakly related to body weight. The correlation coefficient between BMI and cholesterol level in most studies is about 0.1 in women and 0.2 in men (Garn, Bailey, & Block, 1979). Blood pressure correlates better with BMI, usually around 0.4 in middle age (Ernsberger & Nelson, 1988a). Put another way, if you know a woman's BMI, you can predict her cholesterol level with an accuracy only 1% better than pure chance. Blood pressure can be predicted a little better on the basis of BMI, with an accuracy 16% better than chance.

Does hypertension result directly from excess body fat? Obesity and hypertension commonly accompany each other in human populations (Sims, 1982), but the process leading from enlarged fat stores to high blood pressure is unknown. A weakness in our current understanding is the lack of an animal model for obesity-related hypertension. Dogs become hypertensive when their daily diet is supplemented with 2 lb of lard (Rocchini, Moorehead, Wentz, & Deremer, 1987), but this may be a direct effect of excess saturated fat intake. Rats fed an obesity-inducing diet of sweetened lard for one year show a slight increase in blood pressure when measured by one method, but not by a second method (Buñag, Krizsan, & Itoh, 1990). Obesity caused by overfeeding has no effect on blood pressure (Contreras & King, 1989; Ernsberger & Nelson, 1988b). Zucker fatty rats have normal blood pressures (Buñag & Barringer, 1988). Thus, obese animal models do not show elevated blood pressures.

An animal model of hypertension in obesity developed at Case Western Reserve University involves the expression of a specific obesity gene on a background of genetic hypertension (Ernsberger, Koletsky, Baskin, & Collins, 1996; Ernsberger, Koletsky, Baskin, & Foley, 1994; Koletsky, Boccia, & Ernsberger, 1995). In this model, lean and obese siblings are both hypertensive, but the obese animals unexpectedly have somewhat lower blood pressures. Thus, the net impact of genetic obesity on blood pressure is actually protective. However, the association of obesity with reduced blood pressure is lost under certain circumstances. For example, if the animals are fed a diet high in salt, blood pressure will rise markedly in the obese rats so that they are more hypertensive than the lean rats. Another example is weight cycling, wherein the loss of weight on a low-calorie diet is alternated with ad libitum refeeding. Weight-cycled obese rats have very high blood pressures, exceeding those of their lean siblings (Ernsberger, 1994; Ernsberger, Koletsky, Baskin, & Collins, 1996). Therefore, under nutritional stresses such as excess salt consumption or "yo-yo dieting," obesity becomes a liability to the cardiovascular system.

Why do obese animals have normal blood pressures? Weight stability might distinguish obese rats from obese humans. Obese animals maintain steady body weights and consume a constant amount of food on a day-to-day basis. In contrast, obese humans frequently alternate between fasting and bingeing and show large fluctuations in body weight as they lose and then regain a major proportion of their body fat (Blackburn et al., 1989). An animal model of this so-called "yo-yo syndrome" has been characterized (Ernsberger & Nelson, 1988b). Animals made obese by overfeeding developed hypertension only when subjected to periodic supplemented fasts. Blood pressure fell during weight loss, but after then rose, overshooting the original level. Because this form of hypertension occurs during the refeeding period following a fast, it is known as refeeding hypertension. Hypertension results from refeeding in dogs, pigs, mice, and rats (Ernsberger & Koletsky, 1993). Genetically obese animals show even greater refeeding hypertension when weight cycled, and also develop enlarged hearts and significant kidney damage (Ernsberger & Koletsky, 1993; Ernsberger et al., 1994; Ernsberger, Koletsky, Baskin, & Collins, 1996; Koletsky et al., 1995). Thus when obese animals are made to alternately lose and regain weight, they develop diseases comparable to those experienced by obese humans.

For human patients, a fall in blood pressure has been observed immediately following caloric restriction (Landsberg & Young, 1978), leading to guidelines recommending weight loss in hypertensive patients. However, there is little information on long-term changes in blood pressure, particularly during weight regain. Inpatient studies (Jung, Shetty, & James, 1980) show rapid rebound of blood pressure upon full restoration of caloric intake. A report on the effects of weight regain after therapeutic weight loss showed increases in systolic blood pressure as well as cholesterol, triglycerides, and plasma glucose (Pfohl, Luft, Blomberg, & Schmülling, 1994).

The cause of hypertension in obese persons might be the cycles of weight loss and regain they undergo, rather a direct influence of fat tissue. This would explain the weak relationship between obesity and hypertension in cultures and societies in which weight loss practices are uncommon (see Table 2). This "yo-yo hypothesis" requires further testing in human populations.

Weight loss is the most common nondrug treatment recommended for hypertension. However, as is the case for diabetes, the long-term results are disappointing, even when losses are maintained, including massive amounts of weight lost after gastric surgery (Ernsberger & Nelson, 1988a). Promising results have been obtained with trials of multifactorial interventions that have included exercise, sodium restriction, healthful overall diets, and stress management along with weight loss (Beckmann et al., 1995; Whelton et al., 1998). For multifactorial programs, it is impossible to say how much of the blood pressure reduction is due to the small loss of body weight (< 5 kg) that accompanies these lifestyle modifications.

As noted above, cholesterol levels are only weakly correlated with body weight. Indeed, even individuals with so-called morbid obesity selected for gastric surgery do not show elevated cholesterol levels (A. M. Wolf, Beisiegel, Kortner, & Kuhlmann, 1998). The weak relationship between fatness and cholesterol levels can probably be accounted for by dietary factors. A diet high in fat and low in fiber and vegetables can, through separate and independent actions, lead to weight gain and increases in cholesterol, as indicated in the paradigm delineated in Figure 2. Similarly, a sedentary lifestyle independently promotes weight gain and elevated cholesterol. The relevant question is where to intervene. We would argue that modification of dietary and exercise habits is a more direct approach and more likely to achieve long-term results. Moreover, medications with proven effectiveness are available to treat excessive cholesterol levels.

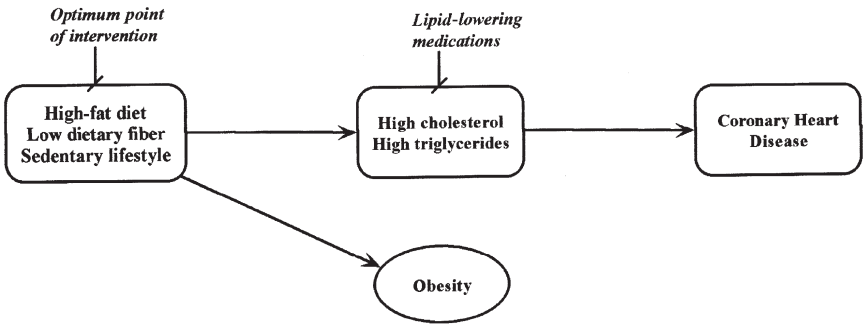


Fig. 2. Hypothetical model for the relationship between dietary saturated fat, obesity, and elevated cholesterol levels.

Type-2 diabetes, hypertension, and elevated cholesterol are primarily of concern because they lead to coronary heart disease, the number one killer in the Western world. What is the relationship between obesity and atherosclerosis? The evidence from prospective studies is contradictory. The Framingham study in particular seems to indicate a higher rate of diagnosed coronary heart disease in obese participants (Higgins, Kannel, Garrison, Pinsky, & Stokes, 1988). However, in the Framingham study weight cycling could account for all of the excess risk associated with obesity (Lissner et al., 1991). Two comprehensive reviews have covered the available literature and concluded that there is no consistent relationship between body weight or body fatness and coronary heart disease (Barrett-Connor, 1985; Williams, Jones, Bell, Davies, & Bourne, 1997).

Arthritis, or more specifically the osteoarthritis associated with old age, has been linked to obesity in cross-sectional and prospective studies (Felson, 1996). In contrast to the diseases mentioned so far, a well-understood process links increased body weight to osteoarthritis through increased wear and tear on the joints. Osteoarthritis is the only disease that has been proven to be directly caused by high body weight. It should be noted, however, than thin persons are not exempt from osteoarthritis.

Gallstones are typically listed as one the health consequences of obesity (Akram et al., 1997; Bray, 1996; Pi-Sunyer, 1993). Even though gallstones are much more common in obese persons than in lean ones, excess body weight is almost certainly not a direct cause of gallstones. That is because large and rapid weight losses are a proven direct cause of gallbladder disease (Everhart, 1993; Vezina et al., 1998). Obese persons are more at risk primarily because they are more likely to engage in crash dieting. An additional role may be played by excess dietary fat, similar to the interplay between lifestyle factors, obesity, and cholesterol (Figure 2).

The Biological Response to Caloric Restriction

What physical changes happen during a weight loss diet, and how long do they take? Timing is an important clue to understanding what is going on in the body. Consider the concept of ideal weight. According to the ideal weight hypothesis, there is a small range of BMI values that we all should attain. If your BMI is higher than this ideal, then your blood sugar, blood pressure, and blood cholesterol should increase proportionately with each excess pound. As you lose weight, your risk factors should decline according to the proportion of excess weight you have removed. Thus if you lose 10% of your excess weight, you should lose 10% of your excess blood pressure. Does this happen? The answer appears to be no. These risk factors are normalized very quickly, in many cases before a significant amount of weight is lost. Blood sugar, of course, drops within a few hours of skipping a meal and stays low all the time when one is on a low-calorie diet. Blood sugar stays low even when

one goes off the diet, because one's tissues readily take up nutrients after a period of deprivation. Blood pressure also drops quickly on a very- low-calorie diet, usually within a week, before there is much loss of body fat (Ernsberger & Nelson, 1988a). On more moderate caloric restriction, there is less of a drop in blood pressure and it takes longer to develop. Drops in cholesterol take a few weeks to register, but the full drop in cholesterol is achieved after only a fraction of excess weight is lost. In fact, "bad" cholesterol (LDL, or low-density lipoprotein) reaches its lowest level 8 weeks into a diet and actually rises with additional weight loss (Andersen, Wadden, Bartlett, Vogt, & Weinstock, 1995). Improvements in cholesterol profile were more related to improved dietary habits such as reduced saturated fat intake than to the amount of weight loss. Therefore, the reductions in risk factors for heart attack that are seen with reduced-calorie regimens are not solely the result of body fat loss. This argues against the ideal-weight hypothesis.

Why do risk factors drop so quickly compared to the slow and gradual loss of body fat? One explanation is the fall in risk factors is a biological response to mild starvation, rather than the result of reducing body fat stores. We tested this idea with a meta-analysis of trials of weight loss for the treatment of blood pressure (Ernsberger & Nelson, 1988a). Comparison of the kilograms of weight lost on the diet to the blood pressure reduction showed no relationship. On the other hand, if we look at the rate of weight loss per week, there was a strong relationship. Gradual weight loss had little effect, whereas there were dramatic falls in blood pressure with rapid weight loss, especially with very-low-calorie formulas. By the same token, diets providing very few calories (300–800 per day) led to large falls in blood pressure, whereas more moderate diets with 1,200–1,800 calories seldom lowered pressure. This means that the process of "going on a diet" and entering a state of deprivation results in a lowering of blood pressure. Part of the benefit may result from the consumption of healthier "diet" foods such as fruits and vegetables and the avoidance of high-fat and high-sodium "junk" foods. In the long run, however, this blood-pressure-lowering effect is not sustained after the diet ends.

Most patients with high cholesterol are treated first with a weight loss regimen before any drug therapies are given. However, despite short-term changes, there is limited long-term effectiveness of weight loss as cholesterol-lowering therapy (Andersen et al., 1995; R. N. Wolf & Grundy, 1983). In one study, obese patients were placed on a 1,000-calorie diet until they got all the way down to their insurance table weight (R. N. Wolf & Grundy, 1983). Importantly, their diet was controlled so that they consumed the same amount and type of dietary fat before and after losing weight. After a temporary dip during the weight loss process, levels of LDL cholesterol returned to match the starting obese level. Thus provided that dietary fat intake is not changed, weight loss does not improve cholesterol levels. One exception to this is weight loss by surgical methods such as gastric or biliopancreatic bypass. By interfering with the absorption of dietary fat, these operations can significantly lower cholesterol. However, even following massive

weight losses of 50 kg or more, a fall in cholesterol level is not always seen (A. M. Wolf et al., 1998). Similarly, the new drug orlistat can lower cholesterol by preventing the uptake of dietary fats from the digestive tract. The effectiveness of these surgical and pharmaceutical interventions does not arise from loss of body fat, but from a direct intestinal action.

Undeniably, weight loss programs can benefit health. This is especially true when these programs emphasize permanent lifestyle changes and encourage exercise and healthier food choices. On the other hand, positive lifestyle changes can be encouraged without a primary focus on weight loss. Thus exercise programs and low-fat diets can yield real and lasting improvements in risk factors while failing to correct obesity (Dengel, Katzel, & Goldberg, 1995). Importantly, improvements in cholesterol and other risk factors stemming from improved diet are maintained as long the dietary guidelines are followed and do not dissipate with time.

The poor effectiveness of weight loss stands in marked contrast to the increasing effectiveness of medications. New and highly potent treatments for type-2 diabetes, hypertension, and high cholesterol have appeared in the last few years. Often new and old drugs can be combined for even greater effectiveness. A drawback of relying on weight loss as a first line of treatment is that chronically ill patients may be denied truly effective pharmaceutical therapy while pursuing the elusive goal of permanent weight loss. Weight reduction should be considered at most an adjunct to treatment rather than a primary goal.

Weight loss not only may be ineffective as a tool for managing chronic disease but may even cause harm in the long run. Weight loss is not usually permanent, regardless of the intervention used. During regain of lost weight, all of the short-term benefits of weight loss are undone, and in many cases risk factors become worse during weight regain than they were at the starting level (Ernsberger, Koletsky, Baskin, & Collins, 1996). Blood pressure shows large increases during the relapse to obesity in humans and in laboratory animals. Worsening of risk factors during regain probably accounts for the increased heart attack deaths seen in persons who lose and regain weight.

Another potentially harmful effect of weight loss regimens is that they can trigger binge eating. Binging is never healthy, but in persons with chronic disease it can do serious harm. Diabetics need to maintain a steady level of food intake to keep their blood sugar levels tightly regulated. Alternately starving and bingeing can compromise blood sugar control. Similarly, chaotic eating patterns can hamper therapy for high blood pressure and cholesterol.

The position of weight loss in medicine today can be compared to the role of bloodletting 150 years ago. Bloodletting became popular because doctors found that if feverish patients were bled, their fever would break and their skin would become cool and clammy. Thus bloodletting improved the symptoms of sick patients. Of course, we now know that blood loss creates a state of shock that lowers body temperature but ultimately increases the risk of death. Similarly,

weight loss produces short-term improvements in symptoms but may not be ultimately beneficial. Before weight loss can be removed from its exalted status as a therapy, a revolution in medicine may be required comparable to the one that brought an end to the practice of bloodletting.

To summarize, weight loss programs can produce many short-term benefits that have been documented in literally thousands of medical studies. However, those few trials with follow-up beyond 6 months have failed to show lasting benefit. Weight loss programs can actually do harm by diverting the patient from more effective and reliable treatments with modern drugs or with sustainable lifestyle changes. Furthermore, when lost weight is regained the patient may be worse off than when she started because of the harmful consequences of weight cycling. All of these limitations of weight loss programs compel the creation of a new paradigm that incorporates the health-promoting aspects of permanent lifestyle changes without a focus on the correction of obesity.

Body Weight and Mortality

How hazardous is obesity? A condition is primarily considered hazardous when it shortens life expectancy. To establish this, it must first be shown that people having the condition consistently die sooner than appropriate controls. Evidence for a causal relationship must then be obtained. Alternatives to the hypothesis of simple causality must be refuted. Furthermore, reversing the condition should extend life.

The relationship between initial body weight, as measured by BMI and subsequent mortality, is complex and varies markedly between different prospective epidemiological studies (Table 2). Most studies have shown a U-shaped relationship between BMI and mortality, with both low and high body weights associated with increased risk of death (Andres, 1980). Others studies have shown no relationship (Keys, 1981, 1989). A few studies have shown a steady decline in mortality with increasing BMI, and a few have shown a steady increase in mortality with increasing weight up to a relative risk (RR) between 1.5 and 2 for the extremely obese. The latter studies, listed in the top few rows of Table 2, have been emphasized in the setting of public health policy concerning body weight. A quantitative meta-analysis of 23 major studies showed a U-shaped curve in the combined data for men and women, with increased mortality when BMI was less than 23 or greater than 28 (Troiano, Frongillo, Sobal, & Levitsky, 1996). To place this in perspective, a BMI of 21 corresponds to the old “ideal weight” set by Metropolitan Life Insurance. Thus, being less than 10% “overweight” or being underweight by any amount raises the risk of death. At the other end of the spectrum, being more than 35% “overweight” also constitutes a hazard.

Which is more important in the overall population, the hazards of underweight or the hazards of overweight? In a study of Finnish women ages 25–64, the leanest

fifth and the fattest fifth of the population both showed a RR of about 1.5 (Rissanen et al., 1991). For women over 65, only underweight was a hazard. Therefore, the impact of underweight and overweight are very nearly the same. Nearly equivalent results have been obtained in many populations, whenever U-shaped distribution of mortality versus BMI has been obtained. Based on his study of 1.8 million Norwegians, Waaler (1984) estimated that 4.3% of deaths in persons aged 30–79 could be attributed to obesity. Especially if the elderly are included, the number of excess deaths attributable to underweight may be higher. Therefore, a rational approach to public health would dictate devoting equal time to treating underweight as overweight.

Some authors acknowledge that moderately fat people have increased life expectancy, but nonetheless argue that obesity is dangerous (Lee & Manson, 1998). It has been claimed that because cigarette smokers weigh an average of 2 to 3 kg less than nonsmokers, the excess mortality among thin people can be explained by the higher numbers of smokers in that group. However, in numerous studies, mild obesity was found to be protective in nonsmokers and smokers alike. Adjustment of mortality data for smoking has no effect on its relationship to body weight. Importantly, only light to moderate cigarette smokers tend to be lean. In many studies, persons who consume at least two packs a day actually weigh more than nonsmokers. Thus, the smokers at the highest risk for disease are not unusually lean.

Another explanation offered for the increased mortality among underweight persons is the following: The reason that thin people are not obese is because they have a hidden, undetectable disease that causes them to lose weight and then, after many years of thinness, causes their death. Thus even though lean people have a shortened lifespan, it is still advantageous to be thin. However, there is no evidence that "occult wasting disease" even exists. Patients with unexplained weight loss tend to either deteriorate or die within a single year, or to regain their lost weight along with their health (Reife, 1995; Wallace, Schwartz, LaCroix, Uhlmann, & Pearlmann, 1995). Significant weight loss is a late symptom in cancer, appearing only after the tumor is large enough to have metabolic effects or cause pain. Because weight loss occurs only in the advanced stages of serious disease, nearly all persons who have become lean because of fatal wasting disease would be screened out of prospective studies during the initial physical examination. Any persons with previously existing fatal wasting disease unintentionally included in such studies should die within the first two years of follow-up. However, in most studies, excluding deaths occurring in the first 5 to 10 years has no effect on the outcome. Finally, it is unlikely that fatal wasting disease is a major cause of thinness in the general population. Genetic predisposition and the desire to conform to cultural and medical standards for body weight are the two most probable causes of leanness.

In the Ontario Longitudinal Study of Aging (Hirdes & Forbes, 1992), mortality was highest in underweight men (BMI < 20; RR = 1.00) and lowest in the overweight group (BMI = 25–30; RR = 0.50). Mortality in the severely obese men remained lower than that of the underweights (BMI > 30; RR = 0.75). Any role for "occult wasting disease" can be ruled out, because only those reporting good or excellent heath at baseline were included. A representative population sample in Italy showed lowest mortality in women at a BMI of 32 and in men at a BMI 29, both in the severely obese range (Seccareccia, Lanti, Menotti, & Scanga, 1998).

Age has a powerful impact on the relationship between body weight and mortality. Studies of people between the ages of 25 and 45, such as first-time life insurance buyers and young nurses, tend to show the greatest hazard of obesity (see Table 2, top two lines). In contrast, among the elderly, low body weight is a strong risk for subsequent death but there is little hazard attributable to obesity until extreme levels (BMI > 35) are reached (Andres, Elahi, Tobin, Muller, & Brant, 1985; Stevens et al., 1998; Tayback, Kumanyika, & Chee, 1990). In nearly all of these studies, subjects with current health problems that could lead to weight loss were excluded. In most cases, smokers were not included in the study, and mortality occurring shortly after weight determination was excluded, so as to avoid any possible influence of "occult wasting disease." Thus, low body weight is a reliable harbinger of decline and death in persons over 60 years of age.

The impact of age on the relative hazard of obesity is illustrated in Figure 3, which shows data from a prospective study of British civil servants that were adjusted for smoking habit (Jarrett, 1986). In the youngest age group in the study, those aged 40–44, the mortality rate doubled from the lightest to the heaviest subgroup. This doubling of risk agrees with a report from the Nurses' Health Study, which found an identical increase in women of about the same age (Manson et al., 1995). The Nurses' Health Study reported its findings only as relative risk, thereby emphasizing the twofold elevation in hazard. What was left unstated is the very low risk of dying—regardless of weight—at these young ages. Expressed differently, at age 44 you have a 98% chance of living to age 54 if you are lean, and 96% odds if you are severely obese (see Figure 3). What is considerably more important from a public health standpoint is the effect of weight on mortality at ages 60–64, where mortality is highest for those who meet life insurance criteria. Obese persons face a 2% greater chance than lean individuals of dying between 44 and 54, but a 6% lesser chance of dying between 64 and 74. As a result, the net adverse impact of obesity on median life expectancy is minimal to nonexistent.

The fact that obese persons have a normal life expectancy presents a paradox, since the incidence of a number of serious risk factors is increased in obesity. The solution to this puzzle is that there are advantages as well as disadvantages to being heavy (Ernsberger & Haskew, 1987). Obese persons are less likely to later develop cancer, as shown in studies in France, Hawaii, Iowa, Massachusetts, Norway, Puerto Rico, and Scotland, as well as the Hypertension Detection and Follow-Up Program

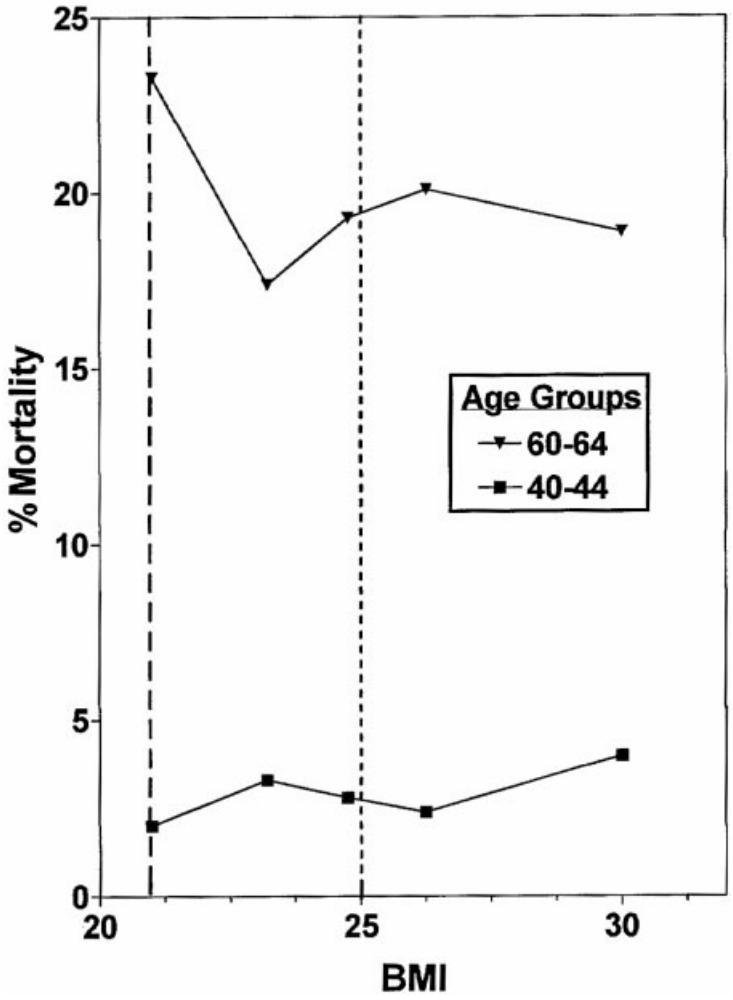


Fig. 3. Mortality rate during 10 years of follow-up as a function or starting BMI in the Whitehall study (Jarrett, 1986). For purposes of illustration, only the youngest (40–44) and oldest (60–64) groups are included. Data were adjusted for smoking. Subjects were British civil servants. The dashed line indicates "ideal weight" defined by life insurance standards (BMI = 21), and dotted line marks the threshold for the current definition of overweight (BMI > 25).

and Seven Countries studies. The obese are also protected against infectious diseases, chronic obstructive pulmonary disease, osteoporosis, mitral valve prolapse, intermittent claudication, renovascular hypertension, eclampsia, premature birth, anemia, type-1 diabetes, peptic ulcer, scoliosis, and suicide (Ernsberger & Haskew, 1987). These health benefits of obesity might potentially offset its hazards.

Obesity is also associated with improved survival in several diseases. Heavy persons with hypertension, type-2 diabetes, and high cholesterol have a more favorable prognosis than thin people with these same ailments (Ernsberger & Haskew, 1987). Obese hypertensives have been shown to outlive lean hypertensives in more than 15 separate controlled prospective studies (Barrett-Connor & Khaw, 1985). In one study, 43% of nonobese hypertensives died, whereas only 26% of obese hypertensives died. In the Systolic Hypertension in the Elderly Program, mortality fell by 35% for each 5 kg/m^2 increment in BMI. Lean type-2 diabetics tend to have a more severe form of the disease than obese diabetics (Ross et al., 1997). Retinopathy is three times more common in lean than in obese type-2 diabetics. Among placebo-treated type-2 diabetics in the University Group Diabetes Program, those who were obese had lower mortality during 5 years of follow-up than did the nonobese (2.8% vs. 7.2%).

Obesity may cushion the risk of high cholesterol. Heavy persons exhibit elevations in literally every proposed risk factor for atherosclerosis. Despite this, a comprehensive review of the medical literature came to the conclusion that obesity is not associated with plaque formation in blood vessels (Barrett-Connor, 1985). Even among persons weighing more than 300 pounds, no increase in coronary plaque has been found at autopsy. Because heavy people have elevated risk factors that fail to translate into a higher incidence of disease, the danger associated with a given risk factor level must differ between the lean and the obese. For example, a total cholesterol of 300 is probably not as grave a sign for a fat patient as for a thin one.

Although hypertension, diabetes, and hyperlipidemia have reduced complications and mortality in heavy persons, this does not mean these conditions are benign in obesity, nor does it mean that diabetics and hypertensives should be encouraged to gain weight, since this may worsen their condition. However, it does mean that the threat to the health and longevity of fat people posed by diabetes and hypertension has been overestimated because of the failure to take into account the ameliorating influence of obesity on these conditions. Thus obesity is associated with a decreased incidence of a few diseases even though the incidence of many other ailments is increased among the obese.

Epidemic increases in the incidence of obesity in the United States and around the world have been documented in numerous independent reports since the 1980s. Figure 4 shows time trends in national data broken down by gender and race. Since 1960, there have been progressive increases in average BMI in all subgroups, paralleling the rising prevalence of obesity. In almost a mirror image pattern, mortality rates have fallen simultaneously. The causes of death contributing to the declines in mortality are those usually linked to obesity, especially heart attack and stroke. If obesity were truly a major contributor to premature death, as some have claimed (Manson et al., 1995) then we would expect a rising death toll, especially with the sharp rise in obesity since 1977.

An example of short-term time trends in a specific population comes from Minneapolis-St. Paul, Minnesota. Between 1981 and 1986, the average BMI in that population rose 1.2 kg/m^2 in women and 0.6 kg/m^2 in men (Sprafka, Burke, Folsom, Luepker, & Blackburn, 1990). Yet during the same time interval and in the same population the incidence of coronary heart disease fell 13% in women and 20% in men. Paralleling the decrease in coronary disease were falls in risk factors: diastolic blood pressure (down 0.9 and 1.1 mm/Hg in women and men, respectively), and cholesterol (down 5.8 and 5.2 mg/dl). Thus even as human populations fatten, risk factors and diseases usually linked to obesity continue to decline. The most likely explanation is that improvements in lifestyle, such as reduced intakes of cholesterol, saturated fat, and sodium and increased exercise, have improved health but not led to widespread loss of weight. Also much of the decline in mortality rates in Western cultures has been credited to improved detection and treatment of hypertension with improved medications. Hypertension is the primary health risk faced by the obese, and if adjustment is made for the higher blood pressures in obese persons, their elevated rates of heart attack and stroke are eliminated (Keys, 1981). Thus improved treatment of hypertension in recent years may have eliminated much of the cardiovascular risk associated with obesity.

Setting aside for the moment the beneficial or ameliorating effects of obesity, there are a number of ailments, including hypertension, that are more common among the obese. Does this mean that obesity is a cause of these diseases? The only way to securely establish this would be to conduct a randomized trial in which one group of obese persons would undergo weight reduction while a control group received comparable counseling on nutrition and exercise without specific advice to lose weight. Any differences in disease incidence or mortality between the groups could then be attributed to the effect of weight loss. Unfortunately, such a trial is impossible, because no safe and effective treatment for obesity exists.

What of the mortality risks of underweight? Would a weight gain program lower the risk of death in excessively lean persons? The answer appears to be yes. In the case of anorexia nervosa, weight gain is the preferred course of treatment and is life saving. The same is also true for protein-calorie malnutrition. There is also evidence that weight gain is beneficial in lean persons suffering from neither anorexia nor malnutrition. Elderly patients enrolled in a weight gain program who increased their weight by at least 5% showed reduced mortality and extended longevity (Keller, 1995). Successful weight gain also reduced the incidence of falls and recurrent infections. In patients with lung disease having a BMI of 25 or less, a gain of 2 kg or more reduced mortality (Schols, Slangen, Volovics, & Wouters, 1998). Thus controlled clinical trials of weight gain in underweights show decreased mortality, but no equivalent trial exists to show benefits of weight loss.

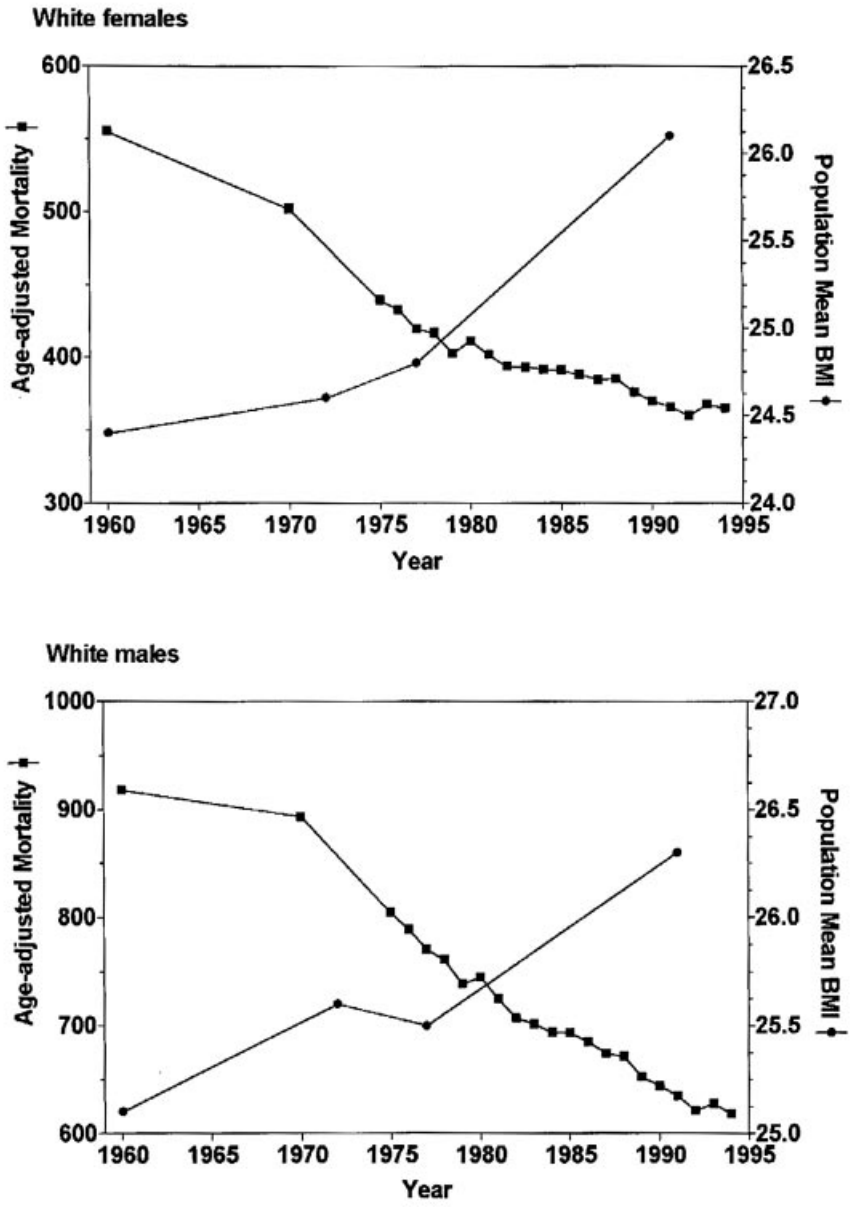
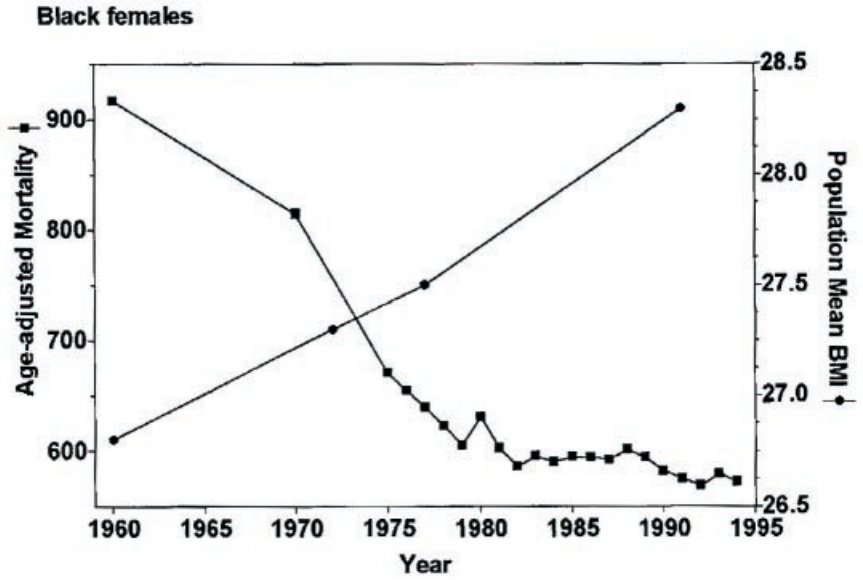


Fig. 4a. Time trends for obesity and total mortality by race and gender between 1960 and 1994. Age-adjusted total mortality data are from the National Center for Health Statistics. Mean BMI by gender and race are from the National Health and Nutrition Examination Surveys (Kuczmarski, Flegal, Campbell, & Johnson, 1994).


Black females
Age-adjusted Mortality
900
800
700
600
28.5
28.0
27.5
27.0
26.5
Population Mean BMI
1960
1965
1970
1975
1980
1985
1990
1995
Year

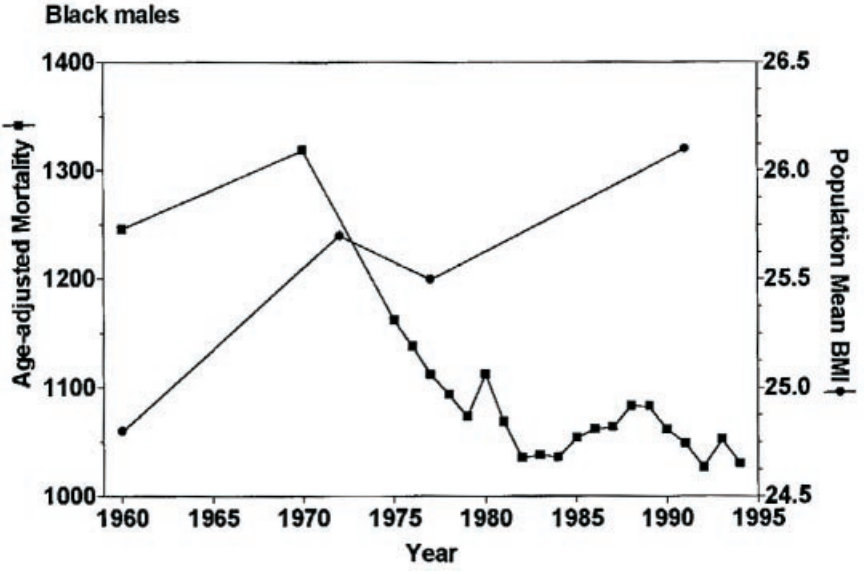

Black males
Age-adjusted Mortality
1400
1300
1200
1100
1000
26.5
26.0
25.5
25.0
24.5
Population Mean BMI
1960
1965
1970
1975
1980
1985
1990
1995
Year

Fig. 4b.

Marked discrepancies in citation rate can be found for reviews covering the hazards of obesity. An outstanding skeptical appraisal of the health hazards of obesity from the prestigious *Annual Reviews in Medicine* (Fitzgerald, 1981) has been cited an average of less than once per year since its publication (0.7 citations a year). A comprehensive critical review with more than 400 references (Ernsberger & Haskew, 1987) has been cited only 2.3 times per year. In contrast, reviews offering much grimmer assessments of the health of obese persons, composed by the director of a hospital weight loss clinic, have been cited at an annual rate of 9.2 (Van Itallie, 1979) and 34.7 (Van Itallie, 1985). Thus articles describing obesity as extremely hazardous are quoted more extensively in the scholarly literature than equivalent articles drawing more skeptical conclusions. This trend can also be seen in media coverage of medical findings, in which extensive attention is devoted to reports of obesity hazards and scant attention is paid to the extensive contrary evidence.

All of the above discussion and all of the studies listed in Table 2 concern healthy people in the general population. In fact, persons with active disease of any sort are automatically excluded from epidemiological studies. However, in medical practice one treats patients afflicted with disease. Medical advice to lose weight is not confined to persons who are otherwise healthy. On the contrary, it is people who are ill who are most likely to be counseled to lose weight. We should therefore ask about the relationship between body weight and mortality in the unwell. In hospitalized patients, BMI upon admission was compared to the odds of dying in the hospital, after adjustment for disease severity (Potter, Schafer, & Bohi, 1988). As shown in Figure 5, the highest risk of death was in people who were underweight (BMI < 21). At all ages, the risk of death declined with increasing weight. For patients aged 50 to 79, the best chance of survival was at a BMI of 40, usually considered "morbidly obese." For patients in their 80s, the optimum BMI is around 32, which is considered "severely obese." The authors of this study considered whether the excess mortality in nonobese patients was caused by malnutrition or chronic illness. To test this, they examined weight change between hospitalizations for those who were hospitalized more than once. There was no increase in risk of death for those who were losing weight prior to hospitalization, indicating that it is long-term, possibly lifelong, leanness that raises the risk of in-hospital death. These findings have been independently confirmed in other studies. The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT) found a lack of overweight (BMI < 25) to be an independent predictor of mortality in hospitalized patients after stratified adjustment for 15 different physiological and demographic variables (Galanos et al., 1997). (The accompanying editorial was entitled "A Mean Outcome for the Lean" [Oud & Haupt, 1997].) Thus even though the absence of obesity may be favorable for young and healthy individuals, with the onset of acute illness or old age, moderate obesity can become protective. These results are consistent with the notion that expanded fat stores facilitate survival when the individual is challenged by illness or aging.

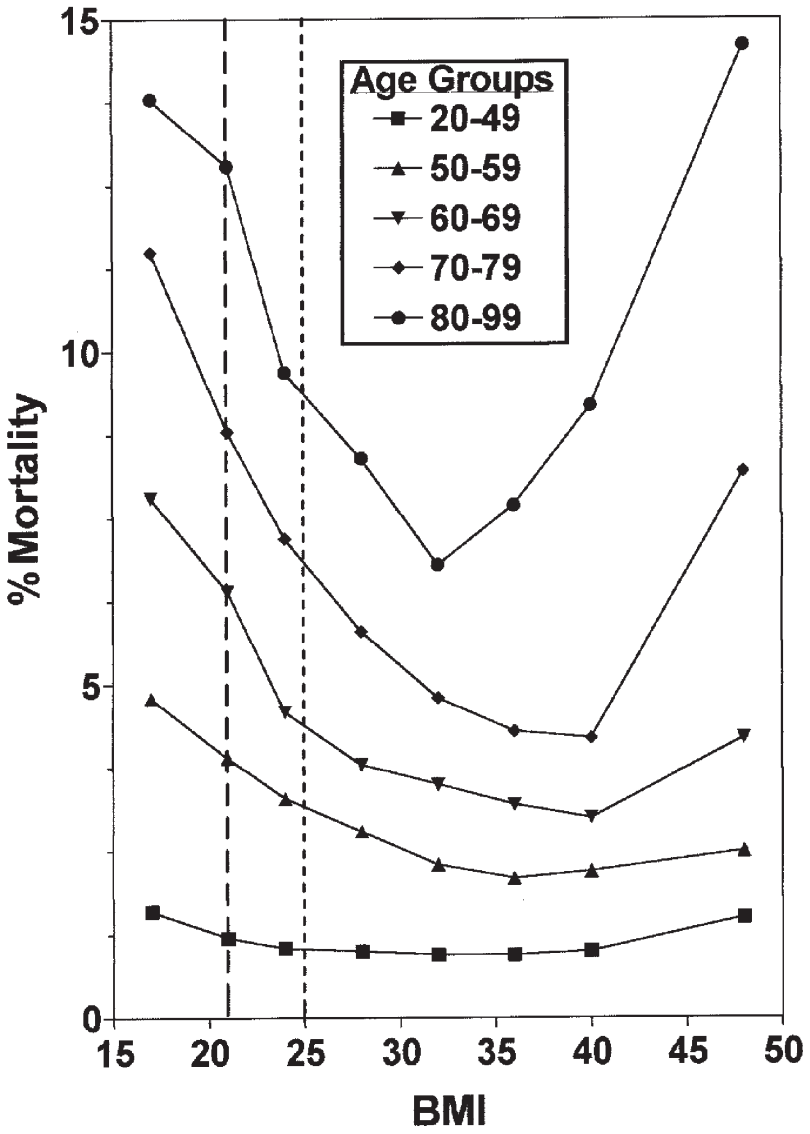


Fig. 5. Relationship between BMI on admission and in-hospital mortality in different age groups (Potter, Schafer, & Bohi, 1988). Mortality is adjusted for diagnosis and other prognostic factors. The dashed line indicates "ideal weight" defined by life insurance standards (BMI = 21), and the dotted line marks the threshold for the current definition of overweight (BMI > 25).

Socioeconomic Status, Culture, Obesity, and Health Risks

Obesity is strongly related to socioeconomic status (SES; Gortmaker, Must, Perrin, Sobol, & Dietz, 1993; Jeffery, French, Forster, & Spry, 1991; Lantz et al., 1998; Morris, Cook, & Shaper, 1992; Sorensen, 1995; Wamala, Wolk, & Orth-Gomér, 1997). Obesity can be either a cause or a consequence of poverty (Sorensen, 1995). Discrimination and stigma can result in unemployment or low-paying work (Gortmaker et al., 1993). Thus it seems that obesity arises first, then low SES results through societal discrimination and stigma. On the other hand, the loss of employment increases the risk of weight gain (Morris et al., 1992), so it is also possible that a decline in SES can presage the development of obesity. Poverty has been strongly linked to low-quality nutrition, which can result in weight gain because excess calories must be consumed to maintain adequate intake of vital nutrients. Persons of low SES have increased intakes of dietary fat and get less exercise, both of which can promote weight gain (Jeffery et al., 1991). Both obesity and low SES are associated with low self-esteem, high job stress and poor health habits (Wamala et al., 1997).

Low SES is a powerful predictor of death from cardiovascular disease. In a representative national U.S. sample, low income was associated with a RR of 3.9 in women and 3.3 in men (Lantz et al., 1998). After adjustment for cigarette smoking, alcohol intake, exercise level, and body weight, the RRs were 3.8 in women and 3.1 in men. Thus known risk factors accounted for only a small portion of the mortality risk of low SES. Evidence points to psychological stress and limited access to health care as the primary source of the high risk of premature death in the lower socioeconomic classes. Low SES is an especially strong predictor of death in diabetics, presumably because of impaired delivery of necessary medical care (Rosengren, Welin, Tsipogianni, & Wilhelmsen, 1989).

After controlling for SES in the Americans' Changing Lives study, the RR from underweight was 2.03 whereas the RR for overweight was 0.94 (Lantz et al., 1998). Thus in comparing individuals with equivalent social status, there is no significant increase in risk of death from high body mass. In the National Health Examination Follow-Up Survey, mortality rates were higher in obese persons (BMI > 30) in poverty compared to the nonpoor obese, whereas poverty had a much smaller adverse effect on survival for leaner persons (Tayback et al., 1990). Similarly, a study in Finland found high risks associated with obesity (BMI > 34) in the upper classes (RR = 1.4 to 1.7) but not in lower social classes (RR = 1.2; Rissanen et al., 1989). Also, underweight (BMI < 19) was not a hazard in the upper classes (RR = 1.1) but was a strong risk in lower classes (RR = 1.9). The contrasting risks of overweight and underweight in high-SES and low-SES groups might account for the discrepancies between different epidemiological studies.

Several epidemiological studies were controlled for SES because they used defined occupational groups (Table 2). The 10-year San Francisco longshoremen

study, for example, showed lower mortality in nonsmokers who were markedly obese (BMI > 29; 6.0% died) than in those who were of "ideal weight" (BMI < 22; 10.2% died; Borhani, Hechter, & Breslow, 1963). An influence of "occult wasting disease" is unlikely, because all the subjects were involved in physically demanding work. Almost identical results were obtained for nonsmoking employees of People's Gas in Chicago: In 14 years, 20.4% of the "ideal weight" (BMI < 23.5) workers died, whereas 16.9% of the markedly obese (BMI > 29) men died (Dyer, Stamler, Berkson, & Lindberg, 1975). The Whitehall Study in England also showed a protective effect of moderate overweight on mortality in British civil servants (Jarrett, Shipley, & Rose, 1982). A comparable study of Paris civil servants showed the highest mortality in those who conformed to the latest weight standards (BMI < 24.4), whereas mortality was 34% lower in those who were overweight (BMI of 24.4 to 27) and 31% lower in those who were obese (BMI > 30; Filipovsky, Ducimetière, Darné, & Richard, 1993). Adjusting the relative risks for smoking and removing the deaths in the first 5 or 10 years of follow-up did not remove the apparent protective effect of obesity. In each of these studies of employment groups, those participants who registered the low body weights associated with increased death rates were not emaciated by any means, but were at or even slightly above weights recommended by the life insurance tables. The use of healthy, actively employed persons rules out any possibility of weight loss due to chronic wasting disease. The inescapable conclusion is that underweight is a significant contributor to excess mortality, and may be equally important to overweight in its impact on longevity in the population.

The studies of body mass and mortality listed in Table 2 are arranged roughly in order of the degree of hazard found to be associated with obesity. A striking relationship, which has not been commented on in any previous review, is that the five studies showing a high hazard of obesity have subjects drawn from the highest SES. This includes suburban nurses, Harvard alumni, persons who can afford individual life insurance policies, residents of an affluent suburb (Framingham, Massachusetts), and others. These are social groups in which the stigma of obesity would be highest. Nurses, in particular, are under strong pressure to lose weight as a healthful example to their patients. In contrast, study populations showing no risk of obesity or even an inverse relationship between body weight and mortality tend to be of low SES and to belong to non-Western cultures that do not value thinness as strongly as affluent Americans. The incidence of obesity was very low in the studies of Harvard alumni, nurses, and insurance policyholders. The average BMI of all these groups was well below the U.S. average. In contrast, obesity was prevalent in the populations where it was perceived as neutral or even advantageous. The world's highest rates of obesity are found in the South Pacific and in Native American groups. Yet in these non-Western cultures, there is no increased risk of cardiovascular disease even with extreme obesity (BMI of up to 40). This raises the possibility that the stigma, discrimination, and stress faced by obese

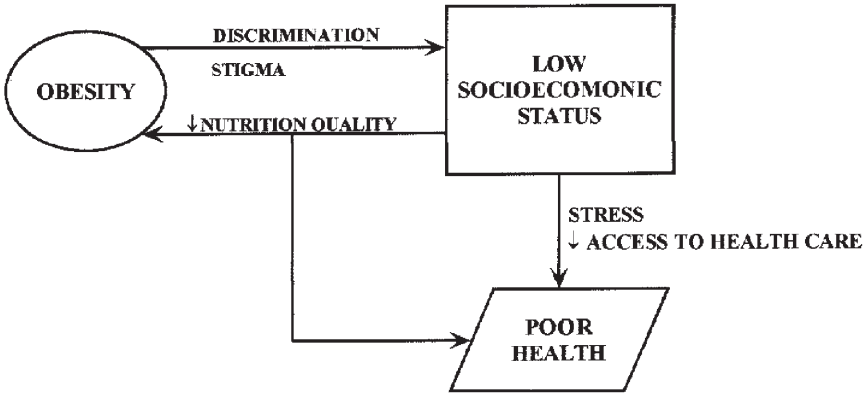


Fig. 6. Hypothetical model for the relationship between SES, obesity, and adverse health outcomes.

persons of high SES in Western cultures may be a major contributor to cardiovascular mortality.

The possible relationships between obesity, SES, and health are schematized in Figure 6. Obesity can lead to low SES through social stigma and the process of discrimination. Obesity is more common among minority groups, including Native Americans, Blacks, Hispanics, and Jews, further magnifying discrimination. Low SES can also contribute to weight gain and obesity by limiting exercise opportunities and diminishing nutritional quality. These factors can promote poor health at the same time as they contribute to obesity. Low SES is a strong independent predictor of poor health and premature death, probably through psychological stress and reduced access to health care.

Weight Cycling and Obesity-Associated Illness

A further difference between the populations at the top and the bottom of Table 2 is the likely prevalence of dieting and participation in weight loss programs. High SES is associated with increased efforts to lose weight (Rodin, 1993). The relative hazard of obesity is higher in younger age groups, which are also most likely to pursue weight loss. Weight loss methods may be hazardous in themselves, as reviewed elsewhere in this issue. Nurses in particular are exposed to opportunities for pharmaceutical, surgical, and very-low-calorie diet interventions, which can be hazardous. There is also strong evidence that the regain of weight that almost always follows successful weight loss can be harmful. Thus the harmful effects of weight cycling may contribute to the high mortality risk of obesity in populations in which weight loss is prevalent, in contrast to the low

mortality risk in populations in which obesity is the norm and likely to be accepted or tolerated.

Fatal consequences of refeeding after starvation are well known in famine victims and anorexics (Weinsier & Krumdieck, 1981). Obese dieters may not be immune to the adverse effects of refeeding after significant weight loss (Brownell & Rodin, 1994). Obese humans typically show repeated loss and regain of large amounts of weight (Blackburn et al., 1989; Rodin, Radke-Sharpe, Rebuffë-Scrive, & Greenwood, 1990). Men with large fluctuations in weight between the ages of 20 and 40 have increased systolic and diastolic blood pressure and cholesterol (Hamm, Shekelle, & Stamler, 1989). These yo-yo dieters are two times more likely to die of coronary heart disease, even after adjustment for known risk factors, than are men with stable or steadily increasing weight (Hamm et al., 1989; Lissner et al., 1991). Fluctuations in body weight have been shown in many other major epidemiological studies to have deleterious cardiovascular effects resulting in increased mortality (Blair, Shaten, Brownell, Collins, & Lissner, 1993; Ernsberger & Koletsky, 1993; Lissner et al., 1991).

A few studies have not found that weight cycling increases the risk of mortality. However, the populations lacking a risk associated with weight cycling tend to be those with low rates of dieting for weight loss, such as a study of elderly men in Baltimore (Lissner, Andres, Muller, & Shimokata, 1990). The lack of an effect of weight cycling in a population with a low level of intentional weight loss implies that minor random fluctuations in weight do not pose a health hazard.

Animal studies strongly support the existence of adverse effects of weight cycling (Ernsberger & Koletsky, 1993; Ernsberger & Nelson, 1988b; Ernsberger et al., 1994; Ernsberger, Koletsky, Baskin, & Collins, 1996; Koletsky et al., 1995). Weight cycling induces hypertension, enlargement of the heart, thickening of the heart wall, increased levels of the stress hormones adrenaline and noradrenaline, progressive kidney damage, redistribution of fat deposits to the abdomen, increased efficiency of weight gain, and exacerbation of obesity. The last effect, progressive weight gain, was found only in genetically obese animals, but not in naturally lean animals. This implies that a genetic susceptibility may determine whether cycles of weight loss and regain lead to progressive accumulation of fat, possibly in humans as well as in rats.

In the Framingham study, the increase in cardiovascular disease in obese patients could be entirely explained by taking two facts into account (Lissner et al., 1991). First, obese people were more like to go up and down in weight than thin people. Second, weight cycling was associated with increased rates of death from cardiovascular disease. Obese people who maintained a high but steady weight had only an average risk of death or cardiovascular disease. This finding raises the possibility that much of increased risk of disease and death in obese people is the result of repeated cycles of weight loss and regain.

Bias, Conflicts of Interest, and Medical Beliefs About Obesity

Given the number of studies with contrary findings, why the emphasis on the few studies that show a strong upward trend of mortality with increasing body weight? One answer is selective citation. Other factors being equal, studies reporting adverse effects of obesity are quoted more frequently than those that are more neutral. Citation analysis can document this. Let us take two articles that appeared in the same issue of *Annals of Internal Medicine* as part of the proceedings of a conference convened by Congress. The first article reviewed more than 100 prospective epidemiological studies and concluded that there was no correlation between obesity and heart disease (Barrett-Connor, 1985). The second article presented a long list of diseases associated with obesity based on cross-sectional studies and made the case for adverse health effects of obesity (Van Itallie, 1985). The antiobesity article was cited an average of 34.7 times per year through 1996, according to the Science Citation Index, whereas the neutral article was cited an average of 9.6 times per year. The lighter citation of the first article cannot be attributed to lower academic standing, because the lead author, Elizabeth Barrett-Connor, is a well-known epidemiologist with more than 339 publications in major medical journals, whereas the second author, Theodore Van Itallie, was the director of a weight loss clinic at Presbyterian-St. Luke's Hospital in New York City at the time of the conference.

Another example of selective citation can be found in two reports, both appearing in the *Journal of the American Medical Association* and both reporting results of the Framingham study. The first report, entitled simply "Body Build and Mortality: The Framingham Study," showed an increased risk of death in underweight but not in overweight (Sorlie, Gordon, & Kannel, 1980) and was accompanied by an editorial entitled "Beware the Lean and Hungry Look." The second article in the same journal, reporting on the very same study, reached the opposite conclusion, stating that underweight persons had the lowest risk and every increment in body weight increased mortality risk (Garrison, Feinleib, Castelli, & McNamara, 1983). The second report made no attempt to explain the discrepancy with the previous report on the same group of Framingham residents. However, the first report covered 5,146 men and 6,829 women. The second report covered 1,976 men and no women. No rationale was given for excluding more than 3,000 men and all of the women from this reanalysis, but obviously the selective inclusion of Framingham subjects could account for the reversal of data trends in the second report. Even though it included only one fifth the number of subjects, the second *Journal of the American Medical Association* report has been cited 7.9 times per year through 1996, whereas the original report has been cited at an annual rate of 5.5 times. Citing authors show a clear preference for articles that assign a high risk to obesity, regardless of journal stature or data quality.

The National Institutes of Health frequently convene panels of experts to discuss important and controversial issues in medicine and to arrive at compromise or consensus statements that are almost universally agreed upon. This process has worked well for many topics, as experts representing a spectrum of opinion are brought together and reach agreement on the current state of knowledge in their field. A major problem with consensus panels, however, is that many of the experts represent special interest groups (Tong, 1991). This is clearly a problem with NIH panels on obesity, on which the multibillion-dollar interests of the weight loss industry have been well represented.

Before examining the specific issues, we must review the possible conclusions that favor the fortunes of the weight loss industry. These are summarized in Table 3. Weight loss clinics, pharmaceutical firms developing and marketing diet pills, and diet industry concerns represent an enormous economic interest. Diet industry sales alone, excluding medical clinics, amount to more than $60 billion a year, as reviewed elsewhere in this issue. These economic interests are favored by proclamations from governmental panels identifying obesity as a major health risk, establishing a very low limit for the definition of obesity, and minimizing the hazards of treatment. The economic interest of pharmaceutical firms is illustrated by a major grant program initiated by Knoll Pharmaceuticals, manufacturers of the diet pill sibutramine. In a letter addressed to physicians across the nation, the company offered generous grant support "to advance the understanding of obesity as a major health problem." Knoll and Wyeth-Ayerst have sponsored continuing education programs across the country with the aim of promoting "awareness" of the hazards of obesity.

Remarkably, each of the precepts in Table 3 has been adhered to precisely by each NIH panel, as detailed below. The congruence between the interests of the diet industry and the content of NIH statements does not establish undue influence of industry over governmental deliberations, but it does suggest the need for reform, particularly of the manner in which expert panels are assembled.

Table 3. Medical Precepts Favoring the Growth and Profitability of the Weight-Loss Industry

Precept	Outcome
Exaggeration of the ill effects of obesity	Facilitation of third-party payments; increased motivation to seek weight control services
Setting body weight standards as low as possible	Expansion of client base
Overstatement of the long-term benefits of weight loss	Increased utilization and reimbursement for services
Minimization of the ill effects of obesity treatments and weight cycling	Repeat utilization of services

In 1979, a panel of weight loss clinic directors and surgeons, chaired by Theodore Van Itallie, was selected by the NIH to evaluate surgical methods of weight loss. The panel gave a strong endorsement to intestinal bypass surgery for weight loss (Van Itallie & Burton, 1979). However, by 1979, severe and even fatal complications of intestinal bypass were known (Halverson, Scheff, Gentry, & Alpers, 1980). Intestinal bypass was virtually abandoned shortly after the panel endorsement was published.

Describing themselves as "an impartial panel of 15 senior level professionals" (Burton, Foster, Hirsch, & Van Itallie, 1985), an NIH panel was convened in 1985 to consider the question of whether obesity constituted a health risk. Nineteen experts on obesity testified to the panel. A remarkable aspect of the consensus statement is that it almost completely contradicted the conclusions of the experts who testified to the panel. A list of these contradictions is provided in Table 4. In each case, the conclusions of the panel favored the weight loss industry (compare Tables 3 and 4). The deliberations might have been affected by the fact that both the panel chair and the chair of the planning committee directed weight loss clinics. When confronted with evidence of systematic bias, the panel chair would only state that the allegation "exceeds the bounds of scientific collegiality" (Hirsch, 1987).

Table 4. Contrasts Between Evidence Presented and Conclusions Reached: 1985 NIH Panel

Evidence presented (Ernsberger, 1987)	Panel conclusion (Burton, Foster, Hirsch, & Van Itallie, 1985
Excess lean body mass is more hazardous than excess fat, because nonobese overweights have the most risk factors (Van Itallie, 1985; Figure 5 therein)	Refers to body weight and body fat synonymously
Insurance height-weight tables derived improperly from faulty data (Harrison, 1985)	Endorsed insurance tables and called for those with common ailments to reduce even further
Poor diet and lack of exercise may be primary causes of disease, with obesity only a bystander (Stallones, 1985)	Identified obesity as a direct cause of disease and a disease unto itself
Genetic factors lead to disease and to obesity, with obesity only a bystander (Iverius & Brunzell, 1985; Stallones, 1985)	Genetic factors not acknowledged
Epidemiologic risk of obesity in children is highly uncertain (Johnston, 1985)	Children must "bring their weight within normal limits"
Obesity is not related to atherosclerosis (Barrett-Connor, 1985)	Obesity causes atherosclerosis
Obesity is actually protective in the Seven Countries Study (Kluthe & Schubert, 1985)	Findings dismissed because study groups are "not representative of the U.S. population"
Weight standards should be adjusted for age (Andres, Elahi, Tobin, Muller, & Brant, 1985)	Weight standards based on insurance customers at age 25. No adjustment for age.

The NIH constituted a panel of obesity experts to serve as a standing expert panel on obesity, known as the National Task Force for the Prevention and Treatment of Obesity. The composition of this governmental panel is shown in Table 5. The Task Force rendered a series of official statements, each published in the *Journal of the American Medical Association*. The first statement covered very-low-calorie diets (VLCDs), referring to liquid diets such as Optifast (provided only by doctors) and Slim-Fast (over-the-counter) that provide 300–500 calories a day (NIH National Task Force, 1993). The panel considered these to be both safe and effective, but only under medical supervision. This position, of course, would strengthen the position of hospital-based weight loss programs, which offer liquid diets under medical supervision. However, the endorsement by the Task Force of liquid diets as a medical intervention came as the Optifast fad, fostered by Oprah Winfrey's temporary weight loss, was fading and most hospitals had terminated their liquid diet programs, including Mt. Sinai Hospital of Cleveland, where Optifast was first formulated.

The second statement concerned weight cycling (NIH National Task Force, 1994). The conclusion, widely repeated in the media, was that weight cycling is not harmful and the increased mortality found in persons who repeatedly lose and regain weight should not deter anyone from joining a weight loss program. The overwhelming evidence that weight cycling promotes cardiovascular disease and death is reviewed in the previous section. Recognition of the hazards of repeated loss and regain of weight is a serious threat to the weight loss industry, however, as they depend on repeat business for their survival. Given the high prevalence of dieting, if only persons who had never dieted before were encouraged to join weight loss programs, the industry would collapse overnight.

The most recent statement from the Task Force concerned long-term treatment of obesity with drugs (NIH National Task Force, 1996). The panel endorsed the use of diet drugs, such as fenfluramine and phentermine, for periods of over 1 year or even for life. The report minimized the concerns over serious and fatal side effects from these drugs, because these risks "must be viewed in the context of the major excess in morbidity and mortality attributable to obesity." A few months after the publication of the panel's conclusions, fenfluramine was withdrawn from the market because of incidences of severe heart damage and a number of fatalities.

In each of its three reports, the Task Force issued opinions that were favorable to weight loss clinics and to pharmaceutical firms marketing diet pills. Could the conflicts of interest listed in Table 5 have played a role? As we pointed out in a letter to *Journal of the American Medical Association*, seven of the nine members of Task Force were directors of weight loss clinics (Ernsberger & Koletsky, 1995). A more complete picture of the conflicts of interest of Task Force members was disclosed as part of their subsequent report (NIH National Task Force, 1996).

None of the arrangements or relationships listed in Table 5 are illegal in any way. However, the remarkably consistent position taken by the Task Force on

Table 5. Conflicts of Interest Among Members of the National Task Force on the Prevention and Treatment of Obesity

Scientific member	Affiliation	Employment conflict	Other conflict
R. L. Atkinson, MD	University of Wisconsin, Madison	Weight loss clinic; performed surgery for weight loss	Knoll Pharmaceuticals
W. H. Dietz, MD, PhD	Tufts University School of Medicine	Weight loss clinic	Knoll Pharmaceuticals; Hoffman-LaRoche
J. P. Foreyt, PhD	Baylor College of Medicine Nutrition Research Clinic	Behavior modification weight loss program	Advisor to Calorie Control Council (industry group); author of popular weight loss book (Warner Press)
N. J. Goodwin, MD	HEALTH WATCH Promotion Service	Unclear	Unknown
J. O. Hill, PhD	University of Colorado, Denver	Behavior modification weight loss program; consultant to Duke Diet and Fitness Center	Advisor to Calorie Control Council (industry group); Proctor & Gamble; Amgen; Knoll Pharmaceuticals; Hoffman-LaRoche; International Life Sciences Institute (industry group)
J. Hirsch, MD (chaired NIH consensus panel)	Rockefeller University	Research weight loss clinic	Hoffman-LaRoche;* Nutrasweet Co;* Diet Center; Weight Watchers; Millennium Co.
F. X. Pi-Sunyer, MD	Columbia University	Weight loss clinic	Scientific Advisory Boards of Weight Watchers International Inc., American Home Products, Wyeth-Ayerst and Knoll Pharmaceuticals; Executive Director, Weight Watchers Foundation; Consultant to Hoffman-LaRoche, Genentech, Eli Lilly; Neurogen; Parke-Davis
R. L. Weinsier, MD, DrPH	University of Alabama, Birmingham	Weight loss clinic	Scientific Advisory Board, Weight Watchers International Inc.; Sandoz Nutrition (makers of Optifast)
R. Wing, PhD	University of Pittsburgh	Behavior modification weight loss program	Scientific Advisory Board, Weight Watchers International Inc.; Eli Lilly; Ross Laboratories; International Life Sciences Institute (industry group)

*Conflict disclosed in NIH National Task Force, 1994. All other conflicts undisclosed prior to 1996.

matters that affect the weight loss industry raises questions about the NIH's selection of panelists. Furthermore, the Task Force endorsed liquid diet products and diet pills when members had accepted payments from the manufacturers of such products. The Task Force is a true governmental body and forms a part of the NIH. An arm of the NIH, the Weight Information Network, distributes copies of the Task Force reports and other writings of the panel members. It also distributes pamphlets, at taxpayer expense, for the lay public, with strongly worded warnings about the dangers of exceeding body weight guidelines. Other pamphlets dismiss or minimize concerns dieters might have about weight cycling, development of gallbladder disease as a result of dieting, or side effects of medication. The underlying message from the Task Force and the NIH itself is that the $60 billion a year invested in the pursuit of thinness in the United States is too little, and considerably more money and attention needs to be devoted to weight control. We ask whether the money and effort expended on the generally unsuccessful pursuit of thinness might be better spent on directly promoting lifestyle change.

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