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# Metabolism

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### Epidemiology of Obesity and Its Link to Heart Disease

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Univariate analyses of many prospective studies have demonstrated that obesity increases the likelihood of developing cardiovascular disease. However, multivariate analyses have yielded more inconsistent results. Some studies have indicated that lean individuals have a greater total mortality than normal-weight individuals, but this may be attributable to the higher proportion of smokers in the lean population. Mexican Americans, a population with a high incidence of obesity, have the same mortality rate as non-Hispanic white Americans, suggesting that obesity does not increase their death rate. In the United States, the percentage of the population that is overweight has increased sharply since the 1970s, but the mortality rate has actually decreased. The increase in body weight has had little effect on mortality, possibly because factors associated with obesity, like hypertension, are treated more effectively. Large-scale clinical trials are required to determine the true effects of obesity on cardiovascular disease, diabetes and total mortality rate.

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**M**ANY PEOPLE, including some clinicians, hold the simplistic view that obesity is simply a matter of overeating and a lack of will power. This may explain the double standard in the treatment of obesity compared with that of hypertension or hyperlipidemia. Whereas patients with the latter are often treated with pharmacological agents, patients with the former are urged to make lifestyle changes. Some of these differences may be explained by the moral dimension that therapists often attach to the problem of obesity.

#### RISK ANALYSES

The relationship between obesity and cardiovascular disease is controversial. A principal reason for this controversy is confusion over the relative merits of univariate versus multivariate analysis from both a scientific and public health perspective.

Univariate models have consistently demonstrated that obesity contributes to cardiovascular disease.<sup>1-3</sup> The Framingham study showed both a univariate and a multivariate relationship between obesity and the incidence of cardiovascular disease. Cardiovascular disease was associated with obesity in both men and women in this study (Fig 1). The incidence of myocardial infarction showed the same obesity-related trend, as did the incidence of sudden death and stroke.

However, when multivariate analyses are used, obesity often ceases to be an independent risk factor. Keys et al. developed multivariate models to predict the occurrence of

cardiovascular disease for various population cohorts.<sup>2</sup> They found that there was a close correlation between observed and predicted cases with these models. This correlation was equally good regardless of whether body mass index (BMI) or skinfolds were included in the model. In multivariate models, the place of obesity as a risk factor is usually taken by other obesity-related conditions, such as hypertension and hyperlipidemia.

#### TOTAL MORTALITY

A prospective study by the American Cancer Society involving more than 750,000 men and women assessed the effect of weight on coronary heart disease.<sup>3</sup> For both men and women, there was a steady increase in heart disease with weight—a univariate relationship. However, when total mortality was examined, excess mortality was also found in the lean population. This has been described as a U-shaped or J-shaped relationship. Total mortality decreased with decreasing body weight until a threshold weight, below which the mortality rate increased as body weight decreased further.

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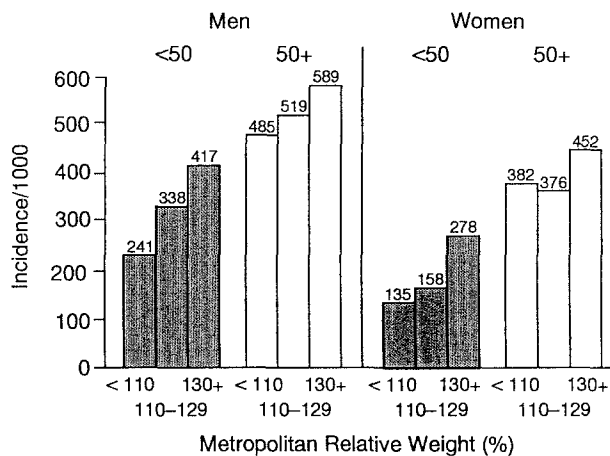
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### 26-year incidence of cardiovascular disease according to Metropolitan Relative Weight at baseline

The Framingham Study  
Univariate Analyses



**Fig 1. Cardiovascular disease was found to increase with increasing weight in both men and women. (Reprinted with permission.<sup>1</sup> © 1983 American Heart Association.)**

There are a number of causes of death from which lean subjects have excess mortality, such as cancer and digestive diseases, which may explain the increased mortality rate in this group.<sup>3</sup> Smokers tend to be lean and smoking may cancel any health advantages of being lean. Data from the American Cancer Society Prospective Study support this assumption, at least in men, as the U-shaped or J-shaped relationship only appears when smokers are included. However, there may be some excess mortality among lean subjects that cannot be attributed purely to cigarette smoking.

### MEXICAN AMERICANS

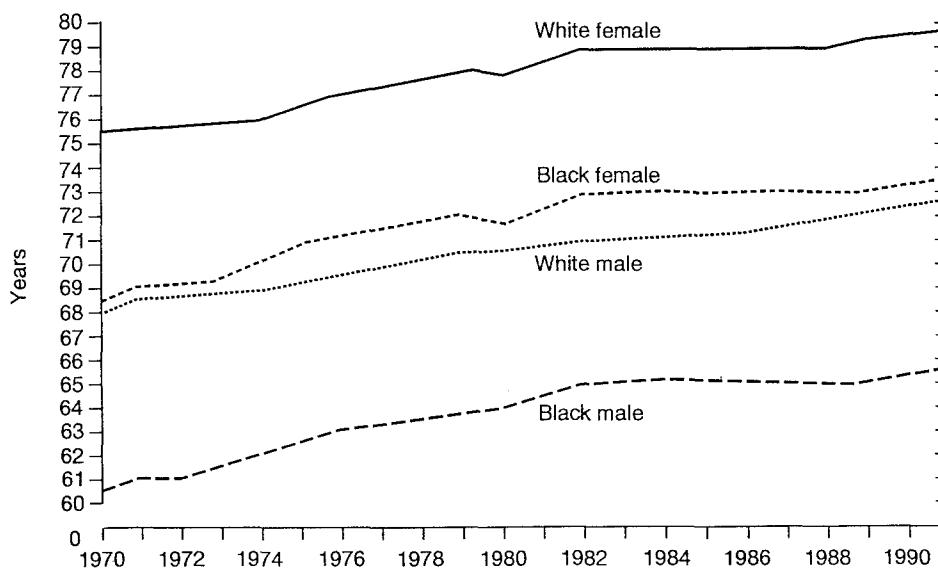
Studies have examined the mortality rates for Mexican Americans in Texas, a group with a high prevalence of obesity and at least a threefold greater risk of diabetes.<sup>4</sup> This population was compared with a non-Hispanic white population in Texas. The mortality rates for Mexican Americans and non-Hispanic whites over the age of 40, both men and women, were similar. The excess obesity in the Mexican Americans did not seem to contribute to an excess total mortality. A similar finding has been reported in Pima Indians, who also have a high incidence of obesity and diabetes. In this population, there is little, if any, relationship between total mortality and degree of obesity.<sup>5</sup>

Populations such as Mexican Americans are declared to be obese when standards derived from white populations are applied. These standards are not necessarily applicable to different racial and ethnic groups. There is little scientific justification to apply white standards of optimum weight for height values to other populations. This practice may have particular implications for the pharmacological treatment of obesity. In the United States, at least, many individuals from specific populations with a high prevalence of obesity as defined for white standards will probably be singled out, perhaps inappropriately, for intervention.

### SECULAR TRENDS IN OVERWEIGHT SUBJECTS

Studies have shown that since the early 1970s the American population has become increasingly overweight.<sup>6</sup> However, at the same time, the age-adjusted mortality rate has decreased consistently from 1970 to the present.<sup>7</sup> The trend towards increasing weight has not prevented a continuing decline in mortality. In fact, there was a steady increase in life expectancy over the 20-year period in both blacks and whites, including black females, which is the group with the greatest increase in overweight subjects (Fig 2). One of the

Life Expectancy by sex and race in the USA, 1970-91



**Fig 2. Life expectancy has steadily increased in the United States over the past 20 years, even in black women, the most obese group.**

factors that might offset any increase in mortality associated with obesity is improved treatment of concomitant diseases, such as hypercholesterolemia. In addition, the treatment of hypertension has been improved and smoking cessation campaigns have greatly reduced the prevalence of smoking in the US population.

#### WEIGHT LOSS

In an analysis of the National Health and Nutrition Examination Survey (NHANES) involving more than 4,600 men and women in the United States aged between 45 and 74 years, weight loss was defined as the maximum lifetime weight minus the weight at the time of the baseline examination.<sup>8</sup> Patients were divided into three groups according to their baseline BMI: lean, moderate, and overweight. They were further divided into those who had lost little or no weight and those who had lost significant weight (at least 15% of maximum body weight). In the lean and moderate groups, those who had lost a significant amount of weight actually had a higher mortality rate than

the those who had lost little weight. One possible explanation is that those who lost significant amounts of weight had a latent disease, such as cancer. These patients may have lost weight involuntarily as a result of their disease. On the other hand, even when early deaths (within 5 or 7 years) were excluded, the adverse effect of weight loss was still apparent. In the obese group, although there was no excess mortality with significant weight loss, there was also no benefit.

#### FUTURE

There is still much to be learned about the relationship between weight loss and mortality. Well-designed, large-scale clinical trials are needed to resolve these issues. Few clinicians would dispute that weight loss confers benefits, such as lowered blood pressure and lipid levels. However, there have been no clinical trials that have directly assessed the effects of weight loss on clinical end points such as cardiovascular disease, diabetes, and total mortality rate.

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