The impact of using different measures of the effect of obesity on mortality across age groups has not been explored. The authors examined this issue by using mortality data from 62,116 men and 262,965 women in the Cancer Prevention Study-I (1960-1972). Measures of effect were calculated separately, by decade of age, for five groups of participants aged 30–79 years. The rate ratio associated with obesity declined with age, from 2.60 (men) and 1.99 (women) for participants aged 30–39 years to 1.24 (men) and 1.15 (women) for those aged 70–79 years. In contrast, the rate differences between obese and reference-weight participants increased with age, from 201 (men) and 112 (women) deaths per 100,000 person-years for those in the youngest decade to 1,379 (men) and 626 (women) deaths per 100,000 person-years for those in the oldest decade. The years of life lost attributable to obesity tended to increase with age but declined for those in the oldest decade. The rate advancement period declined with decade of age. Standardization of estimates to a population changed some age-associated trends. The direction of trends varied regarding the effect of obesity on mortality across age groups, depending on the measure of effect used. Am J Epidemiol 1999; 150:399–407.

The issue of whether the association between weight and mortality changes with age or is constant throughout adulthood has been the subject of much debate (1–7). Traditionally, weight recommendations and standards have been defined by using studies that examine the weight for height or body mass index (BMI) associated with the lowest mortality. Optimal BMI is assessed through cohort studies that follow participants over time and examine associations between BMI at baseline and subsequent mortality. Germane to the debate over optimal body weight are methodological issues involving the analyses of data from these cohort studies (8, 9). In 1987, Manson et al. (9) brought attention to several of these methodological issues in a review of 50 studies on the obesity-mortality relation. They noted that studies have shown no association, a positive association, a J- or U-shaped association, and even an inverse association between weight and total mortality. Reasons cited by these and other authors for discrepant results in the field included lack of control for cigarette smoking, inappropriate adjustments for the biologic effects of obesity, failure to control for cases who had experienced disease-induced weight loss, and inadequate statistical power.

Although much of the debate regarding the impact of age on the BMI-mortality relation has centered on methodological issues, one important issue that to our knowledge has not received attention is the choice of the measure of effect. Relative risks, calculated as rate ratios, are commonly used measures of effect in cohort studies. Recently, we used rate ratios to estimate the impact of BMI on mortality among six age groups by using data from more than 300,000 men and women in the Cancer Prevention Study-I (CPS-I) (10). The BMI associated with optimal survival did not change substantially with age up to age 75 years, and the rate ratio tended to be the lowest when BMI was between 19 and 22. We also compared the magnitude of the BMI-mortality rate ratios among age groups and found that they declined with age. However, comparisons of rate ratios among age groups may be influenced by large differences in age-specific mortality rates. Also, on a population level, the influence of obesity on mortality is affected by the distributions of age and obesity in the population, which are not considered in a comparison...
among age-stratified rate ratios. The purpose of this study was to illustrate the impact of using different measures of effect to evaluate the association between obesity and mortality across age groups.

MATERIALS AND METHODS

Mortality data were selected from CPS-I, which began in 1960 (11). Participants were enrolled in family groups in which at least one member was older than age 45 years, and all household members over age 30 years were eligible for the study. Members of the cohort had higher levels of education than in census figures from the same decade (12), and participants who smoked or had a family history of cancer were oversampled (13). Participants completed a questionnaire on personal health practices and medical history. Height in inches (without shoes) and weight in pounds (wearing indoor clothing) were collected by self-report. The vital status of 98.4 percent of the total cohort was traced through September 1971, and 92.8 percent were traced through September 1972.

Exclusion criteria were determined prior to the analysis and were similar to those used in previous studies (10). We restricted the analyses to White participants who had never smoked. Excluded were participants who were pregnant at baseline, responded by proxy, or were missing data on height or weight or other pertinent variables. Because of the high probability of disease-related weight loss at baseline, we also excluded those who reported an involuntary weight loss of \( \leq 10 \) pounds within 2 years of baseline, died within the first year of follow-up, or reported a history of cancer (other than skin cancer) or heart disease. For the same reason, we excluded participants who responded affirmatively to the question “Are you sick at the present time?” or reported feeling “poor” rather than “fair” or “good” within the past month. For this analysis, we also excluded participants whose BMI was \(<18.5\) (the World Health Organization cutpoint for underweight (14)) or \(\geq 30.0\); and overweight, \(\geq 25\). All measures of effect were calculated separately by gender within five age groups by using SAS software (SAS Institute, Cary, North Carolina). Estimates were calculated by using data from CPS-I except when NHANES was specified. The words “excess” and “attributable” were used synonymously. The measures of effect that were calculated are shown below.

1. Percent dead \( P = \frac{D}{n} \)

where

\[ D = \text{number of deaths over the follow-up period} \]
\[ n = \text{number of subjects in the category} \]

2. Rate ratio \( = \frac{I_{ob}}{I_r} \)

where

\( I_{ob} = D/\text{person-years in the obese or overweight category (i.e., rate)} \)
\( I_r = D/\text{person-years in the BMI reference category} \)

Am J Epidemiol Vol. 150, No. 4, 1999
3. Rate difference = \( I_{ob} - I_r \)
4. Excess death in 100,000 persons = \((P_{ob} - P_r) \times E\) where
   \(P_{ob}\) = percent dead in the obese or overweight category
   \(P_r\) = percent dead in the BMI reference category
   \(E\) = number of persons in the obese or overweight category (for the standardized estimates, we used the age-BMI distribution from NHANES III to calculate \(E\))
5. Years of life lost (YLL) \((16, 17)\) per person = \[ \sum_{i=1}^{n} YLL_i \]
   where
   \(YLL_i\) = for subject \(i\), the difference between age (in years) at death and life expectancy at age of death according to 1960 life expectancy tables \((18)\). For participants who do not die during the follow-up period, \(YLL_i = 0\).
6. Excess YLL per person = \(YLL_{ob} - YLL_r\) where
   \(YLL_{ob}\) = average years of life lost in the obese or overweight category
   \(YLL_r\) = average years of life lost in the BMI reference category
7. Excess YLL per 100,000 persons = \((YLL_{ob} - YLL_r) \times E\)
8. Rate advancement period (RAP) \((19)\) = \(\beta_1 / \beta_2\) where
   \(\beta_1\) and \(\beta_2\) are coefficients from the following Cox proportional hazards model:
   \[ \log(\text{person-year rate}) = \alpha + \beta_1 \text{BMI} + \beta_2 \text{age} \]
9. RAP per 100,000 persons = \(\text{RAP} \times E\)

RESULTS

The study samples from CPS-I and NHANES III are described in table 1. As a result of recruitment practices, the majority of CPS-I participants were aged 40–59 years. In contrast, the distributions of NHANES III participants by age reflect the current national distribution of never-smoking, healthy White adults. Among men in CPS-I and NHANES III, BMI tended to increase with age up to age 60 years. Among women in NHANES III, BMI tended to increase each decade up to age 50–59 years; in CPS-I, there was a similar increase up to age 60–69 years. BMI was higher in NHANES III than in CPS-I participants in every age group, as expected given secular trends in body weight \((20, 21)\).

The results from the mortality follow-up of CPS-I, by age and BMI groups, are shown in table 2. The percentage of the cohort that died during follow-up increased dramatically with age. In the BMI reference category, the percent dead was 35-fold higher among men aged 70–79 years compared with men aged 30–39 years. Among women, this difference was 30-fold. In every age category, the percent dead tended to be higher among those in the preobese and obese groups than among those in the reference group, but the difference was much smaller than it was with age. The differences were always less than threefold and were generally less than twofold.


<table>
<thead>
<tr>
<th>Age in years</th>
<th>CPS-I No.</th>
<th>Height in inches (SE*)</th>
<th>Weight in pounds (SE)</th>
<th>BMI† (SE)</th>
<th>NHANES III No.</th>
<th>Height in inches (SE)</th>
<th>Weight in pounds (SE)</th>
<th>BMI† (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>4,251</td>
<td>69.78 (0.04)</td>
<td>177.7 (0.37)</td>
<td>25.43 (0.05)</td>
<td>361</td>
<td>69.60 (0.15)</td>
<td>185.8 (1.75)</td>
<td>26.90 (0.24)</td>
</tr>
<tr>
<td>40–49</td>
<td>18,869</td>
<td>69.49 (0.02)</td>
<td>179.0 (0.17)</td>
<td>25.83 (0.02)</td>
<td>227</td>
<td>69.19 (0.17)</td>
<td>187.1 (2.44)</td>
<td>27.40 (0.32)</td>
</tr>
<tr>
<td>50–59</td>
<td>21,744</td>
<td>69.03 (0.02)</td>
<td>176.7 (0.16)</td>
<td>25.83 (0.02)</td>
<td>133</td>
<td>69.45 (0.21)</td>
<td>194.4 (3.07)</td>
<td>28.28 (0.42)</td>
</tr>
<tr>
<td>60–69</td>
<td>12,127</td>
<td>68.53 (0.02)</td>
<td>171.6 (0.20)</td>
<td>25.48 (0.03)</td>
<td>179</td>
<td>68.88 (0.19)</td>
<td>185.7 (2.55)</td>
<td>27.43 (0.34)</td>
</tr>
<tr>
<td>70–79</td>
<td>4,127</td>
<td>68.18 (0.04)</td>
<td>164.6 (0.34)</td>
<td>24.70 (0.05)</td>
<td>108</td>
<td>67.79 (0.27)</td>
<td>178.3 (2.82)</td>
<td>27.20 (0.39)</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>21,400</td>
<td>64.16 (0.02)</td>
<td>139.3 (0.16)</td>
<td>23.68 (0.03)</td>
<td>583</td>
<td>64.29 (0.11)</td>
<td>154.8 (1.59)</td>
<td>26.35 (0.27)</td>
</tr>
<tr>
<td>40–49</td>
<td>81,669</td>
<td>63.85 (0.01)</td>
<td>142.7 (0.08)</td>
<td>24.51 (0.01)</td>
<td>442</td>
<td>64.07 (0.12)</td>
<td>156.3 (1.47)</td>
<td>26.78 (0.26)</td>
</tr>
<tr>
<td>50–59</td>
<td>86,930</td>
<td>63.74 (0.01)</td>
<td>146.0 (0.08)</td>
<td>25.20 (0.01)</td>
<td>334</td>
<td>63.53 (0.13)</td>
<td>162.9 (1.96)</td>
<td>28.34 (0.34)</td>
</tr>
<tr>
<td>60–69</td>
<td>49,886</td>
<td>63.64 (0.01)</td>
<td>146.3 (0.10)</td>
<td>25.37 (0.02)</td>
<td>365</td>
<td>62.70 (0.13)</td>
<td>155.9 (1.63)</td>
<td>27.81 (0.27)</td>
</tr>
<tr>
<td>70–79</td>
<td>14,306</td>
<td>63.34 (0.02)</td>
<td>142.2 (0.18)</td>
<td>24.95 (0.03)</td>
<td>344</td>
<td>62.15 (0.15)</td>
<td>146.2 (1.63)</td>
<td>26.68 (0.27)</td>
</tr>
</tbody>
</table>

* CPS-I, Cancer Prevention Study-I; NHANES III, Third National Health and Nutrition Examination Survey; SE, standard error.
† Weight (kg)/height (m²).

Am J Epidemiol Vol. 150, No. 4, 1999
TABLE 2. Percent dead, mortality rate ratio, and mortality rate difference for never-smoking, healthy White men and women, CPS-I* (1960–1972)†

<table>
<thead>
<tr>
<th>BMI range, age in years</th>
<th>No.</th>
<th>Percent dead (1)</th>
<th>Rate ratio (2)</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>p for trend</th>
<th>Rate difference (3)‡</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>p for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18.5–&lt;25.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>1,972</td>
<td>1.52</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40–49</td>
<td>7,504</td>
<td>4.13</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–59</td>
<td>8,682</td>
<td>9.49</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60–69</td>
<td>5,359</td>
<td>25.25</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70–79</td>
<td>2,249</td>
<td>53.62</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25.0–&lt;30.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>1,939</td>
<td>1.86</td>
<td>1.22</td>
<td>0.75</td>
<td>1.98</td>
<td>28</td>
<td>–40</td>
<td>95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40–49</td>
<td>9,732</td>
<td>4.78</td>
<td>1.16</td>
<td>1.00</td>
<td>1.34</td>
<td>54</td>
<td>1</td>
<td>106</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–59</td>
<td>11,171</td>
<td>11.66</td>
<td>1.24</td>
<td>1.14</td>
<td>1.35</td>
<td>195</td>
<td>117</td>
<td>272</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60–69</td>
<td>5,910</td>
<td>27.88</td>
<td>1.12</td>
<td>1.04</td>
<td>1.21</td>
<td>281</td>
<td>105</td>
<td>457</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70–79</td>
<td>1,670</td>
<td>56.65</td>
<td>1.07</td>
<td>0.98</td>
<td>1.17</td>
<td>0.11</td>
<td>403</td>
<td>–105</td>
<td>911</td>
<td>0.02</td>
</tr>
<tr>
<td>≥30</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>340</td>
<td>3.82</td>
<td>2.60</td>
<td>1.36</td>
<td>4.98</td>
<td>201</td>
<td>18</td>
<td>385</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40–49</td>
<td>1,653</td>
<td>7.62</td>
<td>1.89</td>
<td>1.53</td>
<td>2.32</td>
<td>304</td>
<td>185</td>
<td>423</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–59</td>
<td>1,887</td>
<td>15.21</td>
<td>1.66</td>
<td>1.45</td>
<td>1.90</td>
<td>532</td>
<td>368</td>
<td>697</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60–69</td>
<td>858</td>
<td>31.82</td>
<td>1.32</td>
<td>1.16</td>
<td>1.51</td>
<td>745</td>
<td>362</td>
<td>1,128</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70–79</td>
<td>208</td>
<td>60.58</td>
<td>1.24</td>
<td>1.03</td>
<td>1.49</td>
<td>0.01</td>
<td>1,379</td>
<td>95</td>
<td>2,664</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18.5–&lt;25.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>15,476</td>
<td>1.37</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40–49</td>
<td>51,931</td>
<td>2.68</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–59</td>
<td>47,693</td>
<td>5.36</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60–69</td>
<td>25,557</td>
<td>15.15</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70–79</td>
<td>7,920</td>
<td>40.97</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25.0–&lt;30.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>4,444</td>
<td>1.60</td>
<td>1.16</td>
<td>0.89</td>
<td>1.52</td>
<td>18</td>
<td>–16</td>
<td>52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40–49</td>
<td>22,285</td>
<td>3.17</td>
<td>1.18</td>
<td>1.08</td>
<td>1.30</td>
<td>41</td>
<td>18</td>
<td>64</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–59</td>
<td>29,186</td>
<td>6.76</td>
<td>1.27</td>
<td>1.20</td>
<td>1.35</td>
<td>123</td>
<td>92</td>
<td>154</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60–69</td>
<td>18,579</td>
<td>17.43</td>
<td>1.16</td>
<td>1.11</td>
<td>1.21</td>
<td>212</td>
<td>144</td>
<td>280</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70–79</td>
<td>4,972</td>
<td>40.85</td>
<td>1.00</td>
<td>0.95</td>
<td>1.06</td>
<td>0.10</td>
<td>5</td>
<td>219</td>
<td>230</td>
<td>0.04</td>
</tr>
<tr>
<td>≥30</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>1,480</td>
<td>2.70</td>
<td>1.99</td>
<td>1.42</td>
<td>2.78</td>
<td>112</td>
<td>40</td>
<td>183</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40–49</td>
<td>7,453</td>
<td>4.49</td>
<td>1.69</td>
<td>1.50</td>
<td>1.81</td>
<td>154</td>
<td>112</td>
<td>196</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–59</td>
<td>10,051</td>
<td>9.52</td>
<td>1.81</td>
<td>1.68</td>
<td>1.95</td>
<td>364</td>
<td>310</td>
<td>419</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60–69</td>
<td>5,750</td>
<td>22.05</td>
<td>1.50</td>
<td>1.40</td>
<td>1.59</td>
<td>664</td>
<td>546</td>
<td>782</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70–79</td>
<td>1,414</td>
<td>40.26</td>
<td>1.15</td>
<td>1.06</td>
<td>1.26</td>
<td>0.04</td>
<td>626</td>
<td>238</td>
<td>1,014</td>
<td>0.02</td>
</tr>
</tbody>
</table>

* CPS-I, Cancer Prevention Study-I; BMI, body mass index (weight (kg)/height (m²)).
† Parenthetical numbers in the headings indicate formula numbers from Materials and Methods.
‡ Per 100,000 person-years.

The rate ratios and rate differences were significantly higher for obese compared with reference-weight men and women. The rate ratio associated with obesity declined with age for both men and women. Among obese men, the rate ratio was 2.60 in the fourth decade and 1.24 in the eighth decade of life. Among obese women, the same estimates were 1.99 for the youngest group and 1.15 for the oldest group.

The association between rate differences and age was in the opposite direction of that of the rate ratios. The rate differences for both preobesity and obesity increased with age, except among women aged 70–79 years. The mortality rate difference between obese and reference-group men aged 30–39 years was 201 deaths per 100,000 person-years, whereas for men aged 70–79 years, the difference was 1,379 deaths per 100,000 person-years.

For CPS-I and NHANES III, the distributions of men and women aged 30–79 years in each BMI-age category are shown in table 3. The distributions by age and BMI were considerably different in the two sam-

Am J Epidemiol Vol. 150, No. 4, 1999
The largest percentage of men were in the aged 50–59 years, preobese group. Among women, the largest percentage in CPS-I were in the reference-weight, aged 40–49 years group; in NHANES III, the largest per-

TABLE 3. Excess deaths and years of life lost (YLL) attributable to preobesity and obesity, CPS-I* (1960–1972) and NHANES III† (1988–1994)‡

<table>
<thead>
<tr>
<th>BMI* range, age in years</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% distribution of total among persons aged 30–79 years</td>
<td>Excess deaths per 100,000 persons aged 30–79 years (4)</td>
</tr>
<tr>
<td></td>
<td>CPS-I</td>
<td>NHANES III</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-------</td>
<td>------------</td>
</tr>
<tr>
<td>18.5–&lt;25.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>3.23</td>
<td>17.22</td>
</tr>
<tr>
<td>40–49</td>
<td>12.27</td>
<td>9.64</td>
</tr>
<tr>
<td>50–59</td>
<td>14.20</td>
<td>2.07</td>
</tr>
<tr>
<td>60–69</td>
<td>8.77</td>
<td>3.43</td>
</tr>
<tr>
<td>70–79</td>
<td>3.68</td>
<td>1.67</td>
</tr>
<tr>
<td>25.0–&lt;30.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>3.17</td>
<td>19.79</td>
</tr>
<tr>
<td>40–49</td>
<td>15.92</td>
<td>10.56</td>
</tr>
<tr>
<td>50–59</td>
<td>18.27</td>
<td>6.18</td>
</tr>
<tr>
<td>60–69</td>
<td>9.67</td>
<td>5.31</td>
</tr>
<tr>
<td>70–79</td>
<td>2.73</td>
<td>2.77</td>
</tr>
<tr>
<td>≥30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>0.56</td>
<td>8.59</td>
</tr>
<tr>
<td>40–49</td>
<td>2.70</td>
<td>5.53</td>
</tr>
<tr>
<td>50–59</td>
<td>3.09</td>
<td>3.49</td>
</tr>
<tr>
<td>60–69</td>
<td>1.40</td>
<td>2.63</td>
</tr>
<tr>
<td>70–79</td>
<td>0.34</td>
<td>1.11</td>
</tr>
<tr>
<td>Total</td>
<td>100.00</td>
<td>100.0</td>
</tr>
</tbody>
</table>

* CPS-I, Cancer Prevention Study-I; NHANES III, Third National Health and Nutrition Examination Survey; BMI, body mass index (weight (kg)/height (m²)).
† Parenthetical numbers in the headings indicate formula numbers from Materials and Methods.
‡ Numbers do not total 100% because of rounding.

Am J Epidemiol Vol. 150, No. 4, 1999
percentage were in the reference-weight, aged 30–39 years group.

These distributions were used to calculate the number of excess or attributable deaths among 100,000 members of the sample who were aged 30–79 years. The total number of deaths attributable to obesity was larger in the NHANES III standardized estimates (1,333 men, 1,118 women) than in those calculated by using the CPS-I population distribution (1,249 men, 779 women). This finding was due in part to a larger proportion of preobese and obese participants in the standard population than in CPS-I. The standardized estimates of the number of deaths attributable to obesity were relatively stable for men aged 30–59 years and declined in older age groups. For women, the standardized estimates were approximately 110 for those aged 30–49 years, more than doubled for those aged 50–69 years compared with the younger women, and were negative in the oldest group of women. These negative estimates reflect that a slightly lower percentage of women aged 70–79 years died in the preobese and obese groups compared with the reference-weight group.

As expected, more years of life were lost for each death among younger compared with older men and women. For example, reference-weight men and women aged 30–39 years lost approximately 34 years of life with each death, whereas men and women aged 70–79 years who were in the same weight category lost approximately 6 years (data not shown). Despite this difference, the average years of life lost per person was larger for older compared with younger men and women because of the much larger number of deaths among older participants. Years of life lost also varied on the basis of weight. Obese and preobese men and women lost more years of life than did lean men and women in the same age category. However, the impact of age was larger than the impact of BMI. The average years of life lost per person among obese subjects aged 30–39 years (0.91 years for women, 1.06 years for men) was lower than for reference-weight subjects aged 70–79 years (2.52 years for women, 3.03 years for men). The years of life lost per person that were attributable to obesity was highest for men and women in their fifties and sixties.

When we used the standardized estimates, 22,039 and 19,682 years of life lost over the 11-year follow-up period were attributable to overweight in men and women, respectively. Therefore, on average, approximately 2,000 years per 100,000 men and 1,800 years per 100,000 women were lost each year that were attributable to overweight. After standardization, years of life lost attributable to obesity declined with age among men. Among women, the highest estimate was for obese women aged 50–59 years. Among both men and women, the lowest estimates of years of life lost attributable to obesity were for the groups aged 70–79 years, the groups that included the fewest persons in NHANES III.

Rate advancement periods estimate the time periods by which the rate of death was advanced among exposed persons (table 4). This estimate answers the question, How many years older are reference-weight persons when they have the same rate of death as obese persons? A rational estimate could not be calculated for men aged 30–39 years because there was no association between baseline age and mortality in that age range over the 11-year follow-up period. In each of the other age and gender categories, the 11-year death rate increased with advancing baseline age. Among obese men and women, the rate advancement period declined with age. Among men and women aged 40–50 years, obesity advanced the rate of death to that of reference-weight persons who were 5.9 and 6.4 years older, respectively. In persons aged 70–79 years, obesity advanced the death rates by 3.5 years for men and 1.7 years for women.

DISCUSSION

We have shown that the direction of age-associated trends regarding the effect of obesity on mortality varies depending on the measure of effect used. Estimates were presented for the preobese group of men and women, but we emphasized the results for those in the obese group because the magnitude of the effects of BMI is larger and more consistent in that group and better illustrates the contrasts between different measures of effect. The excess percent dead and the rate difference increased with age, the rate ratio and the rate advancement period decreased with age, and the years of life lost per person increased to age 70 years and then declined.

The lack of agreement in these results is in great measure a consequence of comparing trends on the multiplicative versus the additive scale given a situation in which the baseline rate changes dramatically. The more than 30-fold difference in the percent dead among participants in the BMI reference category in the oldest versus the youngest groups illustrates the large range in the size of the baseline rates that form the denominators of risk ratios across age groups. For example, using the percent dead in men, in the youngest group 1.52 percent died in the reference group and 3.82 percent died in the obese group. For the oldest age category, these estimates were 53.62 percent and 60.58 percent, respectively. Examined as a ratio, the risk associated with obesity was greater for the youngest men than for the oldest men.
TABLE 4. Rate advancement period (RAP) estimating the number of years by which the rate of death was advanced among exposed persons, CPS-I* (1960–1972)†

<table>
<thead>
<tr>
<th>BMI* range, age in years</th>
<th>Mean RAP (years/person) in CPS-I sample (8)</th>
<th>RAP (years) per 100,000 persons aged 30–80 years (9)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RAP Lower limit Upper limit $p$ for trend</td>
<td>CPS-I</td>
</tr>
<tr>
<td>-------------------------</td>
<td>---------------------------------------------</td>
<td>-------------</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25.0–&lt;30.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>1.2 –0.1 2.6</td>
<td>19,104</td>
</tr>
<tr>
<td>40–49</td>
<td>2.2 1.3 3.1</td>
<td>40,194</td>
</tr>
<tr>
<td>50–59</td>
<td>1.4 0.7 2.1</td>
<td>13,538</td>
</tr>
<tr>
<td>60–69</td>
<td>1.3 0.4 2.2</td>
<td>3,549</td>
</tr>
<tr>
<td>70–79</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>5.9 3.5 8.3</td>
<td>15,930</td>
</tr>
<tr>
<td>40–49</td>
<td>5.2 3.7 6.6</td>
<td>16,068</td>
</tr>
<tr>
<td>50–59</td>
<td>3.1 1.9 4.4</td>
<td>4,340</td>
</tr>
<tr>
<td>60–69</td>
<td>3.5 1.6 5.3</td>
<td>1,190</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>113,913</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25.0–&lt;30.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–39</td>
<td>2.2 –2.9 7.4</td>
<td>3,850</td>
</tr>
<tr>
<td>40–49</td>
<td>1.9 0.7 3.1</td>
<td>16,663</td>
</tr>
<tr>
<td>50–59</td>
<td>2.3 1.6 3.0</td>
<td>26,404</td>
</tr>
<tr>
<td>60–69</td>
<td>1.3 0.9 1.7</td>
<td>9,503</td>
</tr>
<tr>
<td>70–79</td>
<td>0.3 –0.2 0.7</td>
<td>588</td>
</tr>
<tr>
<td>≥30</td>
<td></td>
<td>6,786</td>
</tr>
<tr>
<td>30–39</td>
<td>11.7 0.8 22.7</td>
<td>18,752</td>
</tr>
<tr>
<td>40–49</td>
<td>6.4 4.4 8.4</td>
<td>23,305</td>
</tr>
<tr>
<td>50–59</td>
<td>5.9 4.9 6.9</td>
<td>8,362</td>
</tr>
<tr>
<td>60–69</td>
<td>3.7 3.1 4.3</td>
<td>952</td>
</tr>
<tr>
<td>70–79</td>
<td>1.7 1.0 2.4</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>115,165</td>
</tr>
</tbody>
</table>

* CPS-I, Cancer Prevention Study-I; BMI, body mass index (weight (kg)/height (m$^2$)).
† Parenthetical numbers in the headings indicate formula numbers from Materials and Methods.

3.82/1.52 = 2.51; oldest men, 60.58/53.62 = 1.13 ). However, when examined as a difference, the estimate was smaller for the youngest compared with the oldest men (youngest men, 3.82 – 1.52 = 2.30; oldest men, 60.58 – 53.62 = 6.96). Far fewer excess deaths are required to double the risk when the denominator is low, and a much larger number is needed when the denominator is high. In this example, the crude risk ratio could never have been as large as 2 for the oldest men, because it is impossible for more than 100 percent of the men to die (107.24 percent mortality would be needed among obese men to produce a risk ratio of 2 when the baseline rate was 53.62 percent). In a time-to-death analysis (using person-years as the denominator), the death rate could have doubled with obesity among the oldest men, but the observed increase was much smaller than required for a doubling.

Not new is the fact that identification of an interaction between risk factors depends on the scale of the dependent variable (22, 23). This study demonstrated this well-known phenomenon. Divergent trends over age groups in additive as opposed to multiplicative measures of effect have been observed for smoking (24, 25) and other risk factors (26). However, we know of no papers that have addressed this issue in evaluating the impact of age on the BMI-mortality relation. In fact, the importance of the measure of effect used to study this issue is rarely mentioned.

Excess years of life lost per person is a combination of the difference in the percentage who died in the obese versus the reference-weight groups (higher for older persons) and the number of years of life lost per death (higher for younger persons). In this analysis, an average of 34 years of life was lost with each death.
among the youngest group and only 6 years among the oldest group. In our calculations of excess years of life lost per person by category, the estimates increased with age up to age 70 years and then declined. Thus, it appeared that the larger differences in the percentages of obese versus reference-weight participants who died dominated the calculation up to age 70 years.

Similar to years of life lost, the rate advancement period reflects not only if but when death occurs (19). Unlike years of life lost, it does not assume that had an exposed case not been exposed, that case would have lived to some predetermined age or that the exposure has no effect on persons who do not become cases during the follow-up period. The rate advancement period conveys information about the premature occurrence of outcomes for risk factors that promote progression of an outcome that increases with age. All-cause death is certainly an outcome that increases with age; therefore, the rate advancement period is appropriate. This measure can be conceptualized as indicating the effect of obesity on death in terms of the effect of aging on death. Here, we calculated the rate advancement period within decades, and thus the denominator of the estimate \( (\beta_2) \) was determined by the effect of age on mortality within 10-year categories. Among women, \( \beta_2 \) increased over the age groups, although in men it was relatively stable after age 40 years. The numerator of the rate advancement period \( (\beta_1) \) is the coefficient associated with BMI within age groups, and this declined with age, as indicated by the decline in the rate ratios. Therefore, the numerator declined with age whereas the denominator increased or stayed the same, and the overall estimate declined.

We have shown only a few of the estimates of effect that potentially could be calculated. Age-associated trends did not vary materially whether we examined the risk of death (from cumulative incidence) or the rate of death (from incidence density), and we did not show estimates by using both rate and risk. Attributable rate (or risk), defined as the proportion of cases due to the exposure among all cases (27), was not shown here. Its association with age is the same as that of the rate ratio (or risk ratio) (RR), which is easily evident from using the following form of the equation for attributable rate: \( 1 - (1/RR) \). Although we did not show the attributable rate or the attributable risk, both can be calculated from the data shown.

Past studies on the impact of age on the BMI-mortality association have emphasized results derived from rate ratios or mortality ratios (10, 28–32). Most studies also show the percent dead or the number dead per person-years in each group, and one study relied most heavily on the log percent dead (33). Analyses to determine the BMI category associated with the minimum mortality within age groups are not influenced by whether the estimate is additive or multiplicative, as long as all measures are based on either risk (deaths/persons) or rates (deaths/person-year). Population standardized results could differ. However, we know of no other papers on the impact of age on the BMI-mortality association that have shown population standardized estimates.

We presented the population-level mortality estimates here not to represent current rates but to illustrate the impact of standardization to a population on estimates of the effect of age on the BMI-mortality relation. Data sets of adequate size to permit comparison of mortality rates among age groups are rare. The CPS-I data set has the advantages of large size and the availability of information, which makes it feasible to control possible confounding by smoking and preexisting disease. Nevertheless, the data are old, and it is likely that the relation between BMI and mortality changed between the years that the CPS-I data and the NHANES III data were collected. Therefore, the standardized population estimates shown here do not represent the current national mortality experience but approximate mortality using relatively current obesity prevalences and past mortality experiences. It is impossible to have true estimates of the impact of any exposure on long-term mortality that are current because, by the nature of the data, time must pass for follow-up information to be collected and analyzed. Nevertheless, the more than 30-year gap between collection of the baseline data for CPS-I and the prevalence data for NHANES III is extreme, and our population standardized estimates should be interpreted with caution.

If there is interest in knowing the impact of an exposure on mortality in a specific population, then standardization to that population is needed. Such information is often useful for public health policy decisions. Nevertheless, a great deal of epidemiologic research is directed toward studying the etiology of disease and identifying exposures that increase the risk of disease in persons. Relative risk, calculated as a risk ratio or a rate ratio, is widely used for this purpose. The ease of controlling for multiple covariates by using Cox proportional hazards models in widely available software packages also contributes to the popularity of relative risk.

No one best measure of effect can be used to quantitatively evaluate the danger of obesity across age groups. Rather, the choice of measures must depend on the context of the evaluation. Choosing the optimum age group for the targeting of weight reduction programs is one issue of great interest (34, 35). None of the estimates shown here can address this issue, because
none deals with changes in mortality associated with weight reduction. Theoretically, these measures do not address deaths that could be prevented were obesity to be prevented. There are several well-known attributes of obesity that should be considered in the interpretation of these estimates for their potential to indicate the benefits of prevention among different age groups. First, the mortality data shown here were from the last 11 years of a 12-year follow-up. This is a very short period of follow-up for mortality in young adult participants. Second, obesity is usually a chronic condition, and few persons are "cured" permanently. Thus, younger persons who survive obesity in their thirties will likely still be obese in their forties. In fact, it is likely that they will be even heavier, as most Americans gain weight as they pass from early adulthood to middle age (36, 37). Targeting obesity prevention at younger persons would seem to be useful, assuming that the preventive effects of the program are maintained into future years. However, decades of experience with weight treatment programs have shown that cessation of treatment is often followed by weight gain (38, 39). Although much less research is available on obesity prevention than on obesity treatment, it is likely that efforts extending into even the seventh or eighth decade of life may be necessary to gain the full benefits of prevention. Effective strategies are needed to prevent obesity over a wide range of ages.

REFERENCES


Am J Epidemiol Vol. 150, No. 4, 1999