Obesity and mortality: a review of the epidemiologic data

Caren G Solomon and JoAnn E Manson

ABSTRACT At least one-third of Americans are obese, as defined by body mass indexes corresponding to body weight \( \geq 120\% \) of ideal body weight, and this figure is rising steadily. Women and nonwhites have particularly high rates of obesity. Obesity greatly increases risks for many serious and morbid conditions, including diabetes mellitus, hypertension, dyslipidemia, coronary artery disease, and some cancers. Obesity is clearly associated with increased risk for mortality, but there has been controversy regarding optimal weight with respect to mortality risk. We review the literature concerning obesity and mortality, with reference to body fat distribution and weight gain, and consider potential effects of sex, age, and race on this relation. We conclude that when appropriate adjustments are made for effects of smoking and underlying disease, optimal weights are below average in both men and women; this appears to be true throughout the adult life span. Central obesity, most commonly approximated by the waist-to-hip ratio, may be particularly detrimental, although this requires further study. Weight gain in adulthood is also associated with increased mortality. These observations support public health measures to reduce obesity and weight gain, including recent recommendations to limit weight gain in the adult years to 4.5 kg (10 lb). Am J Clin Nutr 1997;66(suppl):1044S–50S.

KEY WORDS Body weight, ideal body weight, mortality rate, smoking, central obesity, lifestyle, coronary artery disease, stroke, body mass index

INTRODUCTION

Obesity is a major health problem in the United States. Between 1988 and 1991 more than one-third of US adults were estimated to be overweight or obese as defined by a body mass index (BMI, in kg/m\(^2\)) \( \geq 27.3 \) in women and \( \geq 27.8 \) in men (1), figures that approximately correspond to 120% of desirable weight according to 1983 Metropolitan Life Insurance Company height and weight tables (Table 1) (3). This percentage has been rising consistently over time and most dramatically in recent years in both sexes (Figure 1). Women of all races, but nonwhites in particular, have an especially high prevalence of obesity.

Direct associations between obesity and several diseases, including diabetes mellitus, hypertension, dyslipidemia, and ischemic heart disease (IHD), are well-recognized. Somewhat more controversial is the relation between body weight and all-cause mortality. Although morbid obesity is clearly linked to higher mortality rates (4), the relation between more modest overweight and mortality has been argued, with some investigators reporting a protective effect of modest obesity (5, 6) and others noting optimal longevity at weights below average (7–11). We review the literature on obesity and mortality, with reference to body fat distribution and potential effects of sex, age, and race on this relation.

OVERVIEW OF THE EPIDEMIOLOGIC DATA

Methodologic considerations

Before reviewing the literature, it is important to emphasize that there are several possible explanations for discrepant findings in the relation between body weight and mortality. Possibly, there is some adverse effect of leanness or beneficial effect of excess body weight on overall survival (12). Another explanation is that weight or BMI may be inadequate surrogates for adiposity. For example, weight or BMI may be relatively low in an elderly deconditioned person who has little lean body mass relative to adipose tissue. Reported correlations between BMI and more direct measures of adiposity (eg, underwater weighing) are between 0.6 and 0.8 (13, 14). Likewise, reported correlations between waist-to-hip ratio (WHR), a frequently used marker of central adiposity, and visceral adipose tissue volume as measured by computed tomography are imperfect (15). In addition, such measurements are subject to error. The correlation between self-reported and measured WHR in a subset of participants in the Nurses’ Health Study was 0.70 (16). WHR measurements made at different sites (eg, measuring waist at the site of minimal circumference compared with at the umbilicus) have been noted to correlate differently with various outcome measures (17). Although the imprecision of these measures cannot be ignored, it is important to recognize that any consequent random misclassification would tend to
TABLE 1
Classification of obesity

<table>
<thead>
<tr>
<th>Classification</th>
<th>Relative weight</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% IBW²</td>
<td>Men</td>
</tr>
<tr>
<td>Desirable weight</td>
<td>90-110</td>
<td>20-24</td>
</tr>
<tr>
<td>Overweight</td>
<td>110-120</td>
<td>24-27.8</td>
</tr>
<tr>
<td>Obese</td>
<td>120-180</td>
<td>27.8-40</td>
</tr>
<tr>
<td>Morbidly obese</td>
<td>≥ 180</td>
<td>≥ 40</td>
</tr>
</tbody>
</table>

¹ From Prevention of Myocardial Infarction, Manson JE, Ridker PM, Gaziano MJ, Hennekens CH, eds. (2). Used by permission of Oxford University Press, Inc.

² Ideal body weight.

bias toward the null observed associations between adiposity and mortality.

Alternatively, methodologic problems may underlie null or inverse associations between obesity and mortality. These potential biases, reviewed extensively elsewhere (18), are addressed here briefly. Leanness may be associated with underlying disease (which may or may not be recognizable clinically), with cigarette smoking, or with both; both may independently shorten survival. Furthermore, studies that adjust for potential intermediates in the causal link between obesity and mortality, such as diabetes, hypertension, and dyslipidemia, tend to attenuate estimates of the risk associated with obesity.

The relation between body weight or BMI and mortality

Actuarial data from more than four million men and women suggested initially a direct positive association between body weight and overall mortality rates (7). Several subsequent studies confirmed increased mortality risk with increased relative weights above a certain threshold, but described J- (8-10) or even U- (5, 6) shaped associations between weight and mortality. In each of these studies, potential confounders as described above appear likely explanations of the observed increase in mortality in the very lean.

Some studies showing a J-shaped curve, for example, failed to adjust for smoking. Among participants in the Build Study (8), lean subjects had higher early mortality, whereas the more obese had increased mortality over time, raising the possibility of unrecognized illness in this ostensibly healthy population. The 1975 American Cancer Society study (9) looked at smokers separately and found a much stronger association between leanness and mortality, more specifically cancer mortality, in this group compared with nonsmokers. Among those of both sexes who had never smoked, the nadir of all-cause mortality was observed at weights 10-20% below average.

The Harvard Alumni Study (10), a prospective cohort study of >19,000 middle-aged men, found different relations between BMI and mortality among different types of subjects. A J-shaped relation was observed in the cohort as a whole after adjustment for age, cigarette smoking, and physical activity. Analyses limited to current smokers or to early follow-up revealed a U-shaped association between BMI and mortality. In contrast, when those who had ever smoked and those who died within the first 5 y of follow-up were excluded, there was no evidence of increased mortality in the leanest men (BMI < 22.5), and the lowest mortality was seen for those weighing 20% below average.

A direct positive relation between BMI and mortality was likewise described in a cohort of >8000 Seventh-day Adventist men, in whom leanness is common, characteristically by choice and unlikely to reflect cigarette smoking or underlying illness (19). Seventh-day Adventist men with BMIs in the lowest quintile (<22.3) had the lowest all-cause mortality rates, an observation that remained true even in the subset of those who were extremely lean (BMI < 20).

FIGURE 1. Trends in age-adjusted prevalence of overweight for the US population aged 20-74 y compared with the year 2000 objective (goal). NHES, National Health Examination Survey; NHANES, National Health and Nutrition Examination Survey. Adapted with permission (1).
Obesity is likewise associated with increased mortality risk in women. Although there have been some reports of null associations between BMI and mortality in women (20–22), it appears that these negative studies lacked sufficient power to assess adequately the relation between adiposity and mortality because of too few endpoints in the women studied. In contrast, several larger studies involving women clearly showed strong associations between body weight (7–9) or BMI (11) and all-cause mortality, comparable with associations reported in men. For example, a J-shaped curve described the relation between BMI and all-cause mortality in the Nurses’ Health Study cohort (11). With exclusion of even smokers or those with weight loss in the early years of follow-up (suggesting the possibility of underlying illness), all-cause mortality risk varied directly with BMI.

The direct associations between BMI and mortality noted in the three studies cited above in which there was good control for confounding by smoking and underlying disease are shown in Figure 2 (10, 11, 19).

Central obesity and mortality

The adverse effects of obesity appear to be closely related to the distribution of body fat. Central fat accumulation is frequently estimated by the WHR. Criteria for central obesity have been defined in men as a ratio > 0.95 (23) and in women as a ratio > 0.8 (24). Central accumulation of body fat is strongly associated with insulin resistance and the metabolic abnormalities associated with this condition, including glucose intolerance, high blood pressure, and dyslipidemia (25). Lipolysis in response to hormonal stimulation appears to be greater in abdominal fat than in other fat deposits, and the resultant higher concentrations of circulating fatty acids may act on muscle or liver to inhibit responsiveness to insulin (26).

Presumably in relation to the association of central adiposity with insulin resistance, some studies found WHR to be a stronger predictor than BMI of mortality and morbidity (27, 28). For 1462 Swedish women followed for 12 y, WHR was a significant predictor of all-cause mortality, even after adjustment for BMI and other potential confounders (27). Likewise, WHR was directly associated with all-cause mortality risk over 5 y of follow-up for 41,000 participants in the Iowa Women’s Health Study (28). Compared with women with a WHR in the lowest quintile, the relative risk of death for those with WHRs in the highest quintile was 2.6. In this cohort, BMI was much less predictive than WHR of all-cause mortality.

However, the relative influences of BMI and WHR on mortality risk remain controversial. Among women in the Nurses’ Health Study cohort, BMI was the stronger predictor of all-cause mortality (11). In addition, a recent report from the Manitoba Health Survey, a cross-sectional study of 2792 adults, noted that BMI tended to be a stronger predictor of metabolic abnormalities than WHR, supporting the observation that noncentral obesity is not a benign condition (29).

CAUSE-SPECIFIC MORTALITY

Cardiovascular disease

Coronary artery disease

IHD is closely associated with adiposity, as measured by either relative weight, BMI, or measures of central fat accumulation. The relation between adiposity and IHD is in part mediated by other well-recognized coronary risk factors commonly associated with adiposity, including hypertension (30), non-insulin-dependent diabetes mellitus (NIDDM) (31), and lipid abnormalities (32). Obesity and particularly central obesity, as noted above, are also closely linked with insulin resistance (33), which has likewise been associated with increased cardiovascular risk (34).

Because NIDDM, hypertension, and dyslipidemia are biological intermediates in the path between obesity and coronary morbidity and mortality, the argument has been made that one should not adjust for these in assessing relations between obesity and coronary endpoints. In analyses unadjusted for these coronary risk factors, BMI was reported to be a strong predictor of nonfatal and fatal IHD in female nurses (35). Compared with women whose BMI was < 21, relative risk for IHD was 2.06 (95% CI: 1.72, 2.48) for those with BMIs between 25 and 28.9 and 3.56 (95% CI: 2.96, 4.29) for those with BMIs ≥ 29. Even those who were not overweight by today’s standards (BMI: 23–24.9) had an increased relative risk for IHD compared with lean women (relative risk: 1.46, 95% CI: 1.20, 1.77), underscoring the observation that average weights are greater than ideal weights. In several studies, significant obesity was associated with a twofold or greater increase in cardiovascular mortality risk compared with leanness (7–9).

Nonetheless, even after adjustment for diabetes, hypertension, and hyperlipidemia, overweight was shown to be an independent risk factor for the development of IHD. In > 5000 male and female participants in the Framingham Heart Study, relative weight at the baseline examination was an independent predictor of IHD incidence and coronary mortality in both sexes (36). Effects of obesity on coronary risk were increased with longer follow-up (36, 37), a finding that has been observed in other populations (7–9).

Weight gain over time increases the risk of IHD morbidity and mortality. Compared with participants in the Nurses’ Health Study who gained < 5 kg between the age of 18 y and study inception in 1976 (when women were aged 30–55 y), women who gained 5–7.9 kg had a relative risk for IHD of 1.25 (95% CI: 1.01, 1.55) and those who gained ≥ 20 kg had a relative risk for IHD of 2.65 (95% CI: 2.17, 3.22). Twenty-seven percent of the incidence of IHD in this cohort was felt to be attributable to weight gains ≥ 5 kg after age 18 y (35).

Central accumulation of fat is likewise a strong predictor of IHD risk. Subscapular skinfold thickness, used as an index of central adiposity, was a significant predictor of nonfatal or fatal myocardial infarction in 7692 men in the Honolulu Heart Study over 12 y of follow-up (37). Similarly, in > 100,000 US veterans studied retrospectively, WHR predicted cardiovascular mortality over the subsequent 23 y (38). Women participating in the Iowa Women’s Health Study whose WHRs were in the highest tertile of the cohort had more than three times the risk of mortality from IHD than did women whose WHRs were in the lowest tertile (39). Increases in coronary mortality risk in this study were attenuated but still present after adjustment for BMI, hypertension, and diabetes, among other coronary risk factors.
FIGURE 2. Relative risks for all-cause mortality according to body mass index in three studies that minimized confounding by smoking and underlying disease. See text for details. (A) The Harvard Alumni Study (10), $P$ for trend = 0.0001; (B) The Nurses’ Health Study population (11), $P$ for trend = 7.08, $P < 0.001$; and (C) The Seventh-day Adventist Study (19), $P$ for trend < 0.0001. Analyses in (A) and (B) excluded early follow-up and those who had ever smoked. Figures adapted with permission from the American Medical Association (copyright 1993, the American Medical Association) (10), The New England Journal of Medicine (copyright 1995, Massachusetts Medical Society) (11), and the International Journal of Obesity (19).

Stroke

Obesity is also a risk factor for stroke and stroke mortality. Fatal strokes were reported to be more common with increasing BMI in Seventh-day Adventists (19). Among female participants in the Framingham Heart Study, higher relative weight at baseline was associated with increased risk of ischemic stroke over 26 y of follow-up (39). In addition, WHR was reported to predict 12-y risk of stroke in women in Gothenburg, Sweden (27), and 23-y risk of fatal stroke in US male army veterans (38). The American Cancer Society study also reported an
increase in risk of fatal stroke in the obese, more than 2-fold in men \( \geq 40\% \) overweight and 1.5-fold in women \( \geq 40\% \) overweight (9).

Cancer

High relative weight or BMI has also been associated with increased risk of some cancers. In women, rates of fatal endometrial, ovarian, cervical, breast, and gallbladder cancers were reported to be higher in those \( \geq 40\% \) overweight (9). In men, obesity was associated with increased risk for fatal prostate and colorectal cancers (9). In Harvard alumni who had no smoking history, there was a nonsignificant trend toward increased cancer mortality with increased BMI (\( P = 0.06 \)) (10). Data from the American Cancer Society showed a direct association between relative weight and risk of cancer mortality in men who had never smoked, compared with a U-shaped curve in those who were smokers (9).

Persons with central obesity appear to be at increased risk for cancer mortality, as for cardiovascular disease mortality. In women participating in the Iowa Women's Health Study (28), WHR was directly related to cancer death rates; women in the highest quintile of WHR had almost twice the rate of cancer mortality as did women in the lowest quintile.

Although leanness has also been associated with increased risks of some cancers, including cancers of the lung, stomach, and bladder (9), this seems primarily to reflect effects of cigarette smoking and underlying disease rather than an effect of body weight per se. Although some data do suggest a persistent increase in cancer mortality risk among the very lean even over many years of follow-up, the apparent increase in mortality associated with leanness tends to be greatly minimized or eliminated with exclusion of smokers (9) and early mortality (10).

Other diseases

Mortality from NIDDM is also increased among the obese. Persons in the Build Study who were \( \geq 25\% \) overweight had more than five times the risk of mortality from diabetes as did lean individuals (8). Gastrointestinal disease was another cause of increased mortality among obese participants in that study.

MORTALITY RISK ASSOCIATED WITH OBESITY IN SUBGROUPS OF THE GENERAL POPULATION

The elderly

Weight gain is common with increasing age, and higher weights tend to be accepted and even recommended in the elderly (40). These recommendations are based on observations of greater mortality risk in lean than in obese elderly. For instance, data from 4710 men and women aged \( \geq 55 \) y participating in the National Health and Nutrition Examination Survey (NHANES) suggested that in this age group mortality risk increased little with even significant obesity (BMI > 30), but increased greatly with leanness (BMI < 22) (41). However, the failure to exclude more than the first year of follow-up and to exclude those who were losing weight, as well as the classification of exsmokers as nonsmokers, suggests significant potential for confounding by underlying disease and by smoking. In addition, BMI may be a more imperfect surrogate for adiposity in this age group, in whom lower BMI frequently reflects illness or loss of muscle mass.

Because of the greater prevalence of underlying disease in the elderly, confounding of leanness by unrecognized illness and associated weight loss is particularly likely in this group. When smokers and early mortality were excluded from analyses of elderly Framingham Heart Study participants, there was no significant increase in mortality risk in leaner subjects; conversely, males with BMIs \( \geq 28.5 \) and females with BMIs \( \geq 28.7 \) had significantly increased risks of mortality (relative risks: 1.7 and 2.0, respectively, compared with individuals near average BMI) (42). Similarly, in generally healthy Seventh-Day Adventists aged 70–89 y at completion of follow-up, obesity (BMI > 27.5) but not leanness (BMI \( \leq 22.3 \)) was associated with increased risk for all-cause mortality (19).

Children and adolescents

Obesity has become common in the United States not just in adults, but also in children and adolescents. Between 1988 and 1991, 21% of adolescents aged 12–19 y were overweight, as defined by a BMI above the 85th percentile on the basis of earlier NHANES data adjusted for age and sex (43). Although mortality is rare among obese children and adolescents, these persons are at significantly increased risk of premature mortality later in life. Weight between the ages of 5 and 18 y was a significant predictor of later mortality in > 13 000 persons followed up to 52 y (44). Likewise, BMI between the ages of 13 and 18 y significantly predicted all-cause and IHD mortality among men in the Harvard Growth Study (45). Compared with those whose adolescent BMI was between the 25th and 50th percentile, men with adolescent BMIs above the 75th percentile had nearly twofold the mortality risk over long-term follow-up.

Cardiovascular morbidity and mortality are particular risks in persons obese as children or adolescents. Adolescent BMI above the 75th percentile was associated with a relative risk of IHD mortality of 2.3 among participants in the Harvard Growth Study (45). A similar relative risk for IHD mortality was reported over 32 y of follow-up for males whose BMI at age 18 y was \( \approx 25 \) compared with lean individuals (BMI < 20) (46).

It remains controversial whether obesity in early life is simply a marker for increased risk of adult obesity or whether this condition predicts mortality risk independently of adult BMI. In the Harvard Growth Study, adolescent BMI predicted IHD mortality even after adjustment for adult BMI (45). Nonetheless, among participants in the Nurses' Health Study, BMI at age 18 y was not an independent predictor of IHD after obesity in later life was controlled for (35). During 40 y of follow-up in persons identified between the ages of 2 mo and 16 y as being overweight, both greater obesity at puberty and weight gain in adulthood were associated with increased risks for cardiovascular disease and premature mortality (47).

Nonwhites

Nonwhite race is associated with a particularly high prevalence of obesity. Age-adjusted prevalence of overweight on the basis of data from NHANES III was 48.5% in African American women, 47.2% in Mexican American women, and 39.1% in Mexican American men, rates higher than those reported for
white men and women (1). There are conflicting reports on whether obesity confers similar morbidity and mortality risks in nonwhites as in whites. For example, BMI and abdominal girth were reported to be unassociated with all-cause or IHD mortality over 25–28 y of follow-up in African American women in the Charleston Heart Study, in contrast with significant positive associations between these markers of obesity and mortality in white women (48). Similar negative results were reported for black women enrolled in the Kaiser Foundation Health Plan, in whom baseline BMI failed to predict mortality over the subsequent 15 y (49). However, these studies appear to have had insufficient power to exclude associations between obesity and mortality in African Americans.

Combined data from the Coronary Artery Risk Development in Young Adults Study and the Atherosclerosis Risk in Communities Study indicated a 30% higher risk of cardiovascular disease in obese African American men and women than in leaner African Americans (50). Associations between obesity and lipids, blood pressure, and glucose tolerance were similar among African Americans and whites in this study. Among African American males participating in the Charleston Heart Study, obese subjects were at significantly increased risk for IHD mortality (adjusted relative hazard for 90th compared with 50th percentile: 1.7) (51). There was a U-shaped relation between BMI and all-cause mortality, although the relative hazard associated with high BMI was not significant. Exclusion of smokers from the analysis appeared to attenuate the association between leanness and all-cause mortality. This study failed to find an association between BMI and mortality in white men, leading the authors to speculate that the magnitude of this relation is greater in African American than in white males.

There are fewer data regarding Mexican Americans, but in this group also, associations between obesity and mortality have been questioned. For instance, vital statistics data revealed lower mortality rates among Mexican Americans in Texas than would be expected on the basis of known body weights (52). Nonetheless, known associations between overweight and diabetes and other obesity-associated diseases in this population indicate that mortality risks associated with adiposity in Mexican Americans require further study. Among other populations, such as American Indians and Alaska Natives, increased prevalence of obesity has been closely associated with increases in diabetes, hypertension, and IHD (53). As for other ethnic groups, for these groups more research is needed to quantify mortality risks associated with overweight.

CONCLUSIONS

Obesity is strongly predictive of mortality from all causes combined, cardiovascular disease, and some cancers. Although some data have suggested J- or U-shaped associations between BMI and mortality risks, any apparent adverse effects of leanness appear to be markedly attenuated or completely eliminated with appropriate control for confounding by smoking and underlying disease. Recent data suggest that central obesity may be an even stronger predictor of morbidity and mortality than body weight or BMI, although this remains controversial. The risks associated with obesity, particularly central obesity, may well reflect the association of these anthropometric variables with underlying insulin resistance or hyperinsulinemia. Risks associated with obesity and linked to insulin resistance include diabetes mellitus, hypertension, dyslipidemia, and cardiovascular disease, as well as some cancers, all of which contribute to mortality risk and also result in significant morbidity and cost.

Measures of obesity used in epidemiologic studies are imprecise surrogates for true adiposity. Furthermore, quantitative assessment of the relation between obesity and mortality may be confounded by associated factors. Nonetheless, when confounding is well controlled, there is powerful evidence that obesity is detrimental throughout the life span, any time from childhood to old age. Weight gain over time is associated with particular risk. Better understanding of the relation between adiposity and mortality should come with further research, including mechanistic approaches looking at other markers for insulin resistance, such as insulin concentrations, as predictors of morbidity and mortality. In the meantime, the preponderance of data suggests that prevention of obesity, beginning in childhood and continuing throughout life, should be encouraged to minimize morbidity and improve longevity.

REFERENCES


