THE EFFECT OF AGE ON THE ASSOCIATION BETWEEN BODY-MASS INDEX AND MORTALITY

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ABSTRACT

Background The effect of age on optimal body weight is controversial, and few studies have had adequate numbers of subjects to analyze mortality as a function of body-mass index across age groups.

Methods We studied mortality over 12 years among white men and women who participated in the American Cancer Society’s Cancer Prevention Study I (from 1960 through 1972). The 62,116 men and 262,019 women included in this analysis had never smoked cigarettes, had no history of heart disease, stroke, or cancer (other than skin cancer) at base line in 1959–1960, and had no history of recent unintentional weight loss. The date and cause of death for subjects who died were determined from death certificates. The associations between body-mass index (defined as the weight in kilograms divided by the square of the height in meters) and mortality were examined for six age groups in analyses in which we adjusted for age, educational level, physical activity, and alcohol consumption.

Results Greater body-mass index was associated with higher mortality from all causes and from cardiovascular disease in men and women up to 75 years of age. However, the relative risk associated with greater body-mass index declined with age. For example, for mortality from cardiovascular disease, the relative risk associated with an increment of 1 in the body-mass index was 1.10 (95 percent confidence interval, 1.04 to 1.16) for 30-to-44-year-old men and 1.03 (95 percent confidence interval, 1.02 to 1.05) for 65-to-74-year-old men. For women, the corresponding relative risk estimates were 1.08 (95 percent confidence interval, 1.05 to 1.11) and 1.02 (95 percent confidence interval, 1.02 to 1.03).

Conclusions Excess body weight increases the risk of death from any cause and from cardiovascular disease in adults between 30 and 74 years of age. The relative risk associated with greater body weight is higher among younger subjects. (N Engl J Med 1998;338:1-7.)

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WETHER recommended body weight should remain constant throughout adulthood or should be higher for older adults is controversial. The Department of Agriculture’s 1990 Dietary Guidelines for Americans recommended age-specific ranges of weight for height, with heavier weights indicated for people 35 years of age or older, but age-specific weight recommendations were omitted from the 1995 Dietary Guidelines for Americans, presumably because the information to support the need for different recommended weights was inadequate.

The debate sparked by the dietary guidelines made it evident that more studies were needed to clarify whether age modifies the relation between body weight and mortality. Studies that compare the relations between the body-mass index (the weight in kilograms divided by the square of the height in meters) and mortality among age groups in a single cohort provide evidence to confirm or refute the usefulness of age-specific guidelines, but studies of sufficient size to generate meaningful age-specific estimates are rare. Previous analyses from the American Cancer Society’s Cancer Prevention Study I, a study of personal health habits and mortality, did examine the relation of body weight and mortality in a very large cohort; however, comparisons were made with use of the mean weight within each age group, a measure that varied by as much as 14 lb (6.4 kg) among age groups. Therefore, direct comparisons
among age groups could not be made. Using data on the subjects in the Cancer Prevention Study I, we analyzed the associations between body-mass index and mortality from all causes and from cardiovascular disease in six age groups of healthy white men and women.

**METHODS**

**Subjects**

Over 1 million men and women 30 years of age or older in 26 states were recruited by 68,000 American Cancer Society volunteers between October 1959 and March 1960 to participate in the first Cancer Prevention Study. The participants were enrolled in family groups with at least one member over 45 years of age, and all members of a household over 30 years of age were asked to answer the questionnaire. The cohort was formed as a convenience sample (not a random sample). These subjects had higher levels of educational attainment than the general population in the same decade, and subjects who smoked or had a family history of cancer were oversampled.

In order to avoid confounding by smoking status, we restricted the present analysis to subjects who had never smoked. The subjects were classified as never having smoked if they reported that they did not currently smoke cigarettes and had never smoked cigarettes regularly. Race or ethnic group was obtained from subjects’ choices among categories on a checklist. We had previously found that the relation between body-mass index and mortality was less strong among the black women in this cohort than among the white women. Since the numbers of blacks and members of other minorities were relatively small (<2 percent of the cohort), they were excluded from this analysis.

We also excluded several groups of subjects in order to improve the quality and completeness of the data and to eliminate subjects who may have had weight loss due to illness at the time of the baseline measurements (Table 1). The final sample included 62,116 men and 262,019 women. The men and women whom we excluded were older than those included (mean age, 59 vs. 54 years for men [P<0.001] and 59 vs. 53 years for women [P<0.001]) and had a higher age-adjusted death rate (3191 per 100,000 person-years for men [P<0.001] and above 295 lb (134 kg), whose height was below 56 in. (142 cm) or above 83 in. (211 cm), and those with a body-mass index (BMI) between 14.9 and 48.4. Among women, we excluded those whose weight was below 85 lb (39 kg) or above 270 lb (123 kg), whose height was below 50 in. (127 cm) or above 79 in. (201 cm), and those with a BMI below 14.4 or above 48.4.

**End Points**

The vital status of 98 percent of the total cohort was traced through September 1971, and that of 93 percent through September 1972. Vital status was determined annually in October from 1960 through 1965 and again in 1971 and 1972. Personal inquiries by American Cancer Society volunteers generated reports of the dates and places of all deaths, which were sent to the American Cancer Society central office. Death certificates were then obtained from state health departments and coded by a nosologist. The cause of death was coded according to the codes of the International Classification of Diseases, 7th Revision (ICD-7). Deaths due to cardiovascular disease were identified by ICD-7 codes 330 through 334, 400 through 434, and 450 through 468. Only 0.4 percent of deaths were not coded with an underlying cause.

**Risk Factors**

The study subjects completed a four-page questionnaire on personal health practices and medical history. Weight in pounds and height in feet and inches were written on blank lines after the words “present weight (indoor clothing)” and “height (without shoes).” Body-mass index was calculated from the reported values. In our categorical analyses, the body-mass-index categories were as follows: <19.0, 19.0 to 21.9, 22.0 to 24.9, 25.0 to 26.9, 27.0 to 28.9, 29.0 to 31.9, and ≥32.0. These categories correspond to approximately 50 percent, 90 to 99 percent, 100 to 114 percent, 115 to 119 percent, 120 to 129 percent, 130 to 139 percent, and ≥140 percent of desirable weight according to the 1983 Metropolitan Life Insurance tables.

Educational attainment was assessed in five categories: grammar school, some high school, high-school graduation, some college, and college graduation. Physical activity was assessed by asking, “How much exercise do you get (work or play): none, slight, moderate, or heavy?” Alcohol intake was assessed by asking, “How many cups, glasses, or ‘drinks’ do you usually consume per day (beer, wine, whiskey, gin, etc.)?” We categorized alcohol consumption as none, occasional light, occasional heavy, one drink per day, two to four drinks per day, and five or more drinks per day.

**Statistical Analysis**

We used proportional-hazards analysis (PROC PHREG, SAS Institute, Cary, N.C.) to assess associations between body-mass index and mortality from all causes and from cardiovascular disease. Body-mass index was examined as both a continuous and a categorical variable. Likelihood-ratio tests were used to test for interactions in the proportional-hazards models. The linear trends for the relative risks associated with an increase of 1 in the body-mass index across age groups were tested by weighted linear regression analysis. The inverse of the variance of the risk estimates was used for the weight.
RESULTS

During the 12 years of follow-up, the crude incidence of death ranged from 2 to 3 percent among 30-to-44-year-old women and men to 89 to 91 percent among subjects who were 85 years of age or older at base line (Table 2). The percentage of deaths that were due to cardiovascular disease also increased with age. Among the men, the mean body-mass index was relatively constant (approximately 25.7) from 30 to 74 years of age, but it was lower in the older groups. Among women, the mean body-mass index increased from 23.8 among the 30-to-44-year-olds to 25.2 among those 55 to 64 years old, then declined in the older age categories.

The crude death rates varied among both body-mass-index and age categories. For example, for 30-to-44-year-old women, there were 22 deaths from cardiovascular disease per 100,000 person-years among those with body-mass indexes of 19.0 to 21.9, as compared with 51 per 100,000 person-years among those with indexes of 29.0 to 31.9. For 65-to-74-year-old women, there were 1494 deaths due to cardiovascular disease per 100,000 person-years among those with body-mass indexes of 19.0 to 21.9, as compared with 1854 per 100,000 person-years among those whose body-mass indexes were 29.0 to 31.9. For men and women over 75 years of age, the crude death rate did not increase with body-mass index. For example, among 75-to-84-year-old women, there were 1494 deaths due to cardiovascular disease per 100,000 person-years in the group with indexes of 29.0 to 31.9. For 65-to-74-year-old women, there were 1494 deaths due to cardiovascular disease per 100,000 person-years in the group with indexes of 19.0 to 21.9, as compared with 51 per 100,000 person-years in the group with body-mass index that had five or fewer deaths. For both death from all causes and death from cardiovascular disease, the increase in risk associated with a higher body-mass index tended to be greater among younger subjects.

Using the same covariates, we tested models in the six age groups, with body-mass index examined as a continuous linear term and as a quadratic term (the square of the body-mass index). For men, the linear term for body-mass index was appropriate, whereas for women body-mass index squared was significant in 6 of the 12 tests ($P<0.05$). Because the main focus of this analysis was to compare the effect of excess adiposity among age groups, it was desirable to fit the same model in each age category. Comparisons of the magnitude of the effects indicated that the results of the two models were very similar for women, although some differences in risk ratios were greater than 10 percent. Therefore, we have presented two sets of analyses for the women.

In the first, the quadratic model was fitted in all the age groups, and the body-mass index at the nadir of the relative risk was calculated. In groups of subjects less than 75 years old, the body-mass index at the nadir was below 20.0 for both mortality from all causes and mortality from cardiovascular disease

![Table 2: Outcomes and Body-Mass Indexes at Baseline in the Study Cohort of Healthy White Men and Women Who Had Never Smoked.](image-url)
in all but one test. In that instance the quadratic term was negative (and not statistically significant), and the nadir was not calculated since it had little meaning. In the two oldest age groups, the nadirs for risk were at much higher body-mass indexes (27.4 and 28.5).

In the second series of analyses, models were fitted with only the linear term for body-mass-index.

Figure 3 shows the relative-risk estimates from the models examining body-mass index as a linear term among women and among men. The relative risk associated with increasing body-mass index tended to be slightly lower for women than for men. Among women, body-mass index was positively associated with mortality from all causes and from cardiovascular disease in the four younger age groups. Among
The relative risk associated with an increase in the body-mass index declined with age for both mortality from all causes and mortality from cardiovascular disease among men (P for trend, <0.05 and <0.01, respectively). The interaction between body-mass index and age was statistically significant (P<0.001) for both mortality from all causes and mortality from cardiovascular disease among both men and women.

To illustrate the magnitude of the age-associated decline in the relative risk associated with an elevated body-mass index, we calculated the body-mass index and weight associated with a 20 percent and a 50 percent increase in the risk of death from all causes and from cardiovascular disease, using a body-mass index of 21.0 as the reference value (Table 3). The choice of this reference value was arbitrary, since the model assumes a constant increase in the log of the relative risk across the entire range of body-mass indexes. Nevertheless, the categorical analyses shown in Figures 1 and 2 give some indication that the category 19.0 to 21.9 included the body-mass index associated with minimal risk in the majority of the age categories examined. For both men and women, the increment in body-mass index or weight that was associated with a given increase in risk rose slightly among the three younger age groups but rose more sharply at 65 to 74 years of age.
DISCUSSION

These results suggest that among men and women 30 through 74 years of age, greater body weight increased the risk of death from any cause and death from cardiovascular disease over a 12-year period; however, the relative risk associated with excess weight was higher among younger subjects. Although the various models used to examine relative risk resulted in consistent conclusions, different measures of risk could produce different conclusions because of the large differences in the age-specific mortality rates. For example, whereas the relative risk associated with excess weight was higher among the 30-to-44-year-olds than among the 65-to-74-year-olds, the difference in the crude mortality rates between overweight and lean subjects was larger among the older subjects. Among 30-to-44-year-old women, the difference in the crude rates of death from cardiovascular disease between women with body-mass indexes of 19.0 to 21.9 and those with values of 29.0 to 31.9 was 29 per 100,000 person-years, whereas the difference was 455 per 100,000 person-years among 65-to-74-year-old women. We have emphasized the relative-risk estimate in the presentation of results here because it is the most commonly used measure of effect for the evaluation of the potency of risk factors.12

Approximately 400 events in each age group are required to detect a ratio of relative risks of 1.5, with body-mass index analyzed as a dichotomous variable divided at the median (with an alpha level of 0.05 and 80 percent power).13 For example, if the relative risk of death above the median body-mass-index value as compared with that below the median was 1.33 in one age group and 2.0 in another, approximately 400 deaths would be required in each age group for the study to detect this difference. In many of the studies that have provided age-specific risk estimates of the relation between body-mass index and mortality, there have been too few deaths for the study to make this statistically powerful a comparison.

The Build Study14 and Waaler’s Norwegian study15 had adequate statistical power but did not control for smoking. In the former study, the relation between the body-mass index and mortality was U-shaped, and the body-mass index associated with minimal mortality increased with age. In the Norwegian study, plots of the log of the mortality rate against body-mass-index categories were also U-shaped, but there was no evidence that the body-mass index associated with minimal mortality increased with age.

More recent studies of the effect of age on the relation between body-mass index and mortality have controlled for smoking. In a Finnish cohort of 171,599 women16 and 22,995 men17 who were followed for a median of 12 years, there was a U-shaped relation between body-mass index and mortality from all causes among nonsmoking women 25 to 64 years of age. Among women 65 years of age or older, mortality varied little according to body-mass index; directly comparable analyses were not presented for the men. The 26-year risk of death among 12,576 Seventh-Day Adventist women, a subgroup of the women we studied, was recently reported.18 Among the white women who never smoked and were relatively healthy at base line, the relative risk of death associated with elevated body-mass index was lower for women 55 to 74 years old than for those 30 to 54 years old. The lowest risk of death from any cause among the younger women was found in those who had body-mass indexes from 21.3 to 22.9, but among the older women the lowest risk was in the group with body-mass indexes from 23.0 to 24.8.

Taken together, these studies support the hypothesis that the relative risk of death associated with excess adiposity is lower for older than for younger adults. Variation in specific findings may be attributable to differences in exclusion criteria, in cutoff points for categories of body-mass index, or in the variables controlled for in the analysis, or to unmeasured characteristics of the study subjects.

Although the importance of smoking and preexisting illness as confounders of the relation between body-mass index and mortality has been challenged,19,20 we thought it prudent to avoid potential confounding by these factors.21 Nevertheless, more older subjects than younger ones may have had reduced weight at base line because of preexisting illness. However, the fact that risk did not increase at low body-mass indexes among the older men or all but the oldest women (Fig. 1 and 2) argues against this possibility.

In the Cancer Prevention Study I, all data except those on mortality were obtained by questionnaire from the subjects themselves. In general, self-reported height and weight are highly correlated with measured height and weight (correlation coefficients, >0.9), but heavier persons tend to underestimate their weight more than leaner persons; underreporting of body weight may also increase with age.22,23

In this study, body-mass index was estimated only once, at one age, for each subject. Thus, no conclusions can be drawn about the effect of changes in weight over time.24 The design of this study also did not allow the effects of age to be distinguished from temporal or birth-cohort effects. In addition, the fact that these data were collected between 1959 and 1972 may limit the generalizability of our results. Another limitation is the number of years of follow-up. Twelve-year mortality in a cohort of 30-year-old subjects is very different from that among 85-year-old subjects. In the younger group, all deaths
are premature, whereas none could be termed premature in the older group.

Despite these limitations, the very large number of subjects in a wide range of age groups, the 12 years of follow-up information, and the availability of information on both intended and unintended weight loss made the Cancer Prevention Study I data set a rich resource for these analyses. The numerous exclusions limit the generalizability of the results of our analyses, but they increase the internal validity of those results. In healthy white adults below the age of 75 who have never smoked cigarettes, our results are consistent with the healthy weight ranges proposed in the 1995 Dietary Guidelines for Americans.

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