Obesity has reached epidemic proportions in the United States. Currently, one third of US adults are classified as obese and another one third as overweight. Obesity is also a growing epidemic in other parts of the world. The French, who have enjoyed relatively low rates of obesity and cardiovascular disease (CVD), are also experiencing expanding waistlines.1

Although the health hazards of obesity are widely recognized, the relationship between the middle range of body mass index (BMI) values and mortality is less clear because epidemiologic studies have found linear and curve-linear relationships between BMI and mortality. However, epidemiologic studies of BMI and mortality have been fraught with methodologic problems, including failure to control for cigarette smoking; inappropriate control of biologic effects of obesity, such as hypertension and hyperglycemia; and failure to consider weight loss attributable to subclinical diseases.2

These biases have led to the typical J- or U-shaped relationship between BMI and mortality seen in many epidemiologic studies and to a systematic underestimate of the impact of obesity on premature mortality. For example, in a recent analysis of NHANES (National Health and Nutrition Examination Survey) data sets, Flegal et al3 found that excess mortality attributable to obesity was much lower than reported previously, and that being overweight was associated with a lower mortality compared with normal weight. However, these findings are most likely the result of artifacts attributable to the methodologic flaws mentioned above. In particular, the study failed to exclude persons from the analyses who had chronic diseases at baseline and did not adequately control for smoking, leading to artificially elevated mortality among the lean subjects. Nonetheless, these findings have caused a great deal of confusion among the general public, and commercial interest groups have attempted to exploit the study and dismiss obesity as a public health issue.4

In the current issue of the Hypertension, Thomas et al5 evaluated the impact of overweight on cardiovascular mortality in a large French population (139,562 men and 104,236 women). During an average of 14 years of follow-up, they documented 11,688 deaths (2949 from CVD) among men and 4188 deaths (929 from CVD) among women. This is a self-selected population who came for a health checkup, with a mean age of 43 years for men and 41 years for women and mean BMI values of 24.6 for men and 22.8 for women. The prevalence of overweight and obesity combined was 42% in men and 21% in women. The prevalence of obesity was quite low (~5% in both genders). This large and relatively young population provides a unique opportunity to examine the impact of overweight on cardiovascular mortality.

Two major findings emerged from these analyses. First, in age-adjusted analyses, increasing BMI was strongly associated with increased cardiovascular morality, but the association became nonsignificant after adjusting for cardiovascular risk factors such as hypertension, hypercholesterolemia, and diabetes. These results are not surprising because these variables are on the biological pathway of obesity and CVD. However, they do not imply that BMI is not an independent predictor of mortality, but rather that the effects of BMI on cardiovascular mortality are mediated through these variables. In several previous studies, adjustment for these biologic intermediates attenuated but did not eliminate the association between BMI and CVD mortality, suggesting that other pathways also contribute to the effects.6 Second, in further analyses, the researchers found that the presence of hypertension was the most important factor that led to increased CVD mortality among overweight individuals. In particular, CVD mortality was significantly increased among overweight people only if they were also hypertensive, and the combination of hypertension with hypercholesterolemia or diabetes dramatically increased CVD mortality among overweight individuals. This novel finding deserves careful consideration. Clearly, it underscores the importance of hypertension as a mechanism through which obesity causes CVD. It is now known that obesity causes hypertension through multiple mechanisms, including hyperinsulinemia, renal injuries, increased sympathetic activity, and enhanced salt sensitivity.7

Do these results imply that other cardiovascular risk factors, such as dyslipidemia and diabetes, are not important mediators of obesity and CVD? The answer is no. There is overwhelming evidence that obesity causes dyslipidemia (increased LDL cholesterol and triglycerides and decreased HDL cholesterol) and type 2 diabetes, which, in turn, elevate risk of CVD. It is worth noting that the National Cholesterol Education Program guideline considers diabetes to be a CHD risk equivalent because several studies have shown that a history of diabetes and a history CHD confer similar risks of fatal CHD. Then why in this study does only hypertension

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Editorial Commentary

Overweight and Increased Cardiovascular Mortality

No French Paradox

Frank B. Hu
stand out as important? One possible explanation is that hypertension was much more common and accurately diagnosed than were hypercholesterolemia and diabetes in this population. During the health checkup, >50% of overweight people were diagnosed with hypertension. The diagnosis of dyslipidemia was based on total cholesterol levels rather than on different lipid fractions, and the diagnosis of diabetes was based on self-report. Thus, the more prominent role of hypertension that emerged from these analyses may reflect methodologic differences in measuring these variables rather than a true biological phenomenon.

Because the effects of obesity are largely mediated through metabolic factors, one may ask whether improved treatment of hypertension, diabetes, and dyslipidemia would blunt or even abolish the impact of obesity on cardiovascular mortality. During the past several decades, there has been a substantial decline in cardiovascular mortality in the United States, which has been attributed to decline in smoking and medical and technological advances. Treatment for hypercholesterolemia has improved substantially because of the widespread use of statins, a class of lipid-lowering drugs that has been demonstrated to be efficacious in lowering risk of CVD and to be relatively safe. However, statins reduce only a fraction of the excess risk of CVD risk in primary prevention settings. Typically, a person with the metabolic syndrome has to be put on multiple drugs to reduce blood pressure, treat dyslipidemia, and improve glycemic control, which is costly, can lead to side effects, and often requires lifelong use. It is unrealistic to expect that improved treatment will abolish the adverse effects of obesity on CVD and a fantasy to think that obesity is benign because the treatment of the associated metabolic diseases has improved.

The analyses by Thomas et al provide further evidence that being overweight increases cardiovascular mortality in predominantly middle-aged men and women. Identification of the mechanisms that account for this association remains of academic interest but is largely irrelevant to public health policy because modest weight loss through diet and lifestyle modifications improves nearly all metabolic conditions associated with obesity, including hypertension, blood lipids, and glucose metabolism. Also, current controversy about the exact number of deaths attributable to obesity is unproductive from a public health perspective. We should bear in mind that the burden of obesity is not only an increase in mortality but also an increase in the incidence of numerous major chronic diseases, including CVD, several forms of cancer, and osteoarthritis. Some of these conditions may not be immediate causes of death but increase health care costs and have a significant impact on quality of life. Thus, the estimated impact on mortality does not present the full picture of the burden of obesity on individuals and society. Also, because the prevalence of obesity is changing rapidly, obesity in children and young adults will have a large health impact in the future that has not yet shown up as elevated mortality. It is clear that being overweight is an important risk factor for CVD incidence and mortality, and thus that maintaining a healthy weight through diet and lifestyle in children and adults is the key to preventing CVD. There is no “French paradox” regarding the adverse effects of overweight on CVD incidence and mortality.

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