

## Mortality, Health Outcomes, and Body Mass Index in the Overweight Range

### A Science Advisory From the American Heart Association

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Health hazards of obesity have been recognized for centuries, appearing, for example, in writings attributed to Hippocrates. From the later decades of the 20th century through the present, there have been numerous epidemiological studies of the relationship between excess weight and the total, or all-cause, mortality rate,<sup>1</sup> a critical cumulative measure of the public health impact of any health condition. Using body mass index (BMI), an indicator of relative weight for height (weight [kg]/height [m]<sup>2</sup>) and a frequently used surrogate for assessment of excess body fat, these studies have found linear, U-shaped, or J-shaped relationships between total mortality and BMI. That is, in some studies, both the thin and the obese were more likely to die than those in between. There is, however, always a point at which increasing BMI is associated with increasing mortality risk, but the BMI at which this occurs varies across studies and populations.<sup>2</sup>

Currently,<sup>3</sup> overweight in adults is defined as a BMI of 25.0 to <30.0 kg/m<sup>2</sup> and obesity as a BMI of ≥30.0 kg/m<sup>2</sup> (Table 1). A number of studies have found no significant relationship between BMI in the overweight range and mortality rate<sup>4</sup> and have shown the nadir of mortality risk to be in the overweight range. In particular, commentaries in both the lay press<sup>5–7</sup> and scientific literature<sup>2,8,9</sup> subsequent to recent reports from National Health and Nutrition Examination Surveys (NHANES)<sup>10,11</sup> have highlighted the confusion and controversy regarding this issue. Some have interpreted the recent data to mean that overweight is not detrimental to

health and is not in itself a public health concern and that drawing attention to the need for weight loss in this range will have negative effects on the health and well-being of the general population.<sup>8</sup> Others have argued that the overweight range of BMI harbors substantial health risk<sup>9</sup> and is also a pipeline for later obesity, so that aggressive public health interventions are warranted.

The purpose of the present science advisory is to briefly review and place into context the potential health implications of overweight as distinct from obesity. Clarity on this issue is particularly important given the substantial proportion of the population in the overweight range. Although this advisory discusses the important issue of the BMI–total mortality relationship, it also broadens the topic to include other important considerations, such as outcomes besides total mortality.

We begin with a brief review of population-wide weight trends, then of key methodological issues that influence the evaluation and comparison of studies that attempt to link overweight with mortality, and then we describe selected recent studies to illustrate the potential for drawing conflicting conclusions. The discussion that follows highlights possible differences in the association of BMI and total mortality rate by age, ethnicity, or sex; how body fat distribution may modify the association; and the need to incorporate other considerations, including how overweight relates to a range of other important outcomes, including diabetes mellitus. We conclude with some suggested avenues for future research.

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**Table 1. Classifications of Overweight and Obesity by BMI, Waist Circumference, and Associated Disease Risks**

	BMI, kg/m <sup>2</sup>	Obesity Class	Disease Risk Relative to Normal Weight and Waist Circumference	
			Men ≤102 cm, Women ≤88 cm	Men >102 cm, Women >88 cm
Underweight	<18.5	...	...	...
Normal	18.5–24.9	...	...	...
Overweight	25.0–29.9	...	Increased	High
Obesity	30.0–34.9	I	High	Very high
	35.0–39.9	II	Very high	Very high
Extreme obesity	≥40	III	Extremely high	Extremely high

Reprinted from reference 3.

### Population-Wide Weight Trends

Population-wide increases in BMI levels became apparent when data for adults in the NHANES from the early 1960s were compared with those of the late 1970s.<sup>12,13</sup> Data from successive NHANES cycles show large increases in obesity prevalence and relatively stable overweight prevalence (Table 2), with the most recent data from 2003 to 2004 indicating that two thirds of adults were overweight or obese.<sup>14,15</sup> In addition to these trends, there have been corresponding increases in mean BMI, a shift in the population BMI distribution upward, and a greater shift, or skewing, at higher BMI levels.<sup>16</sup> These trends imply that overweight people are moving into the obese range and being replaced by an influx of persons from the normal weight range.

### Methodological and Conceptual Issues

Studies of the BMI-mortality relationship may suffer from several sources of bias and confounding. Failure or inability to adequately take these into account could explain the U- or J-shaped relationship, at least in some studies, or could distort the location of the true nadir of mortality risk along the BMI distribution, where a U-shaped relationship represents the true causal function.

*Reverse causality* is a term used in the literature to refer to the confounding introduced when occult or preexisting diseases that increase mortality rate also cause weight loss (eg, tobacco-related cancers). Elevated mortality rate at low BMI may reflect a true causal relationship if thin people are disproportionately more susceptible to disease and suffer worse health outcomes, including death, than those at higher BMI levels.

**Table 2. Prevalence of Overweight (BMI 25.0 to <30.0 kg/m<sup>2</sup>) and Obesity (BMI ≥30.0 kg/m<sup>2</sup>) for US Adults 20 to 74 Years of Age, National Health Examination Survey and NHANES**

	Overweight and Obese, %	Overweight, %	Obese, %
1960–1962	44.8	31.5	13.3
1971–1974	47.7	33.1	14.6
1976–1980	47.4	32.3	15.1
1988–1994	56.0	32.7	23.3
1999–2000	64.1	33.1	31.0
2001–2002	65.7	33.6	32.1
2003–2004	67.1	33.2	33.9

Reprinted from reference 15.

In addition, intentional weight loss may be attempted to manage conditions such as diabetes that could affect survival. Such weight loss could result in reclassification of people with these conditions into lower BMI categories. The use of only 1 baseline measurement of a risk factor (eg, blood pressure) has long been known to attenuate (ie, dilute) associations between risk factors and disease. Some have advocated adjusting for this regression dilution bias in studies of the BMI-mortality relationship.<sup>17</sup> Others doubt that attempts to control for either reverse causality or regression dilution bias are important or effective and argue that they do not explain the NHANES results of a lower mortality rate in the overweight range.<sup>18</sup>

Another important consideration is potential overcontrolling by adjustment for weight-related risk factors.<sup>9,19</sup> If BMI contributes to the development of a risk factor (eg, type 2 diabetes mellitus or systemic hypertension), statistical adjustment for such risk factors is misleading with regard to the contribution of BMI. What remains after adjustment is only the residual association of BMI to the outcome, which is not mediated through the weight-related risk factors included in the model.

Lack of statistical power, especially small numbers of disease cases and inadequate length of follow-up, has long been noted as a potential explanation for studies that failed to find relationships between even obesity and mortality. Sjöström<sup>20</sup> noted that the Framingham study, with approximately 5000 participants, required 26 years of follow-up to find a positive relationship.

The choice of the reference group against which to estimate the relative mortality risk of overweight persons is also important. The existence of a J- or U-shaped relationship, with higher mortality among those with lower BMI than among those in the intermediate range of BMI, could be due either to confounding or to a true causal association between low BMI and mortality. Because of this, some have argued that the use of the entire normal range BMI of 18.5 to 25.0 kg/m<sup>2</sup> as a comparison group risks the inclusion of a substantial portion of people with elevated mortality risk at the lower end of this range and will result in an underestimation of the mortality risk, especially of the overweight category. Other problems include the potential for unmeasured confounders in observational studies and, as will be discussed later, potential misclassification bias from use of surrogate markers of body fat, such as BMI, the impact of which varies across population groups.

Such strategies as excluding the first 3 to 5 years of follow-up, conducting studies with long-term follow-up and

testing for interaction between follow-up time and BMI, restricting the analysis to never-smokers, and analysis of presumably healthier occupational cohorts have been used to attempt to deal with these sources of bias in studies of the BMI-mortality relationship.<sup>21–23</sup> However, not all of these strategies are likely to be successful. For example, the exclusion of study participants who die during the first years of follow-up is not necessarily an effective strategy for dealing with confounding due to occult disease.<sup>24</sup>

Two studies serve as examples of these points. First, a recent study from Scotland found indications of reverse causality and a strong masking by smoking of the relationships of overweight and obesity with all-cause and cause-specific mortality.<sup>21</sup> Second, Gu et al<sup>25</sup> found a U-shaped relationship in age-standardized analyses of >150 000 Chinese men and women followed up for 8 years, using a single baseline BMI, with the lowest mortality rates at BMI 24.0 to 24.9 kg/m<sup>2</sup> in men and 25.0 to 26.9 kg/m<sup>2</sup> in women. The U-shaped relationship remained in analyses that excluded smokers and those with prevalent self-reported health conditions such as cardiovascular disease (CVD), cancer, and chronic obstructive pulmonary disease, and with the exclusion of deaths that occurred during the first 3 years of follow-up. There was a small but statistically significant increased risk of all-cause mortality among healthy participants with BMI 27.0 to 29.9 kg/m<sup>2</sup> compared with those with BMI 24.0 to 24.9 kg/m<sup>2</sup> after multivariable adjustment. When the comparison group was those with BMI 18.5 to 24.9 kg/m<sup>2</sup>, there was a significant inverse relationship between mortality and BMI 25.0 to 29.9 kg/m<sup>2</sup>, which illustrates the importance of choice of comparison group.

### Recent Studies on Overweight and All-Cause Mortality

Flegal et al<sup>10</sup> estimated relative risks according to measured BMI groups in the nationally representative NHANES I (baseline 1971 to 1975; nearly 4000 deaths) and NHANES II (1976 to 1980; >2100 deaths) with follow-up through 1992, as well as from NHANES III (baseline 1988 to 1994; >2700 deaths) with follow-up through 2000. The analysis examined 3 strata of age (25 to 59 years, 60 to 69 years, and ≥70 years) and included sex, race (white, black, and other), alcohol consumption categories (0, <0.07, 0.07 to <0.35, and 0.35 oz/d or more), and smoking (never, former, and current). With normal weight (BMI 18.5 to 24.9 kg/m<sup>2</sup>) as the comparison group, obesity was associated with an increased risk of total mortality, particularly at younger ages, and with the most excess deaths occurring with BMI ≥35 kg/m<sup>2</sup>. Relative risks were <1 for overweight in the combined cohorts but were not statistically significant in all age ranges examined, in all participants and those who never smoked alike, or when the first 3 or 5 years of follow-up were excluded. For example, among never-smokers 60 to 69 years old, the relative risk associated with overweight was 0.81 (95% confidence interval [CI] 0.56 to 1.16); with BMI ≥35 kg/m<sup>2</sup>, the relative risk was 2.30 (1.47 to 3.59).

The study by Flegal et al<sup>10</sup> has been criticized for not adequately controlling for smoking and reverse causality, because the data were not simultaneously stratified by smoking and follow-up time because of sample size limitations. In supplemental analyses, Flegal et al<sup>26</sup> reported that, “Even when analyses were restricted to a subset of healthy individuals who had never smoked and deaths occurring in the first part of the study were excluded, the relative risks were still elevated for underweight and below 1 for overweight. . . .” The study also used broad ranges of BMI for comparisons and arguably an inappropriate reference category (ie, BMI 18.5 to 25.0 kg/m<sup>2</sup>). In a more recent study, Flegal et al<sup>11</sup> used similar analytic approaches to those of their earlier report<sup>10</sup> and examined the same data sets, but with extended follow-up. The new study examined specific causes of mortality, again finding decreased overall mortality in the overweight group compared with the same reference category (BMI 18.5 to 25.0 kg/m<sup>2</sup>).

Adams et al<sup>27</sup> reported the results of up to 10 years of mortality follow-up, including 61 317 deaths among 527 265 men and women 50 to 71 years old in the National Institutes of Health–American Association of Retired Persons (NIH-AARP) Diet and Health Study cohort. The extremely large sample size allowed the investigators to examine 10 BMI categories, 6 education categories, 4 alcohol consumption categories, 7 physical activity categories, and a large number of smoking categories. All analyses used a narrow comparison group of high-normal BMI, defined as 23.5 to 24.9 kg/m<sup>2</sup> in both men and women. Overall, that study also showed a U-shaped relationship between BMI and mortality.<sup>27</sup> Compared with those with BMI 23.5 to 24.9 kg/m<sup>2</sup>, mortality was significantly higher in both men and women who were obese at baseline and among those who were underweight (BMI <18.5 kg/m<sup>2</sup>) or who were in the lower range of normal (BMI <23.5 kg/m<sup>2</sup>). In women, there was a significant but small increase in risk among those with BMI 28.0 to 29.9 kg/m<sup>2</sup> (RR 1.07, 95% CI 1.01 to 1.14), whereas in men, there was a significantly lower risk in those with BMI 25.0 to 27.9 kg/m<sup>2</sup>. In subgroup analyses, mortality risk was increased significantly among overweight never-smokers in both sexes, among women who did not have preexisting chronic medical conditions (doctor-diagnosed cancer, heart disease, stroke, emphysema, or end-stage renal disease), and when the first 5 years of follow-up were excluded from the analysis. For example, among women who had never smoked, relative risks were 1.09 (95% CI 0.97 to 1.22) for BMI 25.0 to 26.4 kg/m<sup>2</sup>, 1.21 (1.08 to 1.36) for BMI 26.5 to 27.9 kg/m<sup>2</sup>, and 1.27 (1.14 to 1.42) for BMI 28.0 to 29.9 kg/m<sup>2</sup>. This study has been criticized because the cohort is not a representative sample of the population, as is the NHANES. It included AARP members 50 to 71 years of age from the selected 6 states and 2 metropolitan areas, 18% of whom returned the questionnaire. In addition, all baseline data were collected by self-report, a technique frequently criticized as a potential source of bias in the BMI-mortality relationship. Some have speculated as to the direction of this bias,<sup>28</sup> but there

are few data to directly evaluate the magnitude and direction of bias due to self-reported weight and height. Such studies would add greatly to the literature.

Jee et al<sup>29</sup> reported on >1.2 million Koreans insured by the National Health Insurance Corporation in Korea, approximately 11% of the population. Participants were enrolled from 1992 to 1995 and were followed up through 2004 for mortality, which occurred in >58 000 men and >24 000 women. The analysis excluded events that occurred during the first 2 years of follow-up and anyone who reported certain chronic diseases at baseline (atherosclerotic CVD, cancer, liver disease, diabetes, or a respiratory disease). Participants were grouped into 10 BMI groups, beginning with BMI <18.5 kg/m<sup>2</sup> and continuing to BMI ≥32.0 kg/m<sup>2</sup>. Among women, only those who had never smoked were included, because there were few women who had. The average age of this cohort was 45 years for men and 49 years for women, and the average BMI in both sexes was 23.2 kg/m<sup>2</sup>. The lowest risk of death due to all causes occurred in both sexes in those with BMI 23.0 to 24.9 kg/m<sup>2</sup> who had never smoked, the BMI reference group for all analyses. A significantly higher risk of death was observed in both men and women with BMI <18.5 and ≥30.0 kg/m<sup>2</sup>. After adjustment for age, smoking, alcohol intake, and physical activity, the hazard ratio for total mortality was not statistically significant for either men or women for BMI 25.0 to 26.4 kg/m<sup>2</sup> and 26.5 to 27.9 kg/m<sup>2</sup>. For BMI 28.0 to 29.9 kg/m<sup>2</sup>, hazard ratios were 1.06 (95% CI 1.00 to 1.12) for men and 1.09 (95% CI 1.02 to 1.16) for women. The mortality rate for atherosclerotic CVD was significantly higher for men beginning with BMI 26.5 to 27.9 kg/m<sup>2</sup> among never-smokers and beginning with BMI 28.0 to 29.9 kg/m<sup>2</sup> in those who had ever smoked. In women, atherosclerotic death was significantly higher with BMI 28.0 to 29.9 kg/m<sup>2</sup>. Increased risk for cancer death also occurred in BMI ranges considered overweight in men who had never smoked and in women. Because death registry information alone was used for classification, cause-specific mortality may not be accurate, but total mortality is not affected.

### Prior Studies of Overweight and Mortality

The results of previous studies with long-term (>10 years) follow-up, particularly those that compared the risks of normal-weight individuals with those who are overweight, are mixed, with stronger relationships at the higher end of the overweight range (eg, BMI 27.5 to 30.0 kg/m<sup>2</sup>).<sup>23,30,31</sup> For example, among never-smoking US women with recently stable weight, BMI of 27.0 to 28.9 kg/m<sup>2</sup> (versus <19 kg/m<sup>2</sup>) was linked with a 60% increase in death.<sup>23</sup> However, other long-term studies show no association between the lower<sup>32-34</sup> or higher<sup>33,35,36</sup> range of the overweight category and mortality.

### Potential Modifiers of the BMI-Mortality Association

Further complexity is added by the fact that the association of overweight with mortality may vary according to variables

such as sex, ethnicity, age, and body fat distribution. For example, the association may differ by sex, as in the study by Gu et al<sup>25</sup> in which BMI >27.0 kg/m<sup>2</sup> in men and >30.0 kg/m<sup>2</sup> in women was associated with increased all-cause mortality. Likewise, race/ethnicity may influence risk, with BMI in the overweight range linked to increased rates of death in white men and women in the Cancer Prevention Study II, although there was no significant association for black men or women.<sup>37</sup> Similarly, estimates based on national US data suggest that the BMI associated with minimum mortality is in the overweight range for black men or women but in the normal-BMI range for whites.<sup>38</sup> A higher percentage of body fat at lower BMI has been observed in many Asian compared with non-Asian populations, as well as a high risk of type 2 diabetes mellitus and CVD at low BMI.<sup>39</sup> However, metabolically obese normal weight individuals have been described in other populations, including those of European ancestry, as well.<sup>40</sup> Also, the results of the study by Jee et al<sup>29</sup> in Koreans mentioned above were similar to those of several cohort studies in populations of European descent, which suggests that different cutpoints in Asians may not be necessary. Finally, age may also modify the relationship with overweight, carrying more risk, as measured by relative risk, for younger than for older (eg, ≥65 years) adults.<sup>30</sup> As Stevens et al point out,<sup>41</sup> different answers can be obtained depending on the measure of effect used. In their analysis of the Cancer Prevention Study I, the absolute risk of mortality associated with obesity increased with age, whereas the relative risk decreased.

As noted previously, a major problem with BMI is that it is a surrogate, measuring total body mass. One explanation for a U-shaped relationship between BMI and mortality is that BMI is made up of both fat and fat-free mass, which have opposite effects on health and longevity.<sup>42</sup> Misclassification of individuals or certain groups (eg, the elderly) because of the inherent inadequacy of a surrogate measure is most likely in the middle range of a distribution, typically the overweight range when dealing with BMI. BMI also does not measure fat distribution directly. Waist or waist-to-hip ratio measures are used as proxies for body fat distribution, and in several studies, these are more important indicators of coronary heart disease risk than BMI. For example, Bigaard et al<sup>43</sup> found a strong dose-response relationship between waist circumference and mortality when adjusted for BMI among both men and women, whereas BMI was inversely associated with mortality when adjusted for waist circumference.

The use of BMI as a surrogate for body fat may be particularly problematic in the elderly. Sarcopenic obesity, which is defined as excess fat with low relative lean body mass, is a common problem in the elderly. Thus, BMI is a less accurate measure of body fat in this group, and direct measures of fat and fat distribution may be particularly important in studies of elderly populations. In the Cardiovascular Health Study, a cohort of men and women 65 years of age and older, higher BMI was related to lower mortality risk once the waist circumference was accounted for, whereas higher waist circumference was related to higher mortality

risk after accounting for BMI.<sup>44</sup> Because BMI represents total body mass, BMI adjusted for waist circumference may have better represented the protective effect of lean body mass, which is inversely related to mortality.<sup>45</sup>

## Other Outcomes

### CVD Risk

A focus on total mortality misses the larger picture of the impact of excess body weight on health. First, overweight is more consistently associated with coronary heart disease or CVD mortality than with all-cause mortality, with hazard ratios for higher degrees of overweight (typically BMI in the 27.5 to 29 kg/m<sup>2</sup> range) of 1.4 to 2.8 over 10 to 26 years of follow-up.<sup>23,31,33,36,37</sup> BMI in the lower range of overweight sometimes,<sup>32,33,37</sup> but not always,<sup>23,30,31,33,36</sup> is associated with cardiovascular mortality risk. When present, associations of these outcomes with BMI are generally linear, not U-shaped. Data on stroke are mixed, with borderline increased risk in overweight US male and female health professionals,<sup>46</sup> but studies in overweight British men<sup>33</sup> or mildly overweight elderly Swedes<sup>47</sup> found no increased risk of stroke.

### CVD Risk Factors

Overweight is linked with considerable increases in incidence of CVD risk factors, including type 2 diabetes mellitus,<sup>33,46,48,49</sup> systemic hypertension,<sup>46,49</sup> and dyslipidemia.<sup>46</sup> A number of studies have shown that diabetes risk is significantly elevated in the overweight range for samples of diverse ages.<sup>33,46,48,49</sup> Several studies also show a dose-response pattern of diabetes risk across the overweight range. For example, in a large cohort of British men 40 to 59 years of age, the relative risk of developing diabetes over an average of 14.8 years was 3.58 (95% CI 1.71 to 7.49) for men with BMI 26.0 to 27.9 kg/m<sup>2</sup> and 5.20 (2.44 to 11.04) for those with BMI 28.0 to 29.9 kg/m<sup>2</sup> compared with men whose BMI was 20 to 22.9 kg/m<sup>2</sup>.<sup>33</sup> A recent NHANES analysis reported an increased prevalence of diabetes of 3.75 additional cases per 100 in 1999 to 2004 compared with 1976 to 1980 and estimated that 27% of these cases were among persons in the overweight category.<sup>50</sup>

Overweight is similarly related to systemic hypertension; several studies have found relative risks of 1.4 to 1.7.<sup>46,49</sup> In a predominantly white female cohort 30 to 55 years old at baseline, the relative risk of hypertension increased from 2.55 for BMI 25.0 to 25.9 kg/m<sup>2</sup> (95% CI 2.33 to 2.79) to 4.20 for BMI 28.0 to 30.9 kg/m<sup>2</sup> (95% CI 3.86 to 3.62) over 16 years of follow-up compared with BMI <20.0 kg/m<sup>2</sup>.<sup>51</sup>

In fact, the relationship of CVD mortality with overweight may be influenced by the presence of CVD risk factors. In 1 study from Paris,<sup>52</sup> an excess risk of CVD mortality was found among overweight men and women with weight-related risk factors, particularly among those with systemic hypertension, but not among those without these risk factors. Thus, BMI per se does not necessarily indicate the metabolic fitness (the lack of obesity-related metabolic risk and more favorable body composition) of an individual.<sup>40</sup> Overweight

populations, and even normal-weight groups,<sup>53</sup> likely represent a complex mixture of the metabolically lean and obese due to genetic and environmental factors. These issues indicate that it may be time to readdress the definition and assessment of at risk obesity/overweight.<sup>45</sup>

### Venous Thromboembolic Events

A number of studies, but not all, have shown a 2 to 3 times greater risk of venous thromboembolism among the obese.<sup>54</sup> Fewer studies have specifically examined the overweight group, but emerging evidence indicates that risk of venous thromboembolism may be higher among this group, particularly among those with other thrombosis risk factors.<sup>55,56</sup> In the Leiden Thrombophilia Study,<sup>57</sup> for example, the nonsignificantly higher odds among the overweight compared with the normal-weight participants masked a strong interaction with use of oral contraceptives: There was no association with venous thromboembolism among overweight nonusers of oral contraceptives (odds ratio 0.9, 95% CI 0.4 to 2.0), but there was a strong association among overweight users (odds ratio 10.2, 95% CI 3.8 to 27.3) that was similar to that among obese women who were also oral contraceptive users (odds ratio 9.8, 95% CI 3.0 to 31.8).

### Non-CVD Outcomes

In addition to CVD-related outcomes, there is at least some evidence that overweight is related to a number of other outcomes, including postmenopausal breast cancer<sup>49</sup> and several other cancers,<sup>58</sup> osteoarthritis of the knee requiring arthroplasty,<sup>59</sup> gout,<sup>60</sup> sleep-disordered breathing,<sup>61</sup> gastroesophageal reflux,<sup>62</sup> and symptomatic gallstone disease.<sup>63,64</sup> For example, in the Health Professionals Follow-up Study,<sup>63</sup> the risk of symptomatic gallstone disease in men was increased significantly beginning with BMI 25.0 to 25.8 kg/m<sup>2</sup> (relative risk 1.63, 95% CI 1.24 to 2.16) compared with those with BMI <22.2 kg/m<sup>2</sup>, and measures of abdominal adiposity (waist circumference and waist-to-hip ratio) predicted the risk of developing gallstones independent of BMI. Last, but certainly not least, based on young adult or middle-age BMI, the future cumulative Medicare expenditures were significantly greater for overweight than for normal-weight elderly men and women for CVD and diabetes-related care, as well as for total care for men.<sup>65</sup> Although this study points to the possibility of cost savings from overweight prevention, it does not speak to the costs of weight maintenance or weight loss interventions, which argues for additional research on cost-effective strategies for weight management, especially in the context of CVD and diabetes prevention.

### Evidence of Progressive Danger

Although near-term risk of clinical events such as coronary heart disease death is very low among the young, overweight and obesity are still concerning among children and adolescents. First, excess weight tends to progress. Overweight children in the Bogalusa Study had an increased risk of becoming

obese adults, particularly among blacks and especially among children who were consistently overweight.<sup>66</sup> In young adults in the CARDIA study (Coronary Artery Risk Development In young Adults), those who were initially overweight more often gained large amounts of weight over 10 years than did those who were of normal weight at baseline.<sup>67</sup>

Second, once gained, excess weight is difficult to manage. It is well accepted that long-term maintenance of successful weight loss achieved by behavioral and/or pharmacological means is relatively modest and difficult to maintain, even though there are clear observational and trial data on the benefits of weight loss for control of CVD risk factors.<sup>3</sup> On the other hand, the young adults in the CARDIA study who maintained stable BMI over time had minimal progression of weight-related CVD risk factors and a lower incidence of metabolic syndrome, regardless of baseline BMI.<sup>68</sup>

Third, even among the young, the health consequences of excess body fat are increasingly manifesting themselves. Overweight children and adolescents are at high risk for adverse CVD risk factor levels, including adverse blood pressure, insulin, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglyceride levels.<sup>69</sup> Cardiac structure and function, including left ventricular hypertrophy and excess left ventricular mass relative to cardiac workload, may also be adversely affected by excess fat mass in the young.<sup>70</sup> Finally, there is some evidence that childhood BMI is positively associated with risk of clinical coronary heart disease events in adulthood.<sup>71</sup>

## Conclusions

The relationship between BMI in the overweight range and total mortality risk is controversial. There is evidence of an adverse relationship in some studies but not in others.<sup>4</sup> Some have proposed that methodological issues may mask the true relationships of overweight and obesity with total and cause-specific mortality.<sup>21</sup> Given that nearly one third of the US adult population is overweight, simply debating the relationship between BMI in this range and total mortality misses broader implications.

First, there is considerable evidence that overweight is related to increased risk of other important adverse outcomes besides total mortality. Second, overweight is usually a harbinger of definite obesity and its multiple adverse consequences. Perhaps most importantly, it is critical to consider the overall risk status of patients regardless of BMI, with the realization that those with CVD risk factors such as type 2 diabetes mellitus and systemic hypertension are at particularly increased risk from excess weight and may well benefit from weight loss intervention as part of their treatment.<sup>72,73</sup>

Given this, clinical trials of strategies for the monitoring of and interventions for overweight individuals with above-optimal levels of fasting glucose and blood pressure may be particularly useful, especially with the inclusion of cost-effectiveness analyses. Further research is also needed in several other areas, including studies of intervention strategies and costs for prevention of overweight and obesity, development and trials of the efficacy of weight maintenance strategies for prevention of clinical end points, studies of the translation of efficacious strategies into medical practice and communities, additional studies of various health outcomes related to overweight as distinct from those related to obesity, and studies to better risk-stratify patients by identifying the most appropriate and clinically useful adiposity measures for various groups of patients.

Meanwhile, we cannot afford to wait for this research to begin addressing the problem of overweight in our patients and in our society. Both healthy eating patterns and physical activity have roles in managing weight and CVD risk and should be encouraged in all. Because physical inactivity and excess weight have been independently associated with mortality in several studies,<sup>74</sup> there are additional advantages to overweight and obese persons adopting an active lifestyle, as well as healthy eating habits. In the long term, because weight gain is progressive and weight loss is difficult to maintain, it is vitally important that effective weight maintenance and obesity-prevention approaches be developed and implemented for all individuals above normal weight.

## Disclosures

### Writing Group Disclosures

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Cora E. Lewis	University of Alabama at Birmingham	NHLBI: Longitudinal Studies of CHD Risk Factors in Young Adults (CARDIA)†; NHLBI Vanguard Clinical Centers for the Clinical Trial and Observational Study of the Women's Health Initiative‡; NIDDK Clinical Center for Look AHEAD: Health in Diabetes‡; NIDDK UAB Diabetes Research and Training Center‡	None	None	None	None	None

(Continued)

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Barbara V. Howard	Medstar Research Institute	None	Merck*; Pfizer*; Schering-Plough*	Schering-Plough*	None	Egg Nutrition Council*; Merck*	None
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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (1) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (2) the person owns 5% or more of the voting stock or share of the entity, or owns \$10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

\*Modest.

†Significant.

Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
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